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# Periodic solution for a free boundary problem modeling small plaques

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Plaque formation within arteries is one of the leading causes of death in USA and worldwide. Mathematical models describing the growth of plaque in the arteries (e.g., [1, 2, 3, 5, 6]) were introduced. All of these models include the interaction of the "bad" cholesterols, low density lipoprotein (LDL), and the "good" cholesterols, high density lipoprotein (HDL), in triggering whether plaque will grow or shrink.

Because the blood vessels tend to be circular, 2D cross section model is a good approximation, and the 2D models are studied in [2, 7, 8, 9]. A bifurcation into a 3D plaque was recently studied in [4]. All of these models assume a constant supply of LDL and HDL from the blood vessel.

In reality, nutrient concentration changes with the intake of food, which happens very often in a periodic manner. In this paper, we shall establish a periodic solution when the LDL and HDL supplies from the blood vessel are periodic.

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## 1. Introduction

Atherosclerosis is caused by the build-up of arterial plaque which eventually causes potential heart problems including a heart attack or a stroke. Mathematical models describing the growth of plaque in the arteries (e.g., [1, 2, 3, 5, 6]) were introduced. All of these models include the interaction of the "bad" cholesterols, low density lipoprotein (LDL), and the "good" cholesterols, high density lipoprotein (HDL), in triggering whether plaque will grow or shrink.

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Friedman et al. [2] considered a simplified model involving LDL and HDL cholesterol, macrophages and foam cells. As the blood vessel is a long and thin tube, it is a good approximation to assume that the artery is a radially symmetric infinite cylinder. They further simplified the problem by considering the cross section only, which reduces the problem to a 2D problem. And rigorous mathematical analysis was carried out. Since it is not reasonable to assume that plaques have a strictly radially symmetric shape, systematic symmetry-breaking bifurcation [8, 9, 7, 4] was carried out utilizing the Crandall-Rabinowitz theorem.

All of these models, however, assume a constant supply of LDL and HDL from the blood vessel. In reality, nutrient concentration changes with the intake of food, which happens very often in a periodic manner. Thus we shall assume that the LDL and HDL concentrations within the blood vessel are of the form

$$L_0(t) = L_*(1 + \tau L_1(t)), \qquad H_0(t) = H_*(1 + \tau H_1(t)), \tag{1.1}$$

where $L_1(t)$ and $H_1(t)$ are given periodic $C^2(\mathbb{R})$ functions with period $T$ with

$$\int_0^T L_1(t)dt = \int_0^T H_1(t)dt = 0, \tag{1.2}$$

and

$$\|L_1\|_{C^2[0,T]} \le 1, \qquad \|H_1\|_{C^2[0,T]} \le 1. \tag{1.3}$$

Since the LDL and HDL concentrations in the blood vary around their prevalent values.

We shall study the solution in a small ring of thickness order $O(\varepsilon)$, $\varepsilon > 0$ and take

$$\tau > 0 \text{ to be small.} \tag{1.4}$$

That is, the food intake would not drastically change the prevailing concentration values $L_*$, $H_*$.

A periodic solution is a characterization of the normal fluctuation in reality. This is a solution that will never grow out of control and represent a special stable state. When $L_0(t)$ and $H_0(t)$ are constants, a small radially symmetric stationary plaque was established in [2] and bifurcations of various shape from this small plaque were found [8, 9, 4, 7]. In this paper, we are concerned only with the radially symmetric solution and establish the existence of such a periodic solution of a small plaque.

We refer to [2, 8, 9] for the detailed derivation of the model. Here the variables $L$, $H$, $F$ represent respectively the low density cholesterol, high density cholesterol, foam cells, and $p$ represents the pressure build-up during the cell growing or shrinking process. Given that the blood vessel is a long tube, we assume a 2D cross section radially symmetric domain, with spatial variables in polar coordinate system. Taking into account the periodic nature of the low density cholesterol and high density cholesterol within the blood flow, we find that they satisfy the following equations in the plaque region $\{\Omega(t), t > 0\}$, $\Omega(t) = \{R(t) < r < 1\}$, with a moving boundary $\Gamma(t) = \{r = R(t)\}$ where $0 < R(t) < 1$, and the fixed boundary $\{r = 1\}$ representing the blood vessel wall,

$$\frac{\partial L}{\partial t} - \Delta L = -k_1 \frac{(M_0 - F)L}{K_1 + L} - \rho_1 L, \tag{1.5}$$

$$\frac{\partial H}{\partial t} - \Delta H = -k_2 \frac{HF}{K_2 + F} - \rho_2 H, \tag{1.6}$$

$$\begin{aligned} \frac{\partial F}{\partial t} - D\Delta F - \nabla F \cdot \nabla p = k_1 \frac{(M_0 - F)L}{K_1 + L} - \lambda \frac{F\,(M_0 - F)\,L}{M_0(\gamma + H)} \\ - k_2 \frac{HF}{K_2 + F} + (\rho_3 - \rho_4)\,\frac{(M_0 - F)\,F}{M_0}, \end{aligned} \tag{1.7}$$

$$-\Delta p = \frac{1}{M_0}\Big[\lambda \frac{(M_0 - F)\,L}{\gamma + H} - \rho_3\,(M_0 - F) - \rho_4 F\Big], \tag{1.8}$$

where $\Delta = \partial_{rr} + \frac{1}{r}\partial_r + \frac{1}{r^2}\partial_{\theta\theta}$. The boundary conditions and the free boundary condition are given by

$$\frac{\partial L}{\partial r} = \frac{\partial H}{\partial r} = \frac{\partial F}{\partial r} = 0 \qquad \{r = 1\}, \tag{1.9}$$

$$\frac{\partial p}{\partial r} = 0 \qquad \{r = 1\}, \tag{1.10}$$

$$\frac{\partial L}{\partial \vec{n}} + \beta_1\,(L - L_0(t)) = 0 \qquad \text{on } \Gamma(t), \tag{1.11}$$

$$\frac{\partial H}{\partial \vec{n}} + \beta_1\,(H - H_0(t)) = 0 \qquad \text{on } \Gamma(t), \tag{1.12}$$

$$\frac{\partial F}{\partial \vec{n}} + \beta_2 F = 0 \qquad \text{on } \Gamma(t), \tag{1.13}$$

$$p = \kappa \qquad \text{on } \Gamma(t), \tag{1.14}$$

$$V_n = -\frac{\partial p}{\partial \vec{n}} \qquad \text{on } \Gamma(t), \tag{1.15}$$

where, as indicated in the introduction, $L_0(t)$ and $H_0(t)$ are assumed to be periodic functions rather than constants. Here, $\kappa$ is the curvature in the outward unit normal $\vec{n}$ (i.e., pointing towards the blood region) for $\Gamma(t)$, and in the case of a radially symmetric case $r = R(t)$, $\kappa = -\frac{1}{R(t)}$. All parameters $M_0$, $\lambda$, $\gamma$, $K_i$, $k_i$, $\beta_i$ $(i = 1, 2)$ and $\rho_j$ $(j = 1, 2, 3, 4)$ are positive.

In the simple case where the solutions are assumed to be independent of $\theta$ variable, then we solve from (1.8) that

$$p_r(r,t) = \frac{1}{rM_0}\int_r^1 \Big[\frac{(M_0 - F)\,L}{\gamma + H} - \rho_3 M_0 + (\rho_3 - \rho_4)F\Big](\xi,t)\cdot\xi d\xi. \tag{1.16}$$

Since the curvature of a disk is a constant, the boundary condition (1.14) is no longer needed. Writing the domain as $\{R(t) < r < 1\}$, we find that the term $\nabla F \cdot \nabla p$ in (1.7) becomes $F_r \cdot p_r$, and (1.7), (1.8), (1.15) reduce to

$$\begin{aligned}
&\frac{\partial F}{\partial t} - D\Delta F \\
&\qquad -\frac{F_r}{rM_0}\int_r^1 \Big[\frac{(M_0 - F)\,L}{\gamma + H} - \rho_3 M_0 + (\rho_3 - \rho_4)F\Big](\xi,t)\cdot\xi d\xi \\
&= k_1\frac{(M_0 - F)L}{K_1 + L} - k_2\frac{HF}{K_2 + F} - \lambda\frac{F\,(M_0 - F)\,L}{M_0(\gamma + H)} \\
&\qquad + (\rho_3 - \rho_4)\,\frac{(M_0 - F)\,F}{M_0},
\end{aligned} \tag{1.17}$$

$$\frac{1}{2}\frac{d}{dt}\big[R^2(t)\big] = \frac{-1}{M_0}\int_{R(t)}^1 \Big[\frac{(M_0 - F)\,L}{\gamma + H} - \rho_3 M_0 + (\rho_3 - \rho_4)F\Big]rdr. \tag{1.18}$$

Therefore the equation for $p$ is eliminated and the radially symmetric system then formulates as

$$\text{Problem (P):}\begin{cases}\text{equations (1.5), (1.6), (1.17),}\\ \text{boundary conditions (1.9), (1.11)–(1.13),}\\ \text{free boundary condition (1.18).}\end{cases}$$

Our main result on the periodic small plaque is

**Theorem 1.1.** *Let the assumptions (1.1)–(1.3) hold. For every small $\varepsilon > 0$ and fixed $H_* > 0$, there exists a $L_* = L_*(\varepsilon, H_*)$ such that Problem (P) admits a periodic solution with period $T$ and $R(0) = 1-2\varepsilon$ and $1-3\varepsilon \le R(t) \le 1-\varepsilon$ for all $0 \le t \le T$. In particular,*

$$L_* = \rho_3(\gamma + H_*) + O(\varepsilon + \tau). \tag{1.19}$$

**Remark 1.1.** *Since a periodic solution returns to its original state after one period, the high density cholesterol and the low density cholesterol need to be balanced to produce such a result. Hence the requirement between $L_*$ and $H_*$ is reasonable.*

One of the challenges for establishing this theorem is the complexity of the system. Even for the case of constant nutrient supply, the system does not allow an explicit stationary solution. So we shall explore a variety of *expansion formulas* with respect to $\varepsilon$. Notice that the plaque region disappears when $\varepsilon$ approaches 0, so it is crucial to derive various estimates that are independent of $\varepsilon$ as $\varepsilon \to 0$, and that is the theme throughout this paper.

The remainder of this paper is devoted to proving this theorem.

For convenience, we make a change of variables

$$\widehat{L} = L - L_0(t), \quad \widehat{H} = H - H_0(t), \quad \widehat{F} = F. \tag{1.20}$$

Then Problem (P) is equivalent to the following system:

$$\begin{aligned}\frac{\partial \widehat{L}}{\partial t} - \Delta \widehat{L} = &- \rho_1 \widehat{L} - k_1 \frac{(M_0 - \widehat{F})\widehat{L}}{K_1 + \widehat{L} + L_0(t)} \\ &- k_1 \frac{(M_0 - \widehat{F})L_0(t)}{K_1 + \widehat{L} + L_0(t)} - \rho_1 L_0(t) - L_0'(t),\end{aligned} \tag{1.21}$$

$$\frac{\partial \widehat{H}}{\partial t} - \Delta \widehat{H} = -k_2 \frac{\widehat{H}\widehat{F}}{K_2 + \widehat{F}} - \rho_2 \widehat{H} - k_2 \frac{H_0(t)\widehat{F}}{K_2 + \widehat{F}} - \rho_2 H_0(t) - H_0'(t), \tag{1.22}$$

$$\begin{aligned}&\frac{\partial \widehat{F}}{\partial t} - D\Delta \widehat{F} \\ &\quad - \frac{\widehat{F}_r}{rM_0} \int_r^1 \Big[ \frac{\left(M_0 - \widehat{F}\right)(\widehat{L} + L_0(t))}{\gamma + \widehat{H} + H_0(t)} - \rho_3 M_0 + (\rho_3 - \rho_4)\widehat{F} \Big] \cdot \xi d\xi \\ &= k_1 \frac{(M_0 - \widehat{F})(\widehat{L} + L_0(t))}{K_1 + \widehat{L} + L_0(t)} - k_2 \frac{(\widehat{H} + H_0(t))\widehat{F}}{K_2 + \widehat{F}} \\ &\quad - \lambda \frac{\widehat{F}(M_0 - \widehat{F})(\widehat{L} + L_0(t))}{M_0(\gamma + \widehat{H} + H_0(t))} + (\rho_3 - \rho_4) \frac{(M_0 - \widehat{F})\widehat{F}}{M_0},\end{aligned} \tag{1.23}$$

with boundary conditions

$$\frac{\partial \widehat{L}}{\partial r} = \frac{\partial \widehat{H}}{\partial r} = \frac{\partial \widehat{F}}{\partial r} = 0 \qquad \text{on } \{r = 1\}, \tag{1.24}$$

$$\begin{cases} -\dfrac{\partial \widehat{L}}{\partial r} + \beta_1 \widehat{L} = 0, \; -\dfrac{\partial \widehat{H}}{\partial r} + \beta_1 \widehat{H} = 0, \\ -\dfrac{\partial \widehat{F}}{\partial r} + \beta_2 \widehat{F} = 0 \end{cases} \quad \text{on } \{r = R(t)\}, \tag{1.25}$$

and

(1.26)
$$\frac{1}{2}\frac{d}{dt}\big[R^2(t)\big] = \frac{-1}{M_0}\int_{R(t)}^{1}\Big[\frac{(M_0-\widehat{F})(\widehat{L}+L_0(t))}{\gamma+\widehat{H}+H_0(t)} - \rho_3 M_0 + (\rho_3-\rho_4)\widehat{F}\Big] r dr.$$

## 2. Preliminaries

In this paper, we shall use the function

$$\xi(r) = \frac{1-r^2}{4} + \frac{1}{2}\log r \tag{2.1}$$

a lot when we apply the maximum principle. This function is introduced in [2] and satisfies

$$\begin{aligned} &-\Delta\xi = 1, \quad \xi_r(r) = \frac{1-r^2}{2r}, \\ \text{and} \quad &\xi(r) \le 0, \quad \xi(r) = O(\varepsilon^2) \text{ when } 1-\varepsilon < r < 1. \end{aligned} \tag{2.2}$$

Take

$$c(\beta,\varepsilon) = \frac{1}{\beta}\frac{\varepsilon(2-\varepsilon)}{2(1-\varepsilon)} - \frac{\varepsilon(2-\varepsilon)}{4} - \frac{1}{2}\log(1-\varepsilon) \equiv \frac{\varepsilon}{\beta} + O(\varepsilon^2).$$

Then it is easy to verify that

$$\Big[-\frac{\partial[\xi + c(\beta,\varepsilon)]}{\partial r} + \beta\Big(\xi + c(\beta,\varepsilon)\Big)\Big]_{r=1-\varepsilon} = 0. \tag{2.3}$$

The following continuity lemma is handy when deriving estimates for nonlinear system.

**Lemma 2.1** (See [8, Lemma 5.1])**.** *Let $\{\vec{Q}_\delta^{(i)}\}_{i=1}^M$ be a finite collection of real vectors, and define the norm of the vector by $|\vec{Q}_\delta|_{\max} = \max_{1\le i\le M}|Q_\delta^{(i)}|$. Suppose that $0 < C_1 < C_2$, and*

(i) $|\vec{Q}_0|_{\max} \le C_1$;

(ii) *For any* $0<\delta\le 1$, *if* $|\vec{Q}_\delta|_{\max}\le C_2$, *then* $|\vec{Q}_\delta|_{\max}\le C_1$;
(iii) $\vec{Q}_\delta$ *is continuous in* $\delta$.

*Then* $|\vec{Q}_\delta|_{\max}\le C_1$ *for all* $0<\delta\le 1$.

## 3. Approximation

We start with several lemmas. In order to obtain a periodic solution, we consider the following auxiliary problem

$$\text{Problem (P}^*\text{):}\begin{cases}\text{equations (1.21), (1.22), (1.23),}\\ \text{boundary conditions (1.24), (1.25),}\\ \text{free boundary condition (3.1),}\end{cases}$$

where

$$\frac{1}{2}\frac{d}{dt}\big[R^2(t)\big]=\eta+\frac{-1}{M_0}\int_{R(t)}^1\Big[\frac{(M_0-\widehat{F})(\widehat{L}+L_0(t))}{\gamma+\widehat{H}+H_0(t)}-\rho_3M_0+(\rho_3-\rho_4)\widehat{F}\Big]rdr. \tag{3.1}$$

and the constant $\eta$ satisfies

$$\int_0^T\Big\{\eta+\frac{-1}{M_0}\int_{R(t)}^1\Big[\frac{\big(M_0-\widehat{F}\big)\big(\widehat{L}+L_0(t)\big)}{\gamma+\widehat{H}+H_0(t)}-\rho_3M_0+(\rho_3-\rho_4)\widehat{F}\Big]rdr\Big\}dt=0, \tag{3.2}$$

where the period $T$ is given in (1.3). The introduction of $\eta$ forces the free boundary to be periodic, and later on we shall that $\eta$ can be chosen as 0 to recover the original problem.

As a balance between LDL and HDL is required to produce a periodic solution, we assume

$$L_*=\rho_3(\gamma+H_*)+m(\varepsilon+\tau),\qquad -1<m(\varepsilon+\tau)<1, \tag{3.3}$$

with $m$ a constant to be determined and, as indicated in the introduction, $\varepsilon>0,\tau>0$, $\varepsilon$, $\tau$ are small. The second assumption in (3.3) is crucial, as the various estimates we derive in the following are all independent of $m$, allowing us to freely choose $m$ to allow $\eta$ to be 0.

In what follows we shall establish

$$\eta=O(\varepsilon\tau+\varepsilon^2). \tag{3.4}$$

We shall carefully show that all our estimates, including (3.4), are independent of $m$.

We first consider the initial value problem, with the initial condition satisfying the compatibility conditions:

$$\begin{aligned} \frac{\partial \widehat{L}}{\partial r}(1,0) = \frac{\partial \widehat{H}}{\partial r}(1,0) = \frac{\partial \widehat{F}}{\partial r}(1,0) = 0, \\ -\frac{\partial \widehat{L}}{\partial r}(1-2\varepsilon,0) + \beta_1 \widehat{L}(1-2\varepsilon,0) = 0, \\ -\frac{\partial \widehat{H}}{\partial r}(1-2\varepsilon,0) + \beta_1 \widehat{H}(1-2\varepsilon,0) = 0, \\ -\frac{\partial \widehat{F}}{\partial r}(1-2\varepsilon,0) + \beta_2 \widehat{F}(1-2\varepsilon,0) = 0, \end{aligned} \tag{3.5}$$

with the bounds on the initial data

$$|\widehat{L}(r,0)| \le C_0^* \varepsilon, \quad |\widehat{H}(r,0)| \le C_0^* \varepsilon, \quad 0 \le \widehat{F}(r,0) \le C_0^* \varepsilon, \tag{3.6}$$

and its first order derivatives

$$\Big|\frac{\partial \widehat{L}}{\partial r}(r,0)\Big| \le C_1^* \varepsilon, \quad \Big|\frac{\partial \widehat{H}}{\partial r}(r,0)\Big| \le C_1^* \varepsilon, \quad \Big|\frac{\partial \widehat{F}}{\partial r}(r,0)\Big| \le C_1^* \varepsilon, \tag{3.7}$$

where the constants $C_0^*$ and $C_1^*$ are independent of $\varepsilon$ and $\tau$. We also assume

$$\Big|\frac{\partial \widehat{L}}{\partial t}(r,0)\Big| \le \phi(r), \quad \Big|\frac{\partial \widehat{H}}{\partial t}(r,0)\Big| \le \phi(r), \quad \Big|\frac{\partial \widehat{F}}{\partial t}(r,0)\Big| \le \phi(r), \tag{3.8}$$

with a function $\phi$ defined explicitly later in (3.31). These conditions can be rewritten in terms of the derivatives of the initial data through the use of the equations, but it is clearer to leave the expressions as above.

We take $\varepsilon$ to be small so that

$$C_0^* \varepsilon \le 1, \quad C_1^* \varepsilon \le 1.$$

We let

$$\mathscr{I} = \left\{ (L,H,F) \in (C^2[1-2\varepsilon,1])^3; (L,H,F) \text{ satisfies } (3.5)\text{–}(3.8) \right\}.$$

**Lemma 3.1.** *Assume that the period $T$ is given in (1.3). Given initial conditions $(\widehat{L}(\cdot,0), \widehat{H}(\cdot,0), \widehat{F}(\cdot,0)) \in \mathscr{I}$ and the initial position of the free boundary $R(0) = 1-2\varepsilon$. For small $\varepsilon$, the Problem ($P^*$) admits a unique solution for $0 \le t \le T$.*

*Proof.* This is accomplished by contraction mapping principle. Let

$$\mathscr{R} = \Big\{ R \in C^1[0,T];\ R(0) = R(T) = 1 - 2\varepsilon, |R'(t)| \le \frac{\varepsilon}{T} \Big\}.$$

It is clear that any $R \in \mathscr{R}$ must satisfy

$$1 - 3\varepsilon \le R(t) \le 1 - \varepsilon. \tag{3.9}$$

**Step 1.** Given $R \in \mathscr{R}$, the system (1.21)–(1.23) with boundary conditions (1.24), (1.25) and initial conditions (3.5)–(3.8) admit a unique solution. We use a contraction mapping principle in this step.

Take

$$\Lambda = \left\{ (\overline{L}, \overline{H}, \overline{F});\ \begin{matrix} |\overline{L}| \le C_0^{**}\varepsilon,\ |\overline{H}| \le C_0^{**}\varepsilon,\ 0 \le \overline{F} \le C_0^{**}\varepsilon, \\ |\partial_r \overline{L}| \le C_1^{**}\varepsilon,\ |\partial_r \overline{H}| \le C_1^{**}\varepsilon,\ |\partial_r \overline{F}| \le C_1^{**}\varepsilon. \end{matrix} \right\}, \tag{3.10}$$

where $C_0^{**}$ and $C_1^{**}$ are to be determined, with $C_0^{**}\varepsilon \le 1$, $C_1^{**}\varepsilon \le 1$. For each $(\overline{L}, \overline{H}, \overline{F}) \in \Lambda$, we solve the following linear equations:

$$\begin{aligned} \frac{\partial \widehat{L}}{\partial t} - \Delta \widehat{L} = &- k_1 \frac{(M_0 - \overline{F})\widehat{L}}{K_1 + \overline{L} + L_0(t)} - \rho_1 \widehat{L} \\ &- k_1 \frac{(M_0 - \overline{F})L_0(t)}{K_1 + \overline{L} + L_0(t)} - \rho_1 L_0(t) - L_0'(t), \end{aligned} \tag{3.11}$$

$$\frac{\partial \widehat{H}}{\partial t} - \Delta \widehat{H} = -k_2 \frac{\widehat{H}\overline{F}}{K_2 + \overline{F}} - \rho_2 \widehat{H} - k_2 \frac{H_0(t)\overline{F}}{K_2 + \overline{F}} - \rho_2 H_0(t) - H_0'(t), \tag{3.12}$$

$$\begin{aligned} \frac{\partial \widehat{F}}{\partial t} - D\Delta \widehat{F} - \frac{\widehat{F}_r}{rM_0} \int_r^1 \Big[ &\frac{\left(M_0 - \overline{F}\right)\left(\overline{L} + L_0(t)\right)}{\gamma + \overline{H} + H_0(t)} \\ &- \rho_3 M_0 + (\rho_3 - \rho_4)\overline{F} \Big] \cdot \xi d\xi \\ = k_1 \frac{(M_0 - \widehat{F})(\overline{L} + L_0(t))}{K_1 + \overline{L} + L_0(t)} &- k_2 \frac{(\overline{H} + H_0(t))\widehat{F}}{K_2 + \overline{F}} \\ - \lambda \frac{\widehat{F}\left(M_0 - \overline{F}\right)\left(\overline{L} + L_0(t)\right)}{M_0(\gamma + \overline{H} + H_0(t))} &+ \frac{\rho_3}{M_0}(M_0 - \widehat{F})\overline{F} \\ - \frac{\rho_4}{M_0}(M_0 - \overline{F})\widehat{F}&, \end{aligned} \tag{3.13}$$

$$\frac{\partial \widehat{L}}{\partial r} = \frac{\partial \widehat{H}}{\partial r} = \frac{\partial \widehat{F}}{\partial r} = 0 \qquad \text{on } \{r = 1,\ t > 0\}, \tag{3.14}$$

$$(3.15)\qquad \begin{cases} -\dfrac{\partial \widehat{L}}{\partial r}+\beta_1\widehat{L}=0,\ -\dfrac{\partial \widehat{H}}{\partial r}+\beta_1\widehat{H}=0, \\ -\dfrac{\partial \widehat{F}}{\partial r}+\beta_2\widehat{F}=0, \end{cases} \qquad \text{on}\ \ \{r=R(t)\},$$

and the compatibility conditions:

$$(3.16)\qquad \begin{aligned} \frac{\partial \widehat{L}}{\partial r}(1,0)=\frac{\partial \widehat{H}}{\partial r}(1,0)=\frac{\partial \widehat{F}}{\partial r}(1,0)&=0,\\ -\frac{\partial \widehat{L}}{\partial r}(1-2\varepsilon,0)+\beta_1\widehat{L}(1-2\varepsilon,0)&=0,\\ -\frac{\partial \widehat{H}}{\partial r}(1-2\varepsilon,0)+\beta_1\widehat{H}(1-2\varepsilon,0)&=0,\\ -\frac{\partial \widehat{F}}{\partial r}(1-2\varepsilon,0)+\beta_2\widehat{F}(1-2\varepsilon,0)&=0, \end{aligned}$$

and under our assumptions (3.6)–(3.7) that $\widehat{L}(r,0)$, $\widehat{H}(r,0)$ and $\widehat{F}(r,0)$ satisfy

$$(3.17)\qquad |\widehat{L}(r,0)|\le C_0^*\varepsilon,\quad |\widehat{H}(r,0)|\le C_0^*\varepsilon,\quad 0\le \widehat{F}(r,0)\le C_0^*\varepsilon,$$

$$(3.18)\qquad |\widehat{L}_r(r,0)|\le C_1^*\varepsilon,\quad |\widehat{H}_r(r,0)|\le C_1^*\varepsilon,\quad |\widehat{F}_r(r,0)|\le C_1^*\varepsilon.$$

Define a map $\mathscr{L}:(\overline{L},\overline{H},\overline{F})\to(\widehat{L},\widehat{H},\widehat{F})$. We shall prove that $\mathscr{L}$ maps $\Lambda$ into itself and $\mathscr{L}$ is a contraction, which indicates that the unique fixed point of $\mathscr{L}$ is the unique classical solution of the system (3.11)–(3.17).

Combining (1.3) with (3.10), we immediately obtain

$$\begin{aligned} &\Big|\frac{\partial \widehat{L}}{\partial t}-\Delta\widehat{L}+k_1\frac{(M_0-\overline{F})\widehat{L}}{K_1+\overline{L}+L_0(t)}+\rho_1\widehat{L}\Big|\\ &\qquad=\Big|k_1\frac{(M_0-\overline{F})L_0(t)}{K_1+\overline{L}+L_0(t)}+\rho_1L_0(t)+L_0'(t)\Big|\le\overline{C}, \end{aligned}$$

where $\overline{C}$ is independent of $\varepsilon$, $\tau$, $C_0^{**}$ and $C_1^{**}$. Here and hereafter we shall use the notation $\overline{C}$ to denote various different positive constants independent of $\varepsilon$, $\tau$, $C_0^{**}$ and $C_1^{**}$. It follows that $\overline{C}(\xi(r)+c(\beta_1,\varepsilon))+C_0^*\varepsilon$ is a supersolution for $\pm\widehat{L}$, then, recall (2.2),

$$(3.19)\qquad |\widehat{L}|\le\overline{C}(\xi(r)+c(\beta_1,\varepsilon))+C_0^*\varepsilon\le\overline{C}c(\beta_1,\varepsilon)+C_0^*\varepsilon\le\frac{2\overline{C}}{\beta_1}\varepsilon+C_0^*\varepsilon,$$

where $\xi(r)$ is defined in (2.1). Similarly, we also obtain

$$|\widehat{H}| \leq \frac{2\overline{C}}{\beta_1}\varepsilon + C_0^*\varepsilon. \tag{3.20}$$

The fact $(\overline{L}, \overline{H}, \overline{F}) \in \Lambda$ implies that $\overline{L} + L_0(t) \geq 0$ and $\overline{H} + H_0(t) \geq 0$ for small $\varepsilon$ and $\tau$. By the maximum principle, we clearly have, for $R(t) < r < 1$ and $t > 0$,

$$0 \leq \widehat{F} \leq M_0. \tag{3.21}$$

By (3.10) and (3.21), the right-hand side of equation (3.13) is bounded, i.e.,

$$\Big|\frac{\partial \widehat{F}}{\partial t} - D\Delta\widehat{F} - \frac{\widehat{F}_r}{rM_0}\int_r^1 \Big[\frac{\big(M_0 - \overline{F}\big)\,(\overline{L} + L_0(t))}{\gamma + \overline{H} + H_0(t)} - \rho_3 M_0 + (\rho_3 - \rho_4)\overline{F}\Big] \cdot \xi d\xi\Big| \\ \leq \overline{C}.$$

The extra term involving $\widehat{F}_r$ gets a coefficient of order $O(\varepsilon)$ and alters only in an insignificant manner the computation of the supersolution. One can show that $\overline{C}(\xi(r) + c(\beta_2, \varepsilon)) + C_0^*\varepsilon$ is a supersolution for $\widehat{F}$, so that

$$|\widehat{F}| \leq \overline{C}(\xi(r) + c(\beta_2, \varepsilon)) + C_0^*\varepsilon \leq \overline{C}c(\beta_2, \varepsilon) + C_0^*\varepsilon \leq \frac{2\overline{C}}{\beta_2}\varepsilon + C_0^*\varepsilon.$$

Thus we can take

$$C_0^{**} = C_0^* + 2\overline{C}\max\Big(\frac{1}{\beta_1}, \frac{1}{\beta_2}\Big). \tag{3.22}$$

We next proceed to find $C_1^{**}$. Differentiating the equations in $r$ and applying maximum principle, we find that the system for $r$-derivatives is similar to that for the original functions, with the right-hand sides bounded by $\overline{C}_1$. Furthermore, on $r = 1$, $\widehat{L}_r = \widehat{H}_r = \widehat{F}_r = 0$. On $r = R(t)$, we use the boundary conditions (3.15) to derive

$$\frac{1}{\beta_1}|\widehat{L}_r| \leq C_0^{**}\varepsilon, \quad \frac{1}{\beta_1}|\widehat{H}_r| \leq C_0^{**}\varepsilon, \quad \frac{1}{\beta_2}|\widehat{F}_r| \leq C_0^{**}\varepsilon.$$

Thus a similar argument as above gives us

$$C_1^{**} = C_1^* + \max\Big(\frac{2\overline{C}_1}{\beta_1}, \frac{2\overline{C}_1}{\beta_2}, \beta_1 C_0^{**}, \beta_2 C_0^{**}\Big). \tag{3.23}$$

Above all, we have shown that $(\widehat{L}, \widehat{H}, \widehat{F}) \in \Lambda$, which implies that $\mathscr{L}$ maps $\Lambda$ into itself. We shall next prove that $\mathscr{L}$ is a contraction.

Suppose that $(\widehat{L}_j, \widehat{H}_j, \widehat{F}_j) = \mathscr{L}(\overline{L}_j, \overline{H}_j, \overline{F}_j)$ for $j = 1, 2$, and set

$$\begin{aligned}\mathscr{A} &= \|\overline{L}_1 - \overline{L}_2\|_{L^\infty} + \|\overline{H}_1 - \overline{H}_2\|_{L^\infty} + \|\overline{F}_1 - \overline{F}_2\|_{L^\infty},\\ \mathscr{B} &= \|\widehat{L}_1 - \widehat{L}_2\|_{L^\infty} + \|\widehat{H}_1 - \widehat{H}_2\|_{L^\infty} + \|\widehat{F}_1 - \widehat{F}_2\|_{L^\infty}.\end{aligned}$$

Recalling (3.11)–(3.12), we get, for some constant $\overline{C}^*$ independent of $\varepsilon$,

$$\begin{aligned}\Big|\frac{\partial(\widehat{L}_1 - \widehat{L}_2)}{\partial t} - \Delta(\widehat{L}_1 - \widehat{L}_2)\Big| &\le \overline{C}^*(\mathscr{A} + \mathscr{B}),\\ \Big|\frac{\partial(\widehat{H}_1 - \widehat{H}_2)}{\partial t} - \Delta(\widehat{H}_1 - \widehat{H}_2)\Big| &\le \overline{C}^*(\mathscr{A} + \mathscr{B}).\end{aligned}$$

We now establish the inequality that $\widehat{F}_1 - \widehat{F}_2$ satisfies. By a simple computation, we have

$$\Big|\frac{\partial(\widehat{F}_1 - \widehat{F}_2)}{\partial t} - D\Delta(\widehat{F}_1 - \widehat{F}_2) - \frac{g(\overline{L}_1, \overline{H}_1, \overline{F}_1)}{rM_0}\partial_r(\widehat{F}_1 - \widehat{F}_2)\Big| \le \overline{C}^*(\mathscr{A} + \mathscr{B}),$$

where

$$g(\overline{L}_1, \overline{H}_1, \overline{F}_1) = \int_r^1 \Big[\frac{\big(M_0 - \overline{F}_1\big)\big(\overline{L}_1 + L_0(t)\big)}{\gamma + \overline{H}_1 + H_0(t)} - \rho_3 M_0 + (\rho_3 - \rho_4)\overline{F}_1\Big] \cdot \xi d\xi.$$

By (3.10), we have $|g(\overline{L}_1, \overline{H}_1, \overline{F}_1)| \le C\varepsilon$. Recall that $\partial_r \widehat{F}_i$ $(i = 1, 2)$ are bounded by $C_1^{**}\varepsilon$. Therefore the presence of the term $\frac{g(\overline{L}_1, \overline{H}_1, \overline{F}_1)}{rM_0}\partial_r(\widehat{F}_1 - \widehat{F}_2)$ only presents a minor addition and does not alter the computation of our supersolution. Since we have zero initial conditions for $\widehat{L}_1 - \widehat{L}_2, \widehat{H}_1 - \widehat{H}_2, \widehat{F}_1 - \widehat{F}_2$, the function $\overline{C}^*(\mathscr{A} + \mathscr{B})(\xi(r) + c(\beta_i, \varepsilon))$ clearly serves as a supersolution and therefore by the maximum principle,

$$\begin{aligned}|\widehat{L}_1 - \widehat{L}_2| &\le \overline{C}^*(\mathscr{A} + \mathscr{B})(\xi(r) + c(\beta_1, \varepsilon)),\\ |\widehat{H}_1 - \widehat{H}_2| &\le \overline{C}^*(\mathscr{A} + \mathscr{B})(\xi(r) + c(\beta_1, \varepsilon)),\\ |\widehat{F}_1 - \widehat{F}_2| &\le \overline{C}^*(\mathscr{A} + \mathscr{B})(\xi(r) + c(\beta_2, \varepsilon)),\end{aligned}$$

which implies

$$|\widehat{L}_1 - \widehat{L}_2| \le \overline{C}^{**}(\mathscr{A} + \mathscr{B})\varepsilon,$$

$$|\widehat{H}_1 - \widehat{H}_2| \le \overline{C}^{**}(\mathscr{A} + \mathscr{B})\varepsilon,$$
$$|\widehat{F}_1 - \widehat{F}_2| \le \overline{C}^{**}(\mathscr{A} + \mathscr{B})\varepsilon,$$

where both $\overline{C}^*$ and $\overline{C}^{**}$ are independent of $\varepsilon$ and $\tau$. The above inequalities imply that

$$\mathscr{B} \le \overline{C}^{**}(\mathscr{A} + \mathscr{B})\varepsilon.$$

By taking $\varepsilon$ sufficiently small, we have

$$\frac{\overline{C}^{**}\varepsilon}{1 - \overline{C}^{**}\varepsilon} < 1,$$

so that $\mathscr{L}$ is a contraction mapping. The contraction mapping principle then gives us a unique solution in $\Lambda$ of (1.21)–(1.25) for each fixed $R \in \mathscr{R}$.

**Step 2.** We now have a solution of (1.21)–(1.25) for each fixed $R \in \mathscr{R}$. We next proceed to derive the estimates for $|\widehat{L}_t|$, $|\widehat{H}_t|$ and $|\widehat{F}_t|$. We claim that, for the function $\phi(t)$ in (3.8) still to be determined,

$$|\widehat{L}_t| \le \phi(r),\ |\widehat{H}_t| \le \phi(r),\ |\widehat{F}_t| \le \phi(r),\ R(t) \le r \le 1,\ 0 \le t \le T. \tag{3.24}$$

Notice that in the definition of the closed convex set $\mathscr{R}$, $R$ is assumed to be a $C^1$ function. Differentiating the equations (1.21)–(1.23) in $t$, we obtain the equations for $\widehat{L}_t$, $\widehat{H}_t$ and $\widehat{F}_t$, respectively. Even though the equations are more complex, they are similar in structure as the equations (1.21)–(1.23). For example, for the equation for $\widehat{F}_t$, we have

$$\begin{aligned}
&\partial_t \widehat{F}_t - D\Delta \widehat{F}_t \\
&\qquad - \frac{\partial_r \widehat{F}_t}{rM_0}\int_r^1 \Big[\frac{(M_0 - \widehat{F})(\widehat{L} + L_0(t))}{\gamma + \widehat{H} + H_0(t)} - \rho_3 M_0 + (\rho_3 - \rho_4)\widehat{F}\Big]\cdot \xi d\xi \\
&= \quad \frac{\widehat{F}_r}{rM_0}\int_r^1 \Big\{\frac{M_0 - \widehat{F}}{\gamma + \widehat{H} + H_0(t)}\widehat{L}_t - \frac{(M_0 - \widehat{F})(\widehat{L} + L_0(t))}{(\gamma + \widehat{H} + H_0(t))^2}\widehat{H}_t \\
&\qquad\qquad - \frac{\widehat{L} + L_0(t)}{\gamma + \widehat{H} + H_0(t)}\widehat{F}_t + \frac{M_0 - \widehat{F}}{\gamma + \widehat{H} + H_0(t)}L_0'(t) \\
&\qquad\qquad - \frac{(M_0 - \widehat{F})(\widehat{L} + L_0(t))}{(\gamma + \widehat{H} + H_0(t))^2}H_0'(t)\Big\}\xi d\xi \\
&\qquad + \frac{k_1 K_1 (M_0 - \widehat{F})}{(K_1 + \widehat{L} + L_0(t))^2}\widehat{L}_t - \frac{\lambda}{M_0}\frac{\widehat{F}(M_0 - \widehat{F})}{\gamma + \widehat{H} + H_0(t)}\widehat{L}_t
\end{aligned}$$

$$
\begin{aligned}
&-k_2\frac{\widehat{F}}{K_2+\widehat{F}}\widehat{H}_t+\frac{\lambda}{M_0}\frac{\widehat{F}(M_0-\widehat{F})(\widehat{L}+L_0(t))}{(\gamma+\widehat{H}+H_0(t))^2}\widehat{H}_t\\
&-k_1\frac{\widehat{L}+L_0(t)}{K_1+\widehat{L}+L_0(t)}\widehat{F}_t-\frac{k_2K_2(\widehat{H}+H_0(t))}{(K_2+\widehat{F})^2}\widehat{F}_t\\
&-\frac{\lambda}{M_0}\frac{(M_0-2\widehat{F})(\widehat{L}+L_0(t))}{\gamma+\widehat{H}+H_0(t)}\widehat{F}_t+\frac{\rho_3-\rho_4}{M_0}(M_0-2\widehat{F})\widehat{F}_t\\
&+\frac{k_1K_1(M_0-\widehat{F})L_0'(t)}{(K_1+\widehat{L}+L_0(t))^2}-k_2\frac{\widehat{F}H_0'(t)}{K_2+\widehat{F}}-\frac{\lambda}{M_0}\frac{\widehat{F}(M_0-\widehat{F})L_0'(t)}{\gamma+\widehat{H}+H_0(t)}\\
&+\frac{\lambda}{M_0}\frac{\widehat{F}(M_0-\widehat{F})(\widehat{L}+L_0(t))H_0'(t)}{(\gamma+\widehat{H}+H_0(t))^2}.
\end{aligned}
$$

The equations for $\widehat{L}_t$ and $\widehat{H}_t$ can be computed in a similar manner (and simpler). In summary, we have, for $R(t)<r<1, 0<t<T$,

(3.25)
$$
\begin{cases}
\partial_t\widehat{L}_t-\Delta\widehat{L}_t=a_{1L}\widehat{L}_t+a_{2L}\widehat{H}_t+a_{3L}\widehat{F}_t+a_{4L},\\
\partial_t\widehat{H}_t-\Delta\widehat{H}_t=a_{1H}\widehat{L}_t+a_{2H}\widehat{H}_t+a_{3H}\widehat{F}_t+a_{4H},\\
\partial_t\widehat{F}_t-D\Delta\widehat{F}_t+b_F\partial_r\widehat{F}_t=\displaystyle\int_r^1(\overline{a}_{1F}\widehat{L}_t+\overline{a}_{2F}\widehat{H}_t+\overline{a}_{3F}\widehat{F}_t+\overline{a}_{4F})\xi d\xi\\
\qquad\qquad+a_{1F}\widehat{L}_t+a_{2F}\widehat{H}_t+a_{3F}\widehat{F}_t+a_{4F},
\end{cases}
$$

where $b_F=O(\varepsilon)$, and $a_{jL},a_{jH},a_{jF},\overline{a}_{jF}$ $(j=1,2,3,4)$ are bounded with the bounds depending only on the known quantities.

We next derive boundary conditions for the $t$-derivatives. Obviously, differentiating the boundary conditions with respect to $t$, we obtain at $r=1$,

$$(\widehat{L}_t)_r(1,t)=(\widehat{H}_t)_r(1,t)=(\widehat{F}_t)_r(1,t)=0.$$

To derive the boundary conditions at $r=R(t)$, we differentiate the boundary condition for $\widehat{L}$ in (1.25) in $t$ and obtain

$$-\widehat{L}_{rr}R'-\widehat{L}_{rt}+\beta_1(\widehat{L}_rR'+\widehat{L}_t)=0,\quad r=R(t),\ 0\le t\le T. \tag{3.26}$$

The equation (1.21) together with the estimates in (3.10) imply

$$|\widehat{L}_t-\widehat{L}_{rr}|\le C_0,\quad R(t)\le r\le 1,\ 0\le t\le T, \tag{3.27}$$

for some constant $C_0$ depending only on the given data (i.e., $C_0$ depends only on $\|L_0\|_{C^1[0,T]},\|H_0\|_{C^1[0,T]},M_0,\rho_1,\rho_2,\rho_3,\rho_4,k_1,k_2,K_1,K_2,\lambda,\gamma)$. Combining the estimates (3.26) and (3.27), using also the fact that $R \in \mathscr{R}$, we find, for small $\varepsilon$,

$$|-(\widehat{L}_t)_r + (\beta_1 - R')\widehat{L}_t| \le 1, \quad r = R(t),\ 0 \le t \le T. \tag{3.28}$$

We also have

$$\beta_1 - R' \ge \beta_1 - \frac{\varepsilon}{T} \ge \frac{1}{2}\beta_1.$$

Similarly,

$$|-(\widehat{H}_t)_r + (\beta_1 - R')\widehat{H}_t| \le 1, \quad r = R(t),\ 0 \le t \le T, \tag{3.29}$$

and

$$\Big|-(\widehat{F}_t)_r + \Big(\beta_2 - \frac{1}{D}R'\Big)\widehat{F}_t\Big| \le 1, \quad r = R(t),\ 0 \le t \le T, \tag{3.30}$$

where, for small $\varepsilon$,

$$\beta_2 - \frac{1}{D}R' \ge \frac{1}{2}\beta_2.$$

Choose $\overline{C}$ in the definition (3.31) below such that

$$\Big|\frac{\partial \widehat{L}}{\partial t}(r,0)\Big| \le \phi(r), \quad \Big|\frac{\partial \widehat{H}}{\partial t}(r,0)\Big| \le \phi(r), \quad \Big|\frac{\partial \widehat{F}}{\partial t}(r,0)\Big| \le \phi(r),$$

where

$$\phi(r) \triangleq \frac{1}{\sqrt{\varepsilon}}[\xi(r) - \xi(1-3\varepsilon)] + \max\Big(\frac{4}{\beta_1}, \frac{4}{\beta_2}, \overline{C}\Big). \tag{3.31}$$

Then the function $\phi$ is a supersolution for $\pm\widehat{L}_t, \pm\widehat{H}_t, \pm\widehat{F}_t$. Indeed, for any $0 < \delta \le 1$, if

$$\max_{R(t)\le r\le 1,\ 0\le t\le \delta T} \left\{ \frac{|\widehat{L}_t|}{\phi(r)}, \frac{|\widehat{H}_t|}{\phi(r)}, \frac{|\widehat{F}_t|}{\phi(r)} \right\} \le 2, \tag{3.32}$$

then the right-hand side functions of (3.25) are all bounded by a constant depending only on the known data. Furthermore, for the equation and boundary conditions for $\widehat{F}_t$, the supersolution $\phi$ satisfies

$$\partial_t\phi - D\Delta\phi + b_F\partial_r\phi = D\frac{1}{\sqrt{\varepsilon}} + O(\varepsilon)\frac{1}{\sqrt{\varepsilon}}\frac{1-r^2}{2r} \ge \frac{D}{2\sqrt{\varepsilon}}$$

$$\partial_r \phi = 0, \qquad r = 1,\ 0 < t < T,$$

and

$$\begin{aligned}&-\partial_r\phi + \Big(\beta_2 - \frac{1}{D}R'\Big)\phi\\ &\quad= -\frac{1}{\sqrt{\varepsilon}}O(\varepsilon) + \Big(\beta_2 - \frac{1}{D}R'\Big)\frac{1}{\sqrt{\varepsilon}}O(\varepsilon^2) + \Big(\beta_2 - \frac{1}{D}R'\Big)\max\Big(\frac{4}{\beta_1}, \frac{4}{\beta_2}, \overline{C}\Big)\\ &\quad\geq 2 + O(\varepsilon^{1/2}), \qquad r = R(t),\ 0 < t < T.\end{aligned}$$

The computations for other equations in the system are similar. By maximum principle, for small $\varepsilon$,

$$|\widehat{L}_t| \leq \phi(r),\ |\widehat{H}_t| \leq \phi(r),\ |\widehat{F}_t| \leq \phi(r),\ R(t) \leq r \leq 1,\ 0 \leq t \leq \delta T, \tag{3.33}$$

i.e.,

$$\max_{R(t)\leq r\leq 1,\, 0\leq t\leq \delta T}\Big\{\frac{|\widehat{L}_t|}{\phi(r)}, \frac{|\widehat{H}_t|}{\phi(r)}, \frac{|\widehat{F}_t|}{\phi(r)}\Big\} \leq 1. \tag{3.34}$$

Note that the above estimate is true for $\delta = 0$ since it is assumed in (3.8). The continuity lemma, Lemma 2.1, then implies our $t$ derivative estimates for $\delta = 1$.

With the estimates of $t$ derivatives in hand, we immediately obtain estimates for the second order $r$-derivatives through the equations.

**Step 3.** We now define $\eta$ by (3.2), and define a new $\widetilde{R}(t)$ by (3.1) with $\widetilde{R}(0) = 1 - 2\varepsilon$:

$$\frac{d}{dt}\Big[\frac{\widetilde{R}^2(t)}{2}\Big] = \eta + \frac{-1}{M_0}\int_{R(t)}^1 \Big[\frac{(M_0 - \widehat{F})(\widehat{L} + L_0(t))}{\gamma + \widehat{H} + H_0(t)} - \rho_3 M_0 + (\rho_3 - \rho_4)\widehat{F}\Big] r\,dr,$$

$$\int_0^T \Big\{\eta + \frac{-1}{M_0}\int_{R(t)}^1 \Big[\frac{(M_0 - \widehat{F})(\widehat{L} + L_0(t))}{\gamma + \widehat{H} + H_0(t)} - \rho_3 M_0 + (\rho_3 - \rho_4)\widehat{F}\Big] r\,dr\Big\} dt = 0.$$

We next proceed to show that the map $\mathscr{M} : R \to \widetilde{R} \triangleq \mathscr{M}R$ is a contraction.

First we show $\mathscr{M}$ maps $\mathscr{R}$ into itself. From (3.1), (3.2), (1.1) and (3.3), we find that $|\widetilde{R}'(t)| \leq C(\varepsilon\tau + \varepsilon^2)$, so that $|\widetilde{R}'(t)| \leq \varepsilon/T$ for $0 \leq t \leq T$ if $\tau$ and $\varepsilon$ are small enough.

To show that it is a contraction, take $R_1, R_2 \in \mathscr{R}$. Let $(L_i, H_i, F_i, \eta_i)$ $(i = 1, 2)$ be the corresponding solutions from Step 1. We need to make a change of variables to transform the equations into the same domain:

$$(\widetilde{r},\widetilde{t}) = \Big(1-2\varepsilon\frac{1-r}{1-R_i(t)},t\Big), \quad i=1,2. \tag{3.35}$$

It maps $r=R_i(t)$ $(i=1,2)$ into $\widetilde{r}=1-2\varepsilon$ and keeps the boundary $r=1$ fixed. Notice that under our assumptions,

$$\varepsilon \le 1-R_i(t) \le 3\varepsilon.$$

Under this change of variables,

$$\begin{aligned}
&\frac{\partial}{\partial t} = \frac{\partial}{\partial \widetilde{t}} + \frac{R_i'(t)}{1-R_i(t)}(\widetilde{r}-1)\frac{\partial}{\partial \widetilde{r}} = \frac{\partial}{\partial \widetilde{t}} - \frac{R_i'(t)}{S_i(t)}\,\frac{1-\widetilde{r}}{2\varepsilon}\,\frac{\partial}{\partial \widetilde{r}},\\
&S_i(t) \triangleq \frac{1-R_i(t)}{2\varepsilon}, \quad \frac{1}{2} \le S_i(t) \le \frac{3}{2}, \quad 0 \le \frac{1-\widetilde{r}}{2\varepsilon} \le 1,\\
&S_1(t)-S_2(t) = \frac{R_2(t)-R_1(t)}{2\varepsilon},\\
&\frac{\partial}{\partial r} = \frac{1}{S_i(t)}\frac{\partial}{\partial \widetilde{r}},\\
&\frac{1}{r}\frac{\partial}{\partial r}\Big(r\frac{\partial}{\partial r}\Big) = \frac{1}{S_i^2(t)}\frac{\partial^2}{\partial \widetilde{r}^2} + \frac{1}{1-S_i(t)(1-\widetilde{r})}\,\frac{1}{S_i(t)}\frac{\partial}{\partial \widetilde{r}}.
\end{aligned}$$

Let $\widetilde{L}_i(\widetilde{r},\widetilde{t}) = \widehat{L}_i(r,t)$, $\widetilde{H}_i(\widetilde{r},\widetilde{t}) = \widehat{H}_i(r,t)$ and $\widetilde{F}_i(\widetilde{r},\widetilde{t}) = \widehat{F}_i(r,t)$, $i=1,2$. Then the system is transformed to

$$\begin{aligned}
&\frac{\partial \widetilde{L}_i}{\partial \widetilde{t}} - \frac{1}{S_i^2(t)}\frac{\partial^2 \widetilde{L}_i}{\partial \widetilde{r}^2} + \Big[-\frac{R_i'(t)}{S_i(t)}\,\frac{1-\widetilde{r}}{2\varepsilon} - \frac{1}{1-S_i(t)(1-\widetilde{r})}\,\frac{1}{S_i(t)}\Big]\frac{\partial \widetilde{L}_i}{\partial \widetilde{r}}\\
&\qquad = f_L(\widetilde{L}_i,\widetilde{H}_i,\widetilde{F}_i),\\
&\frac{\partial \widetilde{H}_i}{\partial \widetilde{t}} - \frac{1}{S_i^2(t)}\frac{\partial^2 \widetilde{H}_i}{\partial \widetilde{r}^2} + \Big[-\frac{R_i'(t)}{S_i(t)}\,\frac{1-\widetilde{r}}{2\varepsilon} - \frac{1}{1-S_i(t)(1-\widetilde{r})}\,\frac{1}{S_i(t)}\Big]\frac{\partial \widetilde{H}_i}{\partial \widetilde{r}}\\
&\qquad = f_H(\widetilde{L}_i,\widetilde{H}_i,\widetilde{F}_i),\\
&\frac{\partial \widetilde{F}_i}{\partial \widetilde{t}} - D\frac{1}{S_i^2(t)}\frac{\partial^2 \widetilde{F}_i}{\partial \widetilde{r}^2}\\
&\quad + \Big[-\frac{R_i'(t)}{S_i(t)}\,\frac{1-\widetilde{r}}{2\varepsilon} - \frac{1}{1-S_i(t)(1-\widetilde{r})}\,\frac{1}{S_i(t)}\Big(D + \frac{\widetilde{g}(\widetilde{L}_i,\widetilde{H}_i,\widetilde{F}_i)}{M_0}\Big)\Big]\frac{\partial \widetilde{F}_i}{\partial \widetilde{r}}\\
&\qquad = f_F(\widetilde{L}_i,\widetilde{H}_i,\widetilde{F}_i),
\end{aligned}$$

for $1-2\varepsilon < \widetilde{r} < 1$ and $t > 0$, where

$$\begin{aligned}
f_L(\widetilde{L}_i, \widetilde{H}_i, \widetilde{F}_i) &= -k_1 \frac{(M_0 - \widetilde{F}_i)\widetilde{L}_i}{K_1 + \widetilde{L}_i + L_0(t)} \\
&\qquad - \rho_1 \widetilde{L}_i - k_1 \frac{(M_0 - \widetilde{F}_i)L_0(t)}{K_1 + \widetilde{L}_i + L_0(t)} - \rho_1 L_0(t) - L_0'(t), \\
f_H(\widetilde{L}_i, \widetilde{H}_i, \widetilde{F}_i) &= -k_2 \frac{\widetilde{H}_i \widetilde{F}_i}{K_2 + \widetilde{F}_i} - \rho_2 \widetilde{H}_i - k_2 \frac{H_0(t)\widetilde{F}_i}{K_2 + \widetilde{F}_i} - \rho_2 H_0(t) - H_0'(t), \\
f_F(\widetilde{L}_i, \widetilde{H}_i, \widetilde{F}_i) &= k_1 \frac{(M_0 - \widetilde{F}_i)(\widetilde{L}_i + L_0(t))}{K_1 + \widetilde{L}_i + L_0(t)} - k_2 \frac{(\widetilde{H}_i + H_0(t))\widetilde{F}_i}{K_2 + \widetilde{F}_i} \\
&\qquad - \lambda \frac{\widetilde{F}_i(M_0 - \widetilde{F}_i)(\widetilde{L}_i + L_0(t))}{M_0(\gamma + \widetilde{H}_i + H_0(t))} + \frac{\rho_3 - \rho_4}{M_0}(M_0 - \widetilde{F}_i)\widetilde{F}_i \\
\widetilde{g}(\widetilde{L}_i, \widetilde{H}_i, \widetilde{F}_i) &= S_i(t) \int_{\widetilde{r}}^1 \Big[ \frac{(M_0 - \widetilde{F}_i)(\widetilde{L}_i + L_0(t))}{\gamma + \widetilde{H}_i + H_0(t)} - \rho_3 M_0 \\
&\qquad + (\rho_3 - \rho_4)\widetilde{F}_i \Big] \cdot \Big(1 - S_i(t)(1-\xi)\Big) d\xi.
\end{aligned}$$

It is also clear that, at $\widetilde{r} = 1$,

$$(\widetilde{L}_i)_{\widetilde{r}}(1,t) = (\widetilde{H}_i)_{\widetilde{r}}(1,t) = (\widetilde{F}_i)_{\widetilde{r}}(1,t) = 0,$$

and at $\widetilde{r} = 1 - 2\varepsilon$,

$$\begin{aligned}
-(\widetilde{L}_i)_{\widetilde{r}}(1-2\varepsilon, t) + \beta_1 S_i(t) \widetilde{L}_i(1-2\varepsilon, t) &= 0, \\
-(\widetilde{H}_i)_{\widetilde{r}}(1-2\varepsilon, t) + \beta_1 S_i(t) \widetilde{H}_i(1-2\varepsilon, t) &= 0, \\
-(\widetilde{F}_i)_{\widetilde{r}}(1-2\varepsilon, t) + \beta_2 S_i(t) \widetilde{F}_i(1-2\varepsilon, t) &= 0.
\end{aligned}$$

As in Step 1, define

$$\mathscr{A} = \|\widetilde{L}_1 - \widetilde{L}_2\|_{L^\infty} + \|\widetilde{H}_1 - \widetilde{H}_2\|_{L^\infty} + \|\widetilde{F}_1 - \widetilde{F}_2\|_{L^\infty},$$

where the norms on $\widetilde{L}, \widetilde{H}, \widetilde{F}$ are taken in the transformed domain. We let

$$\mathscr{D} = \frac{1}{\varepsilon}\|R_1 - R_2\|_{L^\infty[0,T]} + \|R_1' - R_2'\|_{L^\infty[0,T]}.$$

Then $\widetilde{L}_1 - \widetilde{L}_2$ satisfies $\widetilde{L}_1(\cdot,0) - \widetilde{L}_2(\cdot,0) = 0$ and

$$\begin{aligned}
&\frac{\partial(\widetilde{L}_1 - \widetilde{L}_2)}{\partial \widetilde{t}} - \frac{1}{S_1^2(t)}\frac{\partial^2(\widetilde{L}_1 - \widetilde{L}_2)}{\partial \widetilde{r}^2} \\
&\qquad + \Big[ -\frac{R_1'(t)}{S_1(t)}\frac{1-\widetilde{r}}{2\varepsilon} - \frac{1}{1 - S_1(t)(1-\widetilde{r})}\ \frac{1}{S_1(t)}\Big]\frac{\partial(\widetilde{L}_1 - \widetilde{L}_2)}{\partial \widetilde{r}} \\
&= \Big[\frac{1}{S_1^2(t)} - \frac{1}{S_2^2(t)}\Big]\frac{\partial^2 \widetilde{L}_2}{\partial \widetilde{r}^2} + \Big[\Big(\frac{R_1'(t)}{S_1(t)} - \frac{R_2'(t)}{S_2(t)}\Big)\frac{1-\widetilde{r}}{2\varepsilon} \\
&\qquad + \frac{1}{1 - S_1(t)(1-\widetilde{r})}\ \frac{1}{S_1(t)} - \frac{1}{1 - S_2(t)(1-\widetilde{r})}\ \frac{1}{S_2(t)}\Big]\frac{\partial \widetilde{L}_2}{\partial \widetilde{r}} \\
&\quad + f_L(\widetilde{L}_1, \widetilde{H}_1, \widetilde{F}_1) - f_L(\widetilde{L}_2, \widetilde{H}_2, \widetilde{F}_2) \\
&\triangleq J_L,
\end{aligned}$$

where by Step 2 and (3.10), we clearly have

$$|J_L| \le C(\mathscr{A} + \mathscr{D})$$

with $C$ independent of $\varepsilon$ and $\tau$. The equations that $\widetilde{H}_1 - \widetilde{H}_2$ and $\widetilde{F}_1 - \widetilde{F}_2$ satisfy are similar. Using maximum principle as in Step 1, we find that the function $C(\mathscr{A} + \mathscr{D})(\xi(r) + 3c(\beta_i, \varepsilon))$ is a supersolution, i.e.,

$$|\widetilde{L}_1 - \widetilde{L}_2| \le C\varepsilon\mathscr{A} + C\varepsilon\mathscr{D}, \tag{3.36}$$

$$|\widetilde{H}_1 - \widetilde{H}_2| \le C\varepsilon\mathscr{A} + C\varepsilon\mathscr{D}, \tag{3.37}$$

$$|\widetilde{F}_1 - \widetilde{F}_2| \le C\varepsilon\mathscr{A} + C\varepsilon\mathscr{D}. \tag{3.38}$$

Taking $3C\varepsilon < \frac{1}{2}$ we find

$$\mathscr{A} \le C\varepsilon\mathscr{D}. \tag{3.39}$$

Notice that in the new variables

$$\begin{aligned}
\frac{d}{dt}\Big[\frac{\widetilde{R}_i^2(t)}{2}\Big] &= \eta_i + \frac{-1}{M_0}\int_{1-2\varepsilon}^{1}\Big[\frac{(M_0 - \widetilde{F}_i)(\widetilde{L}_i + L_0(t))}{\gamma + \widetilde{H}_i + H_0(t)} - \rho_3 M_0 \\
&\qquad + (\rho_3 - \rho_4)\widetilde{F}_i\Big] S_i(t)[1 - S_i(t)(1-\widetilde{r})]d\widetilde{r},
\end{aligned}$$

$$\begin{aligned}
&\int_0^T \Big\{\eta_i + \frac{-1}{M_0}\int_{1-2\varepsilon}^{1}\Big[\frac{(M_0 - \widetilde{F}_i)(\widetilde{L}_i + L_0(t))}{\gamma + \widetilde{H}_i + H_0(t)} - \rho_3 M_0 \\
&\quad + (\rho_3 - \rho_4)\widetilde{F}_i\Big] S_i(t)[1 - S_i(t)(1-\widetilde{r})]d\widetilde{r}\Big\}dt = 0,
\end{aligned}$$

from which and (3.39) it follows that

$$|\eta_1 - \eta_2| \le C(\varepsilon^2 + \varepsilon\tau)\mathscr{D}, \tag{3.40}$$

$$\left|\frac{d[\widetilde{R}_1^2(t) - \widetilde{R}_2^2(t)]}{dt}\right| \le C(\varepsilon^2 + \varepsilon\tau)\mathscr{D}. \tag{3.41}$$

Since $\widetilde{R}_1(0) = \widetilde{R}_2(0) = 1 - 2\varepsilon$, we derive

$$\|(\widetilde{R}_1)^2 - (\widetilde{R}_2)^2\|_{C^1[0,T]} \le C(\varepsilon + \tau)\|R_1 - R_2\|_{C^1[0,T]}. \tag{3.42}$$

Combining with the fact that $1 - 3\varepsilon \le \widetilde{R}_i \le 1 - \varepsilon$, we find

$$\|\widetilde{R}_1 - \widetilde{R}_2\|_{C^1[0,T]} \le C(\varepsilon + \tau)\|R_1 - R_2\|_{C^1[0,T]}, \tag{3.43}$$

and hence we have a contraction if $\varepsilon$ and $\tau$ are small. Thus we have a unique fixed point. □

Notice that with the introduction of $\eta$, the free boundary $r = R(t)$ is already periodic with period $T$, namely, $R(T) = R(0) = 1-2\varepsilon$. To produce a periodic solution, we use another contraction mapping principle. We define a map that will map the initial data at time $t = 0$ to the data after one period $t = T$. Then a fixed point of this map will correspond to a periodic solution. But first we need to show that this map will map an appropriate set of initial data satisfying (3.6), (3.7) and (3.8) into itself. The estimate for (3.8) at $t = T$ was already established in Lemma 3.1. We shall establish (3.6) and (3.7) for $t = T$ in the next lemma, which will serve this purpose. This lemma can be established in our case since *the energy is released* at the boundary at $r = R(t)$ while the domain is small.

**Lemma 3.2.** *The constants $C_0^*$ and $C_1^*$ in (3.6) and (3.7) can be selected such that, at $t = T$,*

$$|\widehat{L}(r,T)| \le C_0^*\varepsilon, \quad |\widehat{H}(r,T)| \le C_0^*\varepsilon, \quad |\widehat{F}(r,T)| \le C_0^*\varepsilon, \tag{3.44}$$

$$|\widehat{L}_r(r,T)| \le C_1^*\varepsilon, \quad |\widehat{H}_r(r,T)| \le C_1^*\varepsilon, \quad |\widehat{F}_r(r,T)| \le C_1^*\varepsilon, \tag{3.45}$$

*and*

$$|R'(t)| \le \frac{\varepsilon}{T} \quad \text{for } 0 \le t \le T. \tag{3.46}$$

*Proof.* We have already established (3.46) and the following estimates:

$$|\widehat{L}(r,t)| \le C_0^{**}\varepsilon, \quad |\widehat{H}(r,t)| \le C_0^{**}\varepsilon, \quad |\widehat{F}(r,t)| \le C_0^{**}\varepsilon, \tag{3.47}$$

$$|\widehat{L}_r(r,t)| \le C_1^{**}\varepsilon, \quad |\widehat{H}_r(r,t)| \le C_1^{**}\varepsilon, \quad |\widehat{F}_r(r,t)| \le C_1^{**}\varepsilon, \tag{3.48}$$

where, by (3.22) and (3.23),

$$C_0^{**} = C_0^* + 2\overline{C}\max\Big(\frac{1}{\beta_1},\frac{1}{\beta_2}\Big),$$
$$C_1^{**} = C_1^* + \max\Big(\frac{2\overline{C}_1}{\beta_1},\frac{2\overline{C}_1}{\beta_2},\beta_1 C_0^{**},\beta_2 C_0^{**}\Big),$$

with the constants $\overline{C}$ and $\overline{C}_1$ independent of $C_0^*$ and $C_1^*$, as long as $\varepsilon$ is small so that $C_0^{**}\varepsilon \le 1, C_1^{**}\varepsilon \le 1$. Thus $\overline{C}(\xi(r)+c(\beta_1,\varepsilon)) + C_0^*\varepsilon e^{-t}$ is a supersolution for $\pm\widehat{L}$ for small $\varepsilon$. Taking $C_0^*$ such that

$$C_0^*(1-e^{-T}) = 2\overline{C}\max\Big(\frac{1}{\beta_1},\frac{1}{\beta_2}\Big), \tag{3.49}$$

then, for small $\varepsilon$,

$$|\widehat{L}(r,T)| \le \overline{C}(\xi(r)+c(\beta_1,\varepsilon)) + C_0^*\varepsilon e^{-T} = \frac{\overline{C}}{\beta_1}\varepsilon + O(\varepsilon^2) + C_0^*\varepsilon e^{-T} \le C_0^*\varepsilon.$$

Then, as in the proof of Lemma 3.1, we also conclude the estimate for $|\widehat{L}_r(r,T)|$. The rest of the proof is similar. □

**Lemma 3.3.** *Assume that $R(0) = 1-2\varepsilon$ and $(\widehat{L}(\cdot,0),\widehat{H}(\cdot,0),\widehat{F}(\cdot,0)) \in \mathscr{I}$. We define the solution $(\widehat{L},\widehat{H},\widehat{F},R,\eta)$ by Lemma 3.1. Then the mapping $\mathscr{N} : (\widehat{L}(\cdot,0),\widehat{H}(\cdot,0),\widehat{F}(\cdot,0)) \to (\widehat{L}(\cdot,T),\widehat{H}(\cdot,T),\widehat{F}(\cdot,T))$ maps $\mathscr{I}$ into itself and is a contraction and therefore admits a unique solution in $\mathscr{I}$. It is clear that this unique solution corresponds to a periodic solution of (P*).*

*Proof.* Lemma 3.2 and (3.24) ensure that $\mathscr{N}$ maps the set $\mathscr{I}$ into itself. Given two set of initial data $(\widehat{L}_i(\cdot,0),\widehat{H}_i(\cdot,0),\widehat{F}_i(\cdot,0))$ $(i=1,2)$, by Lemma 3.1, there exist corresponding unique solutions $(\widehat{L}_i,\widehat{H}_i,\widehat{F}_i,R_i)$ for (P*). We now proceed with the transform (3.35) to map into the same domain. Let $\widetilde{L}_i(\widetilde{r},\widetilde{t}) = \widehat{L}_i(r,t)$, $\widetilde{H}_i(\widetilde{r},\widetilde{t}) = \widehat{H}_i(r,t)$ and $\widetilde{F}_i(\widetilde{r},\widetilde{t}) = \widehat{F}_i(r,t)$. Then, for $1-2\varepsilon < \widetilde{r} < 1$ and $\widetilde{t} > 0$,

$$\frac{\partial \widetilde{L}_i}{\partial \widetilde{t}} - \frac{1}{S_i^2(t)}\frac{\partial^2 \widetilde{L}_i}{\partial \widetilde{r}^2} + \Big[-\frac{R_i'(t)}{S_i(t)}\frac{1-\widetilde{r}}{2\varepsilon} - \frac{1}{1-S_i(t)(1-\widetilde{r})}\frac{1}{S_i(t)}\Big]\frac{\partial \widetilde{L}_i}{\partial \widetilde{r}}$$
$$= f_L(\widetilde{L}_i,\widetilde{H}_i,\widetilde{F}_i),$$
$$\frac{\partial \widetilde{H}_i}{\partial \widetilde{t}} - \frac{1}{S_i^2(t)}\frac{\partial^2 \widetilde{H}_i}{\partial \widetilde{r}^2} + \Big[-\frac{R_i'(t)}{S_i(t)}\frac{1-\widetilde{r}}{2\varepsilon} - \frac{1}{1-S_i(t)(1-\widetilde{r})}\frac{1}{S_i(t)}\Big]\frac{\partial \widetilde{H}_i}{\partial \widetilde{r}}$$
$$= f_H(\widetilde{L}_i,\widetilde{H}_i,\widetilde{F}_i),$$

$$\begin{aligned}&\frac{\partial \widetilde{F}_i}{\partial \widetilde{t}} - D\frac{1}{S_i^2(t)}\frac{\partial^2 \widetilde{F}_i}{\partial \widetilde{r}^2}\\ &\quad+\Big[-\frac{R_i'(t)}{S_i(t)}\ \frac{1-\widetilde{r}}{2\varepsilon} - \frac{1}{1-S_i(t)(1-\widetilde{r})}\ \frac{1}{S_i(t)}\Big(D+\frac{\widetilde{g}(\widetilde{L}_i,\widetilde{H}_i,\widetilde{F}_i)}{M_0}\Big)\Big]\frac{\partial \widetilde{F}_i}{\partial \widetilde{r}}\\ &\qquad\qquad\qquad\qquad = f_F(\widetilde{L}_i,\widetilde{H}_i,\widetilde{F}_i),\end{aligned}$$

where $f_L$, $f_H$, $f_F$ are defined in Step 3 of Lemma 3.1, and

$$S_i(t) = \frac{1-R_i(t)}{2\varepsilon}.$$

Furthermore, $\widetilde{L}_1 - \widetilde{L}_2$ satisfies

$$\begin{aligned}&\frac{\partial(\widetilde{L}_1-\widetilde{L}_2)}{\partial \widetilde{t}} - \frac{1}{S_1^2(t)}\frac{\partial^2(\widetilde{L}_1-\widetilde{L}_2)}{\partial \widetilde{r}^2}\\ &\qquad+\Big[-\frac{R_1'(t)}{S_1(t)}\frac{1-\widetilde{r}}{2\varepsilon} - \frac{1}{1-S_1(t)(1-\widetilde{r})}\ \frac{1}{S_1(t)}\Big]\frac{\partial(\widetilde{L}_1-\widetilde{L}_2)}{\partial \widetilde{r}}\\ &= \Big[\frac{1}{S_1^2(t)} - \frac{1}{S_2^2(t)}\Big]\frac{\partial^2 \widetilde{L}_2}{\partial \widetilde{r}^2} + \Big[\Big(\frac{R_1'(t)}{S_1(t)} - \frac{R_2'(t)}{S_2(t)}\Big)\frac{1-\widetilde{r}}{2\varepsilon}\\ &\qquad+\frac{1}{1-S_1(t)(1-\widetilde{r})}\ \frac{1}{S_1(t)} - \frac{1}{1-S_2(t)(1-\widetilde{r})}\ \frac{1}{S_2(t)}\Big]\frac{\partial \widetilde{L}_2}{\partial \widetilde{r}}\\ &\quad+f_L(\widetilde{L}_1,\widetilde{H}_1,\widetilde{F}_1) - f_L(\widetilde{L}_2,\widetilde{H}_2,\widetilde{F}_2)\\ &\triangleq J_L,\end{aligned}$$

where $|J_L| \le \overline{C}(\mathscr{A}+\mathscr{D})$ with $\overline{C}$ independent of $\varepsilon$ and $\tau$. The equations that $\widetilde{H}_1 - \widetilde{H}_2$ and $\widetilde{F}_1 - \widetilde{F}_2$ satisfy are similar. And as in the proof of Lemma 3.1,

$$|\eta_1 - \eta_2| \le C\varepsilon\tau\mathscr{D} + C\varepsilon\mathscr{A}\,, \tag{3.50}$$

$$\Big|\frac{d[R_1^2(t) - R_2^2(t)]}{dt}\Big| \le C\varepsilon\tau\mathscr{D} + C\varepsilon\mathscr{A}\,, \tag{3.51}$$

where

$$\begin{aligned}\mathscr{A} &\triangleq \|\widetilde{L}_1-\widetilde{L}_2\|_{L^\infty([1-2\varepsilon,1]\times[0,T])} + \|\widetilde{H}_1-\widetilde{H}_2\|_{L^\infty([1-2\varepsilon,1]\times[0,T])}\\ &\quad+\|\widetilde{F}_1-\widetilde{F}_2\|_{L^\infty([1-2\varepsilon,1]\times[0,T])},\\ \mathscr{D} &= \frac{1}{\varepsilon}\|R_1-R_2\|_{L^\infty[0,T]} + \|R_1'-R_2'\|_{L^\infty[0,T]}.\end{aligned}$$

It follows from (3.51) that

$$\|R_1 - R_2\|_{L^\infty[0,T]} \le C\varepsilon\tau\mathscr{D} + C\varepsilon\mathscr{A} + C\varepsilon^2\mathscr{D},$$
$$\|R_1' - R_2'\|_{L^\infty[0,T]} \le C\varepsilon\tau\mathscr{D} + C\varepsilon\mathscr{A} + C\varepsilon^2\mathscr{D}.$$

Choosing $\varepsilon$ and $\tau$ to be small enough, we find

$$\|R_1 - R_2\|_{C^1[0,T]} \le C\varepsilon\mathscr{A}. \tag{3.52}$$

Then we follow the proof of Lemma 3.2, say, to construct supersolutions $\overline{\overline{C}}\mathscr{A}[\xi(r) + 3c(\beta_1,\varepsilon)] + e^{-t}\|\widetilde{L}_1(\cdot,0) - \widetilde{L}_2(\cdot,0)\|_{L^\infty}$ for $\widetilde{L}_1 - \widetilde{L}_2$. After working through all equations, we find

$$\begin{aligned}\|\widetilde{L}_1(\cdot,t) - \widetilde{L}_2(\cdot,t)\|_{L^\infty} + \|\widetilde{H}_1(\cdot,t) - \widetilde{H}_2(\cdot,t)\|_{L^\infty} + \|\widetilde{F}_1(\cdot,t) - \widetilde{F}_2(\cdot,t)\|_{L^\infty}\\ \le \widetilde{C}\varepsilon\mathscr{A} + e^{-t}[\|\widetilde{L}_1(\cdot,0) - \widetilde{L}_2(\cdot,0)\|_{L^\infty} + \|\widetilde{H}_1(\cdot,0) - \widetilde{H}_2(\cdot,0)\|_{L^\infty}\\ + \|\widetilde{F}_1(\cdot,0) - \widetilde{F}_2(\cdot,0)\|_{L^\infty}],\end{aligned}$$

which implies, if $\widetilde{C}\varepsilon \le \frac{1}{2}$,

$$\begin{aligned}\frac{1}{2}\mathscr{A} \le \|\widetilde{L}_1(\cdot,0) - \widetilde{L}_2(\cdot,0)\|_{L^\infty} + \|\widetilde{H}_1(\cdot,0) - \widetilde{H}_2(\cdot,0)\|_{L^\infty}\\ + \|\widetilde{F}_1(\cdot,0) - \widetilde{F}_2(\cdot,0)\|_{L^\infty}.\end{aligned}$$

Taking $\varepsilon$ small so that $2\widetilde{C}\varepsilon + e^{-T} < 1$, we then conclude that the mapping $\mathscr{N}$ is a contraction. □

## 4. Completing the proof

We now proceed to show the existence of a periodic solution of the original problem. All we have to show is that $\eta = 0$ for appropriate data.

**Lemma 4.1.** *For every small $\varepsilon,\tau$ and fixed $H_* > 0$, there exists a $L_* = L_*(\varepsilon, H_*)$ such that the problem $(P^*)$ admits a periodic solution with period $T$, $R(0) = 1 - 2\varepsilon$, and with $\eta = 0$.*

*Proof.* From (3.2), we have

$$\eta = \frac{1}{M_0 T}\int_0^T \int_{R(t)}^1 \Big[\frac{M_0 L_0(t)}{\gamma + H_0(t)} - \rho_3 M_0 + O(\varepsilon)\Big] r dr dt \tag{4.1}$$

$$= \frac{1}{T}\int_0^T \int_{R(t)}^1 \Big[\frac{L_*}{\gamma + H_*} - \rho_3 + O(\varepsilon) + O(\tau)\Big] r dr dt.$$

The integrand in the above expression is of order

$$\Big[m\varepsilon + O(\varepsilon)\Big] + \Big[m\tau + O(\tau)\Big], \quad \varepsilon > 0,\ \tau > 0.$$

and the estimates for all previous lemmas are independent of $m$. It follows that if we choose $m \gg 1$ in (3.3), then $\eta > 0$, and likewise, it is clear that $\eta < 0$ when $m \ll 1$. Notice that the solution is unique within $\mathscr{I}$ and therefore the values $\eta$ various continuously with the changing $m$ value. Thus there must a value $m$ for which $\eta = 0$. This completes the proof. □

**Remark 4.1.** *It is also clear that*

$$L_* = \rho_3(\gamma + H_*) + O(\varepsilon) + O(\tau).$$

## 5. Conclusion

In reality, nutrient concentration changes with the intake of food, which happens very often in a periodic manner. It is therefore biologically reasonable to seek a periodic solution. Indeed, we have rigorously established a periodic small-plaque solution in this paper, once again confirming the strength of the model, established by Friedman et al. [1, 3].

Establishing a small radially symmetric periodic plaque is only the first step. Questions such as stability, and potential bifurcation into non-radially symmetric periodic solutions, are the subject matters for future studies.

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