When plaques block the arteries, atherosclerosis occurs. Severe atherosclerosis would result in fatal cardiovascular diseases such as stroke, heart attack, coronary artery disease, or peripheral artery disease; these are leading causes of death in the world. In the paper, we investigate a free boundary PDE model to describe the formation of an arterial plaque in the early stage of atherosclerosis. The bifurcation analysis is carried out for the model. In particular, we establish the first bifurcation point for the system corresponding to the $n = 1$ mode. The symmetry-breaking stationary solution studied in this paper can be helpful in understanding why there exists arterial plaque that is often accumulated more on one side of the artery than the other.

**KEYWORDS**
atherosclerosis, bifurcations in context of PDEs, free boundary problems for PDEs

**MSC CLASSIFICATION**
35R35; 35B32

1 | INTRODUCTION

Atherosclerosis is the clogging of artery due to the build-up of plaques that are made of cholesterols, fat, and other substances. It may trigger heart diseases, which are the leading causes of death in the United States (cf. previous studies). Recently, several mathematical models have been developed to investigate the formation of plaques. In most models, the growth of a plaque is determined by some critical components including low density lipoprotein (LDL) and high density lipoprotein (HDL). Some of these models are sophisticated, which include a lot of variables. However, they are not feasible to be analyzed theoretically. Friedman et al. proposed a simplified model that combines some of those variables. In order to carry out a bifurcation analysis and reveal the reason why plaques are of asymmetric shapes, we will use the simplified model in this paper. Specifically, we only consider the plaque formation in the early stage of atherosclerosis.

The formation of a plaque originates from the development of a lesion in the inner wall of an artery. Due to the appearance of the lesion, HDL and LDL can move into the tunica intima and become oxidized by free radicals in the intima. After LDL becomes oxidized, oxidized LDL can stimulate the secretion of chemoattractant proteins, which attract macrophage cells (M). Some of these macrophage cells would engulf oxidized LDL and change into foam cells (F), whose accumulation is responsible for the buildup of plaques in the artery. LDL promotes the formation of plaque while simultaneously HDL prevents the process. On the one hand, HDL can revert foam cells back into macrophage cells, which is the so-called reverse cholesterol transport (RCT) effect; on the other hand, HDL can consume free radicals and reduce the oxidation of LDL in the intima. Due to the different effects of LDL and HDL on plaque formation, we always call LDL “bad” cholesterol and HDL “good” cholesterol.
Based on the model in Friedman\textsuperscript{15} Chapters 7 and 8 and Friedman et al\textsuperscript{6}, we assume that an artery is a very long circular cylinder with normalized radius being 1; thus, we only need to consider a cross section of the artery, as shown in Figure 1, which is a 2D problem. The cross section consists of a blood flow region $\Sigma(t)$ and a plaque region $\Omega(t)$, and the moving boundary $\Gamma(t)$ is the interface between these two regions. We denote

$$ L = \text{concentration of LDL}, \quad H = \text{concentration of HDL}, $$

$$ M = \text{density of macrophage cells}, \quad F = \text{density of foam cells}, $$

and the equations for these variables are

$$ \frac{\partial L}{\partial t} - \Delta L = -k_1 \frac{ML}{K_1 + L} - \rho_1 L \quad \text{in } \Omega(t), $$

$$ \frac{\partial H}{\partial t} - \Delta H = -k_2 \frac{HF}{K_2 + F} - \rho_2 H \quad \text{in } \Omega(t), $$

$$ \frac{\partial M}{\partial t} - \Delta M + \nabla \cdot (M\vec{v}) = -k_1 \frac{ML}{K_1 + L} + k_2 \frac{HF}{K_2 + F} + \lambda \frac{ML}{\gamma + H} - \rho_3 M \quad \text{in } \Omega(t), $$

$$ \frac{\partial F}{\partial t} - \Delta F + \nabla \cdot (F\vec{v}) = k_1 \frac{ML}{K_1 + L} - k_2 \frac{HF}{K_2 + F} - \rho_4 F \quad \text{in } \Omega(t), $$

where $\rho_1$, $\rho_2$, $\rho_3$, and $\rho_4$ denote the natural death rate of $L$, $H$, $M$, and $F$, respectively. Equations (1.1)–(1.4) include the aforementioned transitions between macrophages ($M$) and foam cells ($F$): $k_1 \frac{ML}{K_1 + L}$ accounts for the fact that $M$ becomes foam cell by combining with $L$, $k_2 \frac{HF}{K_2 + F}$ describes the removal of foam cell by $H$. For the extra term $\lambda \frac{ML}{\gamma + H}$ in the equation (1.3), we explain it in two parts: The numerator accounts for the fact that oxidized LDL attracts macrophages, and we model the growth of macrophages by $\lambda ML$; on the other hand, since HDL is antagonistic to LDL, this rate is then reduced by $H$.

For simplicity, the combined density of $M$ and $F$ is assumed to be a constant $M_0$ within the plaque; hence,

$$ M + F \equiv M_0 \quad \text{in } \Omega(t). $$

Based on this assumption, $M$ can be replaced by $M_0 - F$; thus, the number of variables is reduced by 1. Moreover, the total mass of $M$ and $F$ in the plaque is varying because of the extra term $\lambda \frac{ML}{\gamma + H}$ and the death terms $\rho_3 M$ and $\rho_4 F$. Together with (1.5), there will be an internal pressure $p$ among the cells (notice that the pressure is relative to the outside pressure, hence its value can be either positive or negative), and the internal pressure would induce a velocity field $\vec{v}$ which is incorporated into Equations (1.3) and (1.4). Since we treat the plaque as porous medium (see justifications in Friedman\textsuperscript{15} Chapters 7 and 8), the relationship between the internal pressure $p$ and the velocity $\vec{v}$ is given by Darcy’s law:

$$ \vec{v} = -\nabla p \quad \text{(the proportional constant is normalized to 1)}. $$

Based on the model in Friedman\textsuperscript{15} Chapters 7 and 8 and Friedman et al\textsuperscript{6}, we assume that an artery is a very long circular cylinder with normalized radius being 1; thus, we only need to consider a cross section of the artery, as shown in Figure 1, which is a 2D problem. The cross section consists of a blood flow region $\Sigma(t)$ and a plaque region $\Omega(t)$, and the moving boundary $\Gamma(t)$ is the interface between these two regions. We denote

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and the equations for these variables are

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$$ \frac{\partial H}{\partial t} - \Delta H = -k_2 \frac{HF}{K_2 + F} - \rho_2 H \quad \text{in } \Omega(t), $$

$$ \frac{\partial M}{\partial t} - \Delta M + \nabla \cdot (M\vec{v}) = -k_1 \frac{ML}{K_1 + L} + k_2 \frac{HF}{K_2 + F} + \lambda \frac{ML}{\gamma + H} - \rho_3 M \quad \text{in } \Omega(t), $$

$$ \frac{\partial F}{\partial t} - \Delta F + \nabla \cdot (F\vec{v}) = k_1 \frac{ML}{K_1 + L} - k_2 \frac{HF}{K_2 + F} - \rho_4 F \quad \text{in } \Omega(t), $$

where $\rho_1$, $\rho_2$, $\rho_3$, and $\rho_4$ denote the natural death rate of $L$, $H$, $M$, and $F$, respectively. Equations (1.1)–(1.4) include the aforementioned transitions between macrophages ($M$) and foam cells ($F$): $k_1 \frac{ML}{K_1 + L}$ accounts for the fact that $M$ becomes foam cell by combining with $L$, $k_2 \frac{HF}{K_2 + F}$ describes the removal of foam cell by $H$. For the extra term $\lambda \frac{ML}{\gamma + H}$ in the equation (1.3), we explain it in two parts: The numerator accounts for the fact that oxidized LDL attracts macrophages, and we model the growth of macrophages by $\lambda ML$; on the other hand, since HDL is antagonistic to LDL, this rate is then reduced by $H$.

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$$ \vec{v} = -\nabla p \quad \text{(the proportional constant is normalized to 1)}. $$
Combining (1.3)–(1.6), we have

\[-\Delta p = \frac{1}{M_0} \left[ \lambda \frac{(M_0 - F)L}{\gamma + H} - \rho_3(M_0 - F) - \rho_4F \right].\tag{1.7}\]

As previously mentioned, \(M\) is replaced by \(M_0 - F\); by (1.4) and (1.7), the equation for \(F\) is

\[\frac{\partial F}{\partial t} - D\Delta F - \nabla F \cdot \nabla p = k_1 \frac{(M_0 - F)L}{K_1 + L} - k_2 \frac{HF}{K_2 + F} - \lambda \frac{F(M_0 - F)L}{M_0(\gamma + H)} + (\rho_2 - \rho_3) \frac{(M_0 - F)F}{M_0}.\tag{1.8}\]

In terms of boundary conditions, no-flux conditions are employed on the blood vessel wall (\(r = 1\)) for all variables (i.e., no exchange through the blood vessel):

\[\frac{\partial L}{\partial r} = \frac{\partial H}{\partial r} = \frac{\partial F}{\partial r} = \frac{\partial p}{\partial r} = 0 \text{ at } r = 1;\tag{1.9}\]

while on the free boundary \(\Gamma(t)\), the following boundary conditions are used:

\[\frac{\partial L}{\partial n} + \beta_1(L - L_0) = 0 \text{ on } \Gamma(t),\tag{1.10}\]

\[\frac{\partial H}{\partial n} + \beta_1(H - H_0) = 0 \text{ on } \Gamma(t),\tag{1.11}\]

\[\frac{\partial F}{\partial n} + \beta_2 F = 0 \text{ on } \Gamma(t),\tag{1.12}\]

\[p = \kappa \text{ on } \Gamma(t),\tag{1.13}\]

where \(L_0\) and \(H_0\) represents the concentration of \(L\) and \(H\) in the blood, respectively. The vector \(n\) denotes the outward unit normal vector on \(\Gamma(t)\), and it points inward to the blood region (as shown in Figure 1). \(\kappa\) is the mean curvature of \(\Gamma(t)\) in the direction of \(n\) (i.e., \(\kappa = -\frac{1}{\kappa(\Gamma(t))}\) if \(\Gamma(t) = \{ r = R(t) \}\)). The explanation of (1.13) can be found in Friedman\textsuperscript{15}Chapters 7 and 8; for simplicity, we normalize the cell-to-cell adhesiveness constant in front of \(\kappa\) to 1.

Finally, the velocity field is assumed to be continuous up to the boundaries; thus, the velocity of the cells on the moving boundary is \(\tilde{v}\). The most convenient way to describe the moving boundary \(\Gamma(t)\) is though its velocity in the normal direction, which is

\[V_n = \tilde{v} \cdot n = -\frac{\partial p}{\partial n} \text{ on } \Gamma(t).\tag{1.14}\]

For Equations (1.1)–(1.14), Friedman et al\textsuperscript{6} studied the radially symmetric case, and a small ringlike plaque was theoretically established. Later on Zhao and Hu\textsuperscript{10} carried out a bifurcation analysis for the system and found a series of bifurcation points for \(n \geq 2\). More specifically, they used \(\mu = \frac{1}{\epsilon} [\lambda L_0 - \rho_3(\gamma + H_0)]\) as the bifurcation parameter and showed that for each \(n \geq 2\), there exists a unique

\[\mu_n = (\gamma + H_0)n^2(1 - n^2) + O(n^5\epsilon),\tag{1.15}\]

such that if \(\mu_n > \mu_c\) (see the definition of \(\mu_c\) in (2.9)), then \(\mu = \mu_n\) is a bifurcation point of the symmetry-breaking stationary solution when \(\epsilon\) is small enough.

Based on further exploration and refinements of the estimates in Zhao and Hu\textsuperscript{10} we shall prove in this paper that \(\mu_1 = O(\epsilon)\) is also a bifurcation point for the system (1.1)–(1.14) by verifying the Crandall-Rabinowitz theorem (Theorem 2.2). Our main result is stated in the following theorem.

**Theorem 1.1.** Assume that \(\mu_c < 0\) and \(\beta_1 \neq \beta_2\). For \(\mu = O(\epsilon)\) defined as the solution to the equation (2.36) with \(n = 1\), we can find a small \(E > 0\), such that for \(0 < \epsilon < E\), then \(\mu = \mu_1\) is a bifurcation point of the symmetry-breaking stationary solution for the system (1.1)–(1.14). Moreover, the free boundary of this bifurcation solution is of the form

\[r = 1 - \epsilon + \tau \cos(\theta) + o(\tau), \text{ where } |\tau| \ll \epsilon.\tag{1.16}\]
In recent years, there are considerable research projects on the bifurcation analysis which are based upon the Crandall-Rabinowitz theorem (see literature\textsuperscript{17–30}). In these papers, the solutions on the \( n = 1 \) bifurcation branch are just \( \epsilon \)-translations of the origin of the radially symmetric solution; after transformation of coordinates, this kind of solutions are still radially symmetric. Therefore, the \( n = 1 \) case is always ignored in previous research on the bifurcation analysis. For our problem, however, the circumstances are very different. There are two boundaries for the system (1.1)–(1.14), with the outer boundary \( r = 1 \) always being fixed. Since the outer boundary is fixed, all the perturbations make changes only on the inner free boundary. Due to this special geometry, the solutions on the \( n = 1 \) bifurcation branch are non-radially symmetric, as shown in the Figure 2.

We want to emphasize that, for technical reasons, Theorem 1.1 was not established in Zhao and Hu.\textsuperscript{10} The primary reason is that, by (1.15), both \( \mu_0 \) and \( \mu_1 \) are of order \( O(\epsilon) \); thus, (1.15) is not enough to guarantee \( \mu_0 \neq \mu_1 \), and hence, the assumption (2) of the Crandall-Rabinowitz theorem cannot be verified. The main goal of this paper is to derive more sophisticated estimates for \( \mu_0 \) and \( \mu_1 \), with which we can then verify the Crandall-Rabinowitz theorem. The \( O(\epsilon) \) expansion given in (1.15) is not enough to be utilized for \( \mu_0 \) and \( \mu_1 \), and we will go to order \( O(\epsilon^2) \) to obtain the necessary estimates.

The structure of this paper is as follows. We collect some preliminaries in Section 2 and give some useful estimates in Section 3. The proof to the main result, Theorem 1.1, is presented in Section 4. We conclude, in Section 5, by discussing the biological implications of the result of this paper.

2 | PRELIMINARIES

2.1 | A small radially symmetric stationary solution

We denote the radially symmetric stationary solution of the system (1.1)–(1.14) by \((L_*, H_*, F_*, p_*)\). Dropping all the time derivatives, and writing the system in polar coordinates in the domain \( \Omega_* = \{1 - \epsilon < r < 1\} \), we obtain the equation for \((L_*, H_*, F_*, p_*)\):

\[
\begin{align*}
-\Delta L_* &= -k_1 \frac{(M_0 - F_*)L_*}{K_1 + L_*} - \rho_1 L_* \quad \text{in} \quad \Omega_*, \\
-\Delta H_* &= -k_2 \frac{H_*F_*}{K_2 + F_*} - \rho_2 H_* \quad \text{in} \quad \Omega_*, \\
-\Delta F_* &= \frac{1}{M_0} \left[ \frac{\lambda (M_0 - F_*)L_*}{\gamma + H_*} - \rho_3 (M_0 - F_*) - \rho_4 F_* \right] \quad \text{in} \quad \Omega_*, \\
\frac{\partial L_*}{\partial r} &= \frac{\partial H_*}{\partial r} = \frac{\partial F_*}{\partial r} = \frac{\partial p_*}{\partial r} = 0, \quad r = 1, \\
-\frac{\partial L_*}{\partial r} + \beta_1 (L_* - L_0) &= 0, \quad -\frac{\partial H_*}{\partial r} + \beta_1 (H_* - H_0) = 0, \quad -\frac{\partial F_*}{\partial r} + \beta_2 F_* = 0, \quad r = 1 - \epsilon, \\
p_* &= -\frac{1}{1 - \epsilon}, \quad r = 1 - \epsilon, \\
\frac{\partial p_*}{\partial r} &= 0, \quad r = 1 - \epsilon.
\end{align*}
\]
There are many parameters in the system. As in Zhao and Hu, \(^{10}\) we keep all parameters fixed except \(L_0\) and \(\rho_4\). For convenience, rather than using \(L_0\), we use \(\mu = \frac{1}{\varepsilon} [\lambda L_0 - \rho_3 (\gamma + H_0)]\) as our bifurcation parameter and let \(\rho_4 = \rho_4(\mu)\). The existence theorem for the radially symmetric solution has been established in Zhao and Hu\(^ {10}\) and is stated as follows:

**Theorem 1.2.** Define

\[
\mu_c = \frac{\rho_3}{\rho_1} \left( \frac{\gamma + H_0}{2} \left( \frac{\lambda k_1 M_0}{\lambda K_1 + \rho_3 (\gamma + H_0)} + \rho_1 \right) - \rho_2 H_0 \right). \tag{2.9}
\]

For every \(\mu > \mu_c\) and \(\mu_c < \mu < \mu^*\), we can find a small \(\varepsilon^* > 0\), and for each \(0 < \varepsilon < \varepsilon^*\), there exists a unique \(\rho_4\) such that the system (2.1)–(2.8) admits a unique solution \((L^*, H^*, F^*, p^*)\).

**Remark** 2.1. By ODE theories, the solution \((L^*, H^*, F^*, p^*)\) can be extended to the bigger region \(\Omega_{3\varepsilon} = \{1 - 2\varepsilon < r < 1\}\) while maintaining \(C^\infty\) regularity. For notational convenience, we still use \((L^*, H^*, F^*, p^*)\) to denote the extended solution.

## 2.2 Bifurcation theorem

Next we state a simple version of the Crandall-Rabinowitz theorem, which is critical in the bifurcation analysis.

**Theorem 2.2.** (Crandall-Rabinowitz theorem\(^ {31}\)) Let \(X, Y\) be real Banach spaces and \(F(x, \cdot)\) a \(C^p\) map, \(p \geq 3\), of a neighborhood \((0, \mu_0)\) in \(X \times \mathbb{R}\) into \(Y\). Suppose

1. \(F(0, \mu) = 0\) for all \(\mu\) in a neighborhood of \(\mu_0\).
2. \(\ker F_x(0, \mu_0)\) is one dimensional space, spanned by \(x_0\).
3. \(\text{Im } F_x(0, \mu_0) = Y_1\) has codimension 1.
4. \(F_{\mu x}(0, \mu_0) x_0 \notin Y_1\).

Then \((0, \mu_0)\) is a bifurcation point of the equation \(F(x, \mu) = 0\) in the following sense: In a neighborhood of \((0, \mu_0)\), the set of solutions \(F(x, \mu) = 0\) consists of two \(C^{p-2}\) smooth curves \(\Gamma_1\) and \(\Gamma_2\) which intersect only at the point \((0, \mu_0)\); \(\Gamma_1\) is the curve \((0, \mu)\) and \(\Gamma_2\) can be parameterized as follows:

\[
\Gamma_2 : (x(\varepsilon), \mu(\varepsilon)), |\varepsilon| \text{ small, } (x(0), \mu(0)) = (0, \mu_0), \ x'(0) = x_0.
\]

## 2.3 Preparations for the bifurcation theorem

In order to tackle the existence of symmetry-breaking stationary solutions to system (1.1)–(1.14), we would like to apply the Crandall-Rabinowitz theorem. The preparations are the same as in Zhao and Hu\(^ {10}\) and are similar as those in previous works.\(^ {17-30}\)

We consider a family of perturbed domains \(\Omega_r = \{1 - \varepsilon + \bar{R} < r < 1\}\) and denote the corresponding inner boundary by \(\Gamma_r : r = 1 - \varepsilon + \bar{R}, \bar{R} = \varepsilon S(\theta), |\theta| \ll \varepsilon\) and \(|S| \leq 1\). Let \((L, H, F, p)\) be the solution of the system:

\[
\begin{align*}
-\Delta L &= -k_1 \frac{(M_0 - F)L}{K_1 + L} - \rho_1 L \quad \text{in } \Omega_r, \\
-\Delta H &= -k_2 \frac{HF}{K_2 + F} - \rho_2 H \quad \text{in } \Omega_r, \\
-D\Delta F - \nabla F \cdot \nabla p &= k_1 \frac{(M_0 - F)L}{K_1 + L} - k_2 \frac{HF}{K_2 + F} - \lambda \frac{F(M_0 - F)L}{M_0 (\gamma + H)} + (\rho_3 - \rho_4) \frac{(M_0 - F)F}{M_0} \quad \text{in } \Omega_r, \\
-\Delta p &= \frac{1}{M_0} \left[ \lambda \frac{(M_0 - F)L}{\gamma + H} - \rho_3 (M_0 - F) - \rho_4 \right] \quad \text{in } \Omega_r, \\
\frac{\partial L}{\partial r} &= \frac{\partial H}{\partial r} = \frac{\partial F}{\partial r} = \frac{\partial p}{\partial r} = 0, \quad r = 1, \\
\frac{\partial L}{\partial n} + \beta_1 (L - L_0) &= 0, \quad \frac{\partial H}{\partial n} + \beta_1 (H - H_0) = 0, \quad \frac{\partial F}{\partial n} + \beta_2 F = 0 \quad \text{on } \Gamma_r, \\
p &= \kappa \quad \text{on } \Gamma_r.
\end{align*}
\]
The existence and uniqueness of such a solution is guaranteed in Zhao and Hu\textsuperscript{10}. We then define a function $\mathcal{F}$ as

$$
\mathcal{F}(\tau S, \mu) = -\frac{\partial p}{\partial n}|_{r_\tau}.
$$

(2.17)

It is clear that $(L, H, F, p)$ is a symmetry-breaking stationary solution if and only if $\mathcal{F}(\tau S, \mu) = 0$. Next we introduce the Banach spaces:

$$
X^{l+a} = \{ S \in C^{l+a}(\Sigma), S \text{ is } 2\pi - \text{periodic in } \theta \},
$$

(2.18)

$$
X_1^{l+a} = \text{closure of the linear space spanned by } \{ \cos(n\theta), n = 0, 1, 2, \ldots \} \text{ in } X^{l+a}.
$$

It has been shown in Zhao and Hu\textsuperscript{10} that the mapping $\mathcal{F}(., \mu) : X_1^{l+a} \to X_1^{l+a}$ is continuous and bounded for any $l > 0$.

Notice that the Fréchet derivatives of $\mathcal{F}$ are involved in the conditions of the Crandall-Rabinowitz theorem. In order to compute these Fréchet derivatives, we expand $(L, H, F, p)$ in $\tau$ as below:

$$
L = L_1 + \tau L_1 + O(\tau^2),
$$

(2.19)

$$
H = H_1 + \tau H_1 + O(\tau^2),
$$

(2.20)

$$
F = F_1 + \tau F_1 + O(\tau^2),
$$

(2.21)

$$
p = p_1 + \tau p_1 + O(\tau^2).
$$

(2.22)

The rigorous justification for (2.19)–(2.22) can be found in Zhao and Hu.\textsuperscript{10} Substituting (2.19)–(2.22) into the system (2.10)–(2.16), and dropping all the higher order terms in $\tau$, we can obtain the system for $(L_1, H_1, F_1, p_1)$, which is also called the linearized system of (2.10)–(2.16).

Next we set the perturbation as $S(\theta) = \cos(n\theta)$ since the set $\{ \cos(n\theta) \}_{n=0}^\infty$ is a basis of the Banach space $X_1^{l+a}$ which is defined in (2.18). Therefore, we only need to seek solutions of the form

$$
L_1 = L_1^n \cos(n\theta), \ H_1 = H_1^n \cos(n\theta),
$$

(2.23)

$$
F_1 = F_1^n \cos(n\theta), \ p_1 = p_1^n \cos(n\theta).
$$

(2.24)

From Zhao and Hu\textsuperscript{10}(4.7)-(4.16), we know that the equations for $(L_1^n, H_1^n, F_1^n, p_1^n)$ are (Recall that $\Omega^*$ denotes the annulus $1 - \epsilon \leq r \leq 1$):

$$
-\frac{\partial^2 L_1^n}{\partial r^2} - \frac{1}{r} \frac{\partial L_1^n}{\partial r} + \frac{n^2}{r^2} L_1^n = f_5(L_1^n, H_1^n, F_1^n) \text{ in } \Omega^*,
$$

(2.25)

$$
-\frac{\partial^2 H_1^n}{\partial r^2} - \frac{1}{r} \frac{\partial H_1^n}{\partial r} + \frac{n^2}{r^2} H_1^n = f_6(L_1^n, H_1^n, F_1^n) \text{ in } \Omega^*,
$$

(2.26)

$$
-\frac{\partial^2 F_1^n}{\partial r^2} - \frac{1}{r} \frac{\partial F_1^n}{\partial r} + \frac{n^2}{r^2} F_1^n = \frac{1}{D} \left( f_5(L_1^n, H_1^n, F_1^n) + \frac{\partial F_1^n}{\partial r} + \frac{\partial p_1^n}{\partial r} \right) \text{ in } \Omega^*,
$$

(2.27)

$$
-\frac{\partial^2 p_1^n}{\partial r^2} - \frac{1}{r} \frac{\partial p_1^n}{\partial r} + \frac{n^2}{r^2} p_1^n = f_6(L_1^n, H_1^n, F_1^n) \text{ in } \Omega^*,
$$

(2.28)

$$
\frac{\partial L_1^n}{\partial r} = \frac{\partial H_1^n}{\partial r} = \frac{\partial F_1^n}{\partial r} = \frac{\partial p_1^n}{\partial r} = 0, \ r = 1,
$$

(2.29)

$$
\frac{\partial L_1^n}{\partial r} + \beta_1 L_1^n = \frac{\partial^2 L_1^n}{\partial r^2} - \beta_1 \frac{\partial L_1^n}{\partial r} \bigg|_{r=1-\epsilon}, \ r = 1 - \epsilon,
$$

(2.30)

$$
\frac{\partial H_1^n}{\partial r} + \beta_1 H_1^n = \frac{\partial^2 H_1^n}{\partial r^2} - \beta_1 \frac{\partial H_1^n}{\partial r} \bigg|_{r=1-\epsilon}, \ r = 1 - \epsilon.
$$

(2.31)
- $\frac{\partial F^n}{\partial r} + \beta_2 F^1_1 = \frac{\partial^2 F^3}{\partial r^2} - \beta_2 \frac{\partial F^3}{\partial r} \bigg|_{r=1-\epsilon}, \ r = 1 - \epsilon,$ 

where $f_5, f_6, f_7,$ and $f_8$ are all bounded by linear functions of $|L_1^n|, |H_1^n|,$ and $|F^n_1|$. In particular, $f_8$ is given by

$$f_8(L_1^n, H_1^n, F^n_1) = \frac{1}{M_0} \left[ \frac{(M_0 - F_s)L_1^n}{\gamma + H_s} - \frac{L_1^n}{\gamma + H_s} - \frac{L_1^n}{(\gamma + H_s)^2} + (\rho_3 - \rho_4)F^n_1 \right],$$

which will be used in the discussion in Section 4.

Now recall that $\mathcal{F}(0, \mu) = \frac{\partial p}{\partial r} \bigg|_{r=1-\epsilon} = 0$ by (2.8), we can utilize the expansions (2.19)–(2.22) to derive (more rigorous proof can be found in Zhao and Hu)

$$\mathcal{F}(tS, \mu) - \mathcal{F}(0, \mu) = -\frac{\partial p}{\partial r} \bigg|_{r=1-\epsilon} + O(|r|^2||S||^{c+\alpha}(\Sigma)) = r \left[ \frac{\partial^2 p_s}{\partial r^2} \bigg|_{r=1-\epsilon} \right] S(\theta) + \frac{\partial p_1}{\partial r} \bigg|_{r=1-\epsilon} + O(|r|^2||S||^{c+\alpha}(\Sigma)),$$

which leads to the Fréchet derivative of $\mathcal{F}$ at $(0, \mu)$ as below:

$$[\mathcal{F}_g(0, \mu)] S(\theta) = \frac{\partial^2 p_s}{\partial r^2} \bigg|_{r=1-\epsilon} S(\theta) + \frac{\partial p_1}{\partial r} \bigg|_{r=1-\epsilon}.$$ Substituting $S(\theta) = \cos(n\theta)$ and (2.24) into the above equation, we further obtain

$$[\mathcal{F}_g(0, \mu)] \cos(n\theta) = \left( \frac{\partial^2 p_s(1-\epsilon)}{\partial r^2} + \frac{\partial p_1^n(1-\epsilon)}{\partial r} \right) \cos(n\theta).$$

Based on the second assumption of the Crandall-Rabinowitz theorem (Theorem 2.2), we shall consider the Kernel of $\mathcal{F}_g(0, \mu)$. Therefore, we denote $\mu = \mu_n$ to be the solution of the equation (the existence and uniqueness of such a solution can be found in Zhao and Hu)

$$\frac{\partial^2 p_s(1-\epsilon)}{\partial r^2} + \frac{\partial p_1^n(1-\epsilon)}{\partial r} = 0.$$ 

Clearly, for each $n \geq 0$, $[\mathcal{F}_g(0, \mu)] \cos(m\theta) = 0$ if and only if $\mu = \mu_n$.

For each fixed $n \geq 0$ and $\mu = \mu_n$, it was shown in Zhao and Hu that for sufficiently small $\epsilon > 0$ (depending on $n$), we have

$$[\mathcal{F}_g(0, \mu_n)] \cos(m\theta) \neq 0, \text{ if } m \neq n \text{ and } n \neq 1.$$

From there, it was then concluded that for $n \geq 2$, $\mu = \mu_n$ is a bifurcation point. To show $n = 1$ is also a bifurcation point, we just need to establish

$$[\mathcal{F}_g(0, \mu_1)] \cos(m\theta) \neq 0, \text{ for } m \neq 1.$$ 

It has already been established in Zhao and Hu for all $m \geq 2$, so it remains to verify (2.38) for $m = 0$.

### 3 USEFUL ESTIMATES AND LEMMAS

A lot of estimates were derived in Zhao and Hu. In order to obtain a better estimate than (1.15) for the cases $n = 0$ and 1, here we collect some formulas from Zhao and Hu (i.e., (2.11)–(2.13) and (4.47)–(4.52) in Zhao and Hu) which will be useful in this paper. (Note that we only consider the cases when $n = 0$ and 1; hence, we do not need the higher order terms of $\epsilon$ in the expansions. In fact, for $n \geq 2$, $O(\epsilon)$ order is already enough to distinguish the $\mu_n$'s.)

$$L_n(r) = L_0 - \frac{\epsilon}{\beta_1} \left( \frac{k_1 M_0 L_0}{k_1 + L_0} + \rho_1 L_0 \right) + O(\epsilon^2)$$
\[
\begin{align*}
\frac{\rho_3(\gamma + H_0)}{\lambda} + e \left[ \frac{\mu - \rho_3(\gamma + H_0)}{\beta_1} \right] \frac{k_1 M_0}{\lambda K_1 + \rho_3(\gamma + H_0)} + \frac{\rho_1}{\lambda} + e L_s + O(e^2)
\end{align*}
\]

\[(\lambda) = \rho_3(\gamma + H_0) + e L_s + O(e^2),
\]

\[
H_s(r) = H_0 - e \frac{\rho_2 H_0}{\beta_1} + O(e^2) \triangleq H_0 + e H_s^1 + O(e^2).
\]

\[
F_s(r) = e \frac{k_1 M_0 L_0}{\beta_2 D(K_1 + L_0)} + O(e^2)
\]

\[
e \frac{\rho_3(\gamma + H_0)}{\beta_2 D} \frac{k_1 M_0}{\lambda K_1 + \rho_3(\gamma + H_0)} + O(e^2) \triangleq e F_s^1 + O(e^2).
\]

\[
L_s^2(r) = \frac{1}{\beta_1} \left( \frac{\partial^2 L_s}{\partial r^2} - \beta_1 \frac{\partial L_s}{\partial r} \right) + O(e) = \frac{\partial}{\partial r} L_s^1 + O(e).
\]

\[
H_s^2(r) = \frac{1}{\beta_1} \left( \frac{\partial^2 H_s}{\partial r^2} - \beta_1 \frac{\partial H_s}{\partial r} \right) + O(e) = -H_s^1 + O(e).
\]

\[
F_s^2(r) = \frac{1}{\beta_1} \left( \frac{\partial^2 F_s}{\partial r^2} - \beta_1 \frac{\partial F_s}{\partial r} \right) + O(e) = -F_s^1 + O(e).
\]

The following lemma is from Zhao and Hu\(^{10}\) (Lemma 2.2). It includes a relationship among the parameters, which will be used later.

**Lemma 3.1.** For the radially symmetric stationary solution \((L_s, H_s, F_s, p^s)\), the following estimates holds

\[
M_0(\lambda L_s^1 - \rho_3 H_s^1) \over \gamma + H_0 - \rho_4 F_s^1 = O(e);
\]

in other words, \(\rho_4\) can be expressed as

\[
\rho_4 = \frac{1}{F_s^1} \frac{M_0}{\gamma + H_0} (\lambda L_s^1 - \rho_3 H_s^1) + O(e).
\]

Notice that Equations (2.25)–(2.28) are of similar structures. For convenience, we denote the operator \(\mathcal{L}_n \triangleq \frac{\partial^2}{\partial r^2} - 1, \frac{\partial}{\partial r} + \frac{\nu^2}{r^2}\). For this special operator, one can easily verify the following lemmas (special cases of \(n = 0\) and 1 in Zhao and Hu\(^{10}\) Lemma 4.2 with the case \(n = 1\) modified to satisfy \(\psi_1(1) = \psi'_1(1) = 0\))

**Lemma 3.2.** The general solution of \((\eta \text{ is a constant})\)

\[
\mathcal{L}_n[\psi] \triangleq -\psi'' - \frac{1}{r} \psi' + \frac{n^2}{r^2} \psi = \eta + f(r), \quad 1 - \epsilon < r < 1,
\]

\(\psi'_1(1) = 0,\)

is given by

\[
\psi - \psi_1 = \begin{cases} Ar + \frac{1}{r} \left( A + K[f](1) \right) + K[f](r) & n = 1, \\ A + K[f](r) & n = 0, \end{cases}
\]

where

\[
K[f](r) = \begin{cases} \frac{r}{2} \int_r^1 f(s) ds + \frac{r}{2} \int_{r-e}^r s^2 f(s) ds & n = 1, \\ -r \int_r^1 \left( \log \frac{s}{r} \right) s f(s) ds & n = 0; \end{cases}
\]

in addition, \(\psi_1(r)\) satisfies

\[
\mathcal{L}_n[\psi_1] = -\psi''_1 - \frac{1}{r} \psi'_1 + \frac{n^2}{r^2} \psi_1 = \eta, \quad 1 - \epsilon < r < 1, \quad \psi'_1(1) = 0, \psi_1(1) = 0,
\]

Alternation Strategy
and is given by

$$\psi_1 = \begin{cases} \eta \left( -\frac{1}{6r} + \frac{1}{2} r - \frac{1}{3} r^2 \right) & n = 1, \\ \eta \left( \frac{1}{6} r + \frac{1}{2} \log r \right) & n = 0. \end{cases} \quad (3.13)$$

The special solution $K[f]$ satisfies

$$|K[f](r)| \leq \frac{e}{2} \|f\|_{L^{\infty}}, |K[f]'(r)| \leq \frac{e}{2} \|f\|_{L^{\infty}}, n = 1,$$

and

$$|K[f](r)| \leq c \|f\|_{L^{\infty}}, |K[f]'(r)| \leq c \|f\|_{L^{\infty}}, n = 0. \quad (3.14)$$

The proof is the same as in Zhao and Hu.\(^{10}\) We add one more restriction on $\psi_1$, that is, $\psi_1(1) = 0$, but it does not affect the proof. Since $\psi_1(1) = \psi_1'(1) = 0$, and by (3.12),

$$\psi''_1(1) = -\eta + \left( -\frac{1}{r} \psi'_1 + \frac{n}{r} \psi_1 \right) \bigg|_{r=1} = -\eta. \quad (3.15)$$

In addition, differentiating the equation (3.12) and evaluating at $r = 1$, we further obtain

$$\psi''_1(1) = \left( -\frac{r \psi''_1 - \psi'_1}{r^2} + \frac{n^2 \psi'_1 - 2r \psi_1}{r^4} \right) \bigg|_{r=1} = -\psi''_1(1) = \eta. \quad (3.16)$$

Based on the above two equations, it then follows from the Taylor series that, for $1 - \epsilon \leq r \leq 1$,

$$\psi_1(r) = \psi_1(1) + \psi_1'(1)(r-1) + \frac{\psi''_1(1)}{2} (r-1)^2 + \ldots = -\eta (r-1)^2 + O(\epsilon^3), \quad (3.17)$$

and

$$\psi'_1(r) = \psi'_1(1) + \psi''_1'(1)(r-1) + \frac{\psi''''_1(1)}{2} (r-1)^2 + \ldots = -\eta(r-1) + \frac{\eta}{2} (r-1)^2 + O(\epsilon^3). \quad (3.18)$$

In particular, we have

$$\psi_1(1 - \epsilon) = -\frac{\eta}{2} \epsilon^2 + O(\epsilon^3), \quad (3.19)$$

$$\psi'_1(1 - \epsilon) = -\epsilon \eta + \frac{\eta}{2} \epsilon^2 + O(\epsilon^3). \quad (3.20)$$

**Lemma 3.3.** *If in addition to (3.9), we further assume the boundary condition

$$-\psi'(1 - \epsilon) + \beta \psi(1 - \epsilon) = G, \quad (3.21)$$

then the coefficient $A$ in (3.10) can be explicitly computed as: for $n = 1$

$$A = \frac{G + \psi'(1 - \epsilon) - \beta \psi_1(1 - \epsilon) - \beta K[f](1 - \epsilon) K[f]'(1 - \epsilon) - \frac{1}{(1-\epsilon)^2} K[f]'(1) \frac{\beta}{1-\epsilon} K[f]'(1)}{-1 + \frac{1}{(1-\epsilon)^2} + \beta (1 - \epsilon) + \frac{\beta}{1-\epsilon}}, \quad (3.22)$$

and for $n = 0$,

$$A = \frac{1}{\beta} \left[ G + \psi'(1 - \epsilon) - \beta \psi_1(1 - \epsilon) - \beta K[f](1 - \epsilon) + K[f]'(1 - \epsilon) \right]. \quad (3.23)$$

**Lemma 3.4.** *If $f(r) = O(\epsilon)$ in (3.9), and the assumptions in Lemma 3.3 hold, then for $1 - \epsilon \leq r \leq 1$,

$$\psi(r) = \frac{G}{\beta} + \epsilon \left( \frac{\eta}{\beta} - \frac{G}{\beta^2} \right) + O(\epsilon^2) \quad n = 1, \quad (3.24)$$

$$\psi(r) = \frac{G}{\beta} + \epsilon \frac{\eta}{\beta} + O(\epsilon^2) \quad n = 0. \quad (3.25)$$
Proof. Based on Lemma 3.2, if \( f(r) = O(\varepsilon) \) in (3.9), we have in either \( n = 0 \) or \( n = 1 \) case,

\[
K[f](r) = O(\varepsilon^2), \quad K[f]'(r) = O(\varepsilon^2).
\]

Substituting these two estimates into (3.21) and (3.22), recalling also (3.18) and (3.19), we obtain

\[
A = \frac{G + e\eta + O(\varepsilon^2)}{2(2\beta + e) + O(\varepsilon^2)} = \frac{G}{2\beta} + e \left( \frac{\eta}{2\beta^2} - \frac{G}{2\beta^2} \right) + O(\varepsilon^2) \quad n = 1,
\]

\[
A = \frac{G + e\eta + O(\varepsilon^2)}{\beta} = \frac{G}{\beta} + e \frac{\eta}{\beta} + O(\varepsilon^2) \quad n = 0.
\]

Since \( A \) is the only coefficient in (3.10), we can now substitute the above expressions for \( A \) into (3.10) to derive, for \( 1 - \varepsilon \leq r \leq 1 \),

\[
\psi(r) = A \left( r + \frac{1}{r} \right) + O(\varepsilon^2) = 2A + O(\varepsilon^2) = \frac{G}{\beta} + e \left( \frac{\eta}{\beta^2} - \frac{G}{\beta^2} \right) + O(\varepsilon^2) \quad n = 1,
\]

\[
\psi(r) = A + O(\varepsilon^2) = \frac{G}{\beta} + e \frac{\eta}{\beta} + O(\varepsilon^2) \quad n = 0.
\]

This completes the proof. \( \Box \)

Notice that in this lemma, the difference between \( n = 1 \) and \( n = 0 \) cases starts from \( O(\varepsilon) \) terms; furthermore, the difference in \( O(\varepsilon) \) terms is \( e \frac{G}{\beta^2} \), which is determined only by \( G \) and \( \beta \).

Lemma 3.2, together with Lemmas 3.3 and 3.4, is applied to equations for \( L_1^n, H_1^n, \) and \( F_1^n \). Notice that the boundary condition for \( p_1^n \) is

\[
p_1^n(1 - \varepsilon) = \frac{1 - n^2}{(1 - \varepsilon)^2},
\]

which is of a different form from (3.20), we hence need the following lemma that can be easily verified:

**Lemma 3.5.** If in addition to (3.9), we further assume the boundary condition for \( \psi \)

\[
\psi(1 - \varepsilon) = \frac{1 - n^2}{(1 - \varepsilon)^2}, \tag{3.25}
\]

then the coefficient \( A \) in (3.10) is solved as

\[
A = \frac{-\psi_1(1 - \varepsilon) - K[f](1 - \varepsilon) - \frac{1}{1 - \varepsilon} K[f]'(1)}{1 - \varepsilon + \frac{1}{1 - \varepsilon}}, \quad n = 1,
\]

\[
A = -\psi_1(1 - \varepsilon) - K[f](1 - \varepsilon), \quad n = 0.
\]

**Lemma 3.6.** If \( f(r) = O(\varepsilon^2) \) in (3.9), and the assumptions in Lemma 3.5 hold, then for \( n = 0, 1 \) and \( 1 - \varepsilon \leq r \leq 1 \),

\[
\psi'(1 - \varepsilon) = e\eta + e^2 \frac{\eta}{2} + O(\varepsilon^3). \tag{3.26}
\]

Proof. If \( f = O(\varepsilon^2) \) in (3.9), by Lemma 3.2, we have

\[
K[f](r) = O(\varepsilon^2), \quad K[f]'(r) = O(\varepsilon^3).
\]

In order to estimate \( \psi'(1 - \varepsilon) \), we differentiate (3.10) and evaluate the derivative at \( r = 1 - \varepsilon \),

\[
\psi'(1 - \varepsilon) = \psi_1'(1 - \varepsilon) + A - \frac{1}{(1 - \varepsilon)^2} \left( A + K[f]'(1) \right) + K[f]'(1 - \varepsilon) \quad n = 1,
\]

\[
\psi'(1 - \varepsilon) = \psi_1'(1 - \varepsilon) + K[f]'(1 - \varepsilon) \quad n = 0.
\]
Combining with the expression of \( A \) in Lemma 3.5, recalling also (3.16)–(3.19), we further derive \( A = O(\epsilon^2) \), and in both cases,

\[
\psi'(1 - \epsilon) = \epsilon \eta + \epsilon^2 \eta + O(\epsilon^3) \quad n = 0, 1,
\]

which completes the proof. \( \square \)

### 4 Proof of Theorem 1.1

As mentioned before, the key is to show \( \mu_0 \neq \mu_1 \). Since they are the same on the order of \( O(\epsilon) \), we shall derive higher order approximations for \( \mu_0 \) and \( \mu_1 \). Hence, the estimates (3.4)–(3.6) for \( L^n_1, H^n_1 \), and \( F^n_1 \) are not enough for the purpose of this paper—we need more information about the higher order terms in \( \epsilon \). To do that, we denote

\[
L^n_1 = \frac{\mu}{\lambda} - L^1 + \epsilon L^n_{11} + O(\epsilon^2),
\]

\[
H^n_1 = -H^1 + \epsilon H^n_{11} + O(\epsilon^2),
\]

\[
F^n_1 = -F^1 + \epsilon F^n_{11} + O(\epsilon^2),
\]

and we proceed to estimate \( L^n_{11}, H^n_{11} \), and \( F^n_{11} \) based on Lemmas 3.2, 3.3, and 3.4.

Recall first the equations for \( L^n_1, H^n_1 \), and \( F^n_1 \) are (\( \Omega \)- denotes the annulus \( 1 - \epsilon \leq r \leq 1 \):

\[
- \frac{\partial^2 L^n_1}{\partial r^2} - \frac{1}{r} \frac{\partial L^n_1}{\partial r} + \frac{n^2}{r^2} L^n_1 = f_5(L^n_1, H^n_1, F^n_1) \text{ in } \Omega_1,
\]

\[
- \frac{\partial^2 H^n_1}{\partial r^2} - \frac{1}{r} \frac{\partial H^n_1}{\partial r} + \frac{n^2}{r^2} H^n_1 = f_6(L^n_1, H^n_1, F^n_1) \text{ in } \Omega_1,
\]

\[
- \frac{\partial^2 F^n_1}{\partial r^2} - \frac{1}{r} \frac{\partial F^n_1}{\partial r} + \frac{n^2}{r^2} F^n_1 = \frac{1}{D} \left( f_1(L^n_1, H^n_1, F^n_1) + \frac{\partial F^n_1}{\partial r} \frac{\partial p^n_1}{\partial r} + \frac{\partial F^n_1}{\partial r} \frac{\partial p^n_1}{\partial r} \right) \text{ in } \Omega_1,
\]

\[
\frac{\partial L^n_1}{\partial r} = \frac{\partial H^n_1}{\partial r} = \frac{\partial F^n_1}{\partial r} = 0, \quad r = 1,
\]

\[
- \frac{\partial L^n_1}{\partial r} + \beta_1 L^n_1 = \frac{\partial^2 L^n_1}{\partial r^2} - \beta_1 \frac{\partial L^n_1}{\partial r} \bigg|_{r=1-\epsilon}, \quad r = 1 - \epsilon,
\]

\[
- \frac{\partial H^n_1}{\partial r} + \beta_1 H^n_1 = \frac{\partial^2 H^n_1}{\partial r^2} - \beta_1 \frac{\partial H^n_1}{\partial r} \bigg|_{r=1-\epsilon}, \quad r = 1 - \epsilon,
\]

\[
- \frac{\partial F^n_1}{\partial r} + \beta_1 F^n_1 = \frac{\partial^2 F^n_1}{\partial r^2} - \beta_1 \frac{\partial F^n_1}{\partial r} \bigg|_{r=1-\epsilon}, \quad r = 1 - \epsilon.
\]

For the right-hand sides of (4.4)–(4.6), we can write them as the form \( \eta + O(\epsilon) \), and we shall claim that \( \eta \) is independent of \( n \). In fact, we notice that the \( O(1) \) terms of \( L^n_1(r), H^n_1(r) \), and \( F^n_1(r) \) in (4.1)–(4.3) are constants, and are independent of \( n \). Moreover, it has been proved in Zhao and Hu\(^{10} \) that \( \frac{\partial F^n_1}{\partial r}, \frac{\partial p^n_1}{\partial r} = O(\epsilon) \), and \( \frac{\partial F^n_1}{\partial r}, \frac{\partial p^n_1}{\partial r} \) are both bounded. Hence, the extra two terms in (4.6), \( \frac{\partial F^n_1}{\partial r}, \frac{\partial p^n_1}{\partial r} \), do not affect the \( O(1) \) term \( \eta \).

Using Lemma 3.4, we find that the difference between \( L^n_1(r) \) and \( L^n_0(r) \) starts from \( O(\epsilon) \) terms. As a matter of fact, by (3.23), (3.24), and (3.4),

\[
L^n_1 - L^n_0 = -\frac{\epsilon}{\beta_1} \left( \frac{\partial^2 L^n_1}{\partial r^2} - \beta_1 \frac{\partial L^n_1}{\partial r} \right) \bigg|_{r=1-\epsilon} + O(\epsilon^2) = \frac{\epsilon}{\beta_1} \left( L^n_1 - \frac{\mu}{\lambda} \right) + O(\epsilon^2).
\]

From (4.1), \( L^n_1 = \frac{\mu}{\lambda} - L^n_1 + \epsilon L^n_{11} + O(\epsilon^2) \), and \( L^n_0 = \frac{\mu}{\lambda} - L^n_1 + \epsilon L^n_{11} + O(\epsilon^2) \); combining with the above equation, we further have

\[
L^n_{11} - L^n_{11} = \frac{1}{\beta_1} \left( L^n_1 - \frac{\mu}{\lambda} \right)^2.
\]
Similarly, we can derive
\[
H_{11}^1 - H_{11}^0 = \frac{1}{\beta_1} H_1^1,
\]
\[
F_{11}^1 - F_{11}^0 = \frac{1}{\beta_2} F_1^1.
\]

Next we consider the equation for \( p_1^n \):
\[
- \frac{\partial^2 p_1^n}{\partial r^2} - \frac{1}{r} \frac{\partial p_1^n}{\partial r} + \frac{n^2}{r^2} p_1^n = f_8(L_1^n, H_1^n, F_1^n) \quad \text{in} \quad \Omega_s,
\]
where by (2.34),
\[
\frac{\partial p_1^n}{\partial r}(1) = 0, p_1^n(1 - e) = \frac{1 - n^2}{(1 - e)^2},
\]
In order to apply Lemmas 3.2, 3.5, and 3.6, we shall rewrite \( f_8 \) in the form \( f_8 = \eta + f(r) \), where \( f(r) = O(e^2) \). More specifically, we denote,
\[
f_8(L_1^n, H_1^n, F_1^n) = \eta_n + O(e^2),
\]
and we now proceed a long and tedious journey to compute \( \eta_n = \eta_n(e) \). Substituting (3.1)–(3.3) and (4.1)–(4.3) all into the equation of \( f_8 \), we have
\[
M_0 f_8 = \lambda \left( \frac{M_0 - F_1}{\gamma + H_0 + e H_1^n} - \frac{\rho (r + H_0)}{\gamma + H_0 + e H_1^n} \right) + (\rho_3 - \rho_4) (\gamma + H_0)^2 + O(e^2).
\]

We notice that all the terms in the first bracket \([ \ldots ]\) of (4.16) are independent of \( n \); hence, if we calculate \( \eta_1 - \eta_0 \), these terms are cancelled out. As a result,
\[
\eta_1 - \eta_0 = \frac{e}{M_0} \left( \lambda M_0 H_1^n \frac{(L_1^n - L_1^0)}{\gamma + H_0} - \frac{M_0 \rho_3 (H_1^n)^2}{\gamma + H_0^0} - \frac{M_0 \rho_3 (H_1^n)}{\gamma + H_0} - \rho_4 (F_1^0 - F_1^0) \right).
\]
In addition, by Lemma 3.6, we immediately have

\[
\frac{\partial p_1^m(1 - \epsilon)}{\partial r} = c\eta_n + \epsilon^2\eta_n + O(\epsilon^3). \tag{4.18}
\]

Notice that in Zhao and Hu, we have derived explicit dependence of \(O(\epsilon)\) and \(O(\epsilon^2)\) terms on \(n\), it was needed over there since (2.37) needs to be verified for all \(m \neq n\); in particular, \(m\) can approach \(\infty\). The situation here is different, we only need to show (2.38) for \(m = 0\), as the remaining \(m\)'s are already proved in Zhao and Hu. Thus, all the above expansions of \(O(\epsilon^2)\) and \(O(\epsilon^3)\) terms are for fixed \(n = 0\) and \(n = 1\), and explicit dependence on \(n\) is not required here.

Now we are ready to prove our main result Theorem 1.1.

**Proof of Theorem 1.1.** In the Crandall-Rabinowitz theorem (Theorem 2.2), we choose the Banach spaces \(X = X_1^{4+\sigma}\) and \(Y = X_1^{4+\sigma}\). In order to prove \(\mu = \mu_1\) is a bifurcation point, it is required to verify the four conditions of the Crandall-Rabinowitz theorem at this point. First of all, the differentiability of the map \(F\) follows the same argument as in the papers, and the condition (1) in the Crandall-Rabinowitz theorem is naturally satisfied. For the remaining conditions, we need to prove

\[
[F_\varepsilon(0, \mu_1)] \cos m\theta \neq 0, \text{ for } \forall m \neq 1. \tag{4.19}
\]

As is mentioned, it has been established in Zhao and Hu that there exists a bound \(E_2 > 0\), when \(0 < \epsilon < E_2\), we have (4.19) to be true for each \(m \geq 2\). Hence, it suffices to show

\[
[F_\varepsilon(0, \mu_1)] \cos(0\theta) = [F_\varepsilon(0, \mu_1)] 1 \neq 0, \text{ i.e., } \mu_0 \neq \mu_1, \tag{4.20}
\]

and we shall prove it by contradiction.

Recall that \(\mu_0\) is the solution to the equation

\[
\frac{\partial^2 p_1(1 - \epsilon; \mu)}{\partial r^2} + \frac{\partial p_1^0(1 - \epsilon; \mu)}{\partial r} = 0.
\]

For the contrary, assuming \(\mu_0 = \mu_1\), we then have

\[
\frac{\partial p_1^1(1 - \epsilon)}{\partial r} - \frac{\partial p_1^0(1 - \epsilon)}{\partial r} = 0. \tag{4.21}
\]

On the other hand, it follows from (4.18) and (4.17) that

\[
\frac{\partial p_1^1(1 - \epsilon)}{\partial r} - \frac{\partial p_1^0(1 - \epsilon)}{\partial r} = \epsilon(\eta_1 - \eta_0) + \frac{\epsilon^2}{2}(\eta_1 - \eta_0) + O(\epsilon^3)
\]

\[
= \frac{\epsilon^2}{M_0} \left[ \frac{\lambda M_0}{\gamma + H_0} (L_{11} - L_{11}^0) - \frac{\rho_3 M_0}{\gamma + H_0} (H_{11} - H_{11}^0) - \frac{\rho_4 (F_{11} - F_{11}^0)}{\beta_1} \right] + O(\epsilon^3).
\]

Substituting the estimates for \(L_{11} - L_{11}^0, H_{11} - H_{11}^0\), and \(F_{11} - F_{11}^0\) (i.e., (4.11)–(4.13)) into the above equation, recalling also (3.7) in Lemma 3.1 and the fact that \(\mu_0, \mu_1 = O(\epsilon)\) by (1.15), we further have

\[
\frac{\partial p_1^1(1 - \epsilon)}{\partial r} - \frac{\partial p_1^0(1 - \epsilon)}{\partial r} = \epsilon^2 \left[ \frac{\lambda}{\gamma + H_0} \frac{1}{\beta_1} (L_{11} - \frac{\mu_0}{\lambda}) - \frac{\rho_3}{\gamma + H_0} \frac{H_{11}^1}{\beta_1} - \frac{\rho_4}{\beta_1} \frac{F_{11}^1}{M_0} \right] + O(\epsilon^3)
\]

\[
= \epsilon^2 \left[ \frac{1}{\beta_1} \frac{\lambda L_{11} - \rho_2 H_{11}}{\gamma + H_0} - \frac{1}{\beta_2} \frac{\rho_4 F_{11}^1}{M_0} - \frac{\mu_0}{\beta_1 (\gamma + H_0)} \right] + O(\epsilon^3)
\]

\[
= \epsilon^2 \left( \frac{1}{\beta_1} - \frac{1}{\beta_2} \right) \frac{\rho_4 F_{11}^1}{M_0} + O(\epsilon^3).
\]
We have assumed that $\beta_1 \neq \beta_2$. Since the sign of $\frac{\partial p_1(1-c)}{\partial r} - \frac{\partial p_0(1-c)}{\partial r}$ is dominated by $\left(\frac{1}{\beta_1} - \frac{1}{\beta_2}\right) \frac{\rho_0 k_1}{M_\infty}$, we can easily find a bound $E_2 > 0$, such that when $0 < \epsilon < E_2$,

$$\frac{\partial p_1(1-c)}{\partial r} - \frac{\partial p_0(1-c)}{\partial r} \neq 0,$$

which contradicts with the statement (4.21). Hence, we have $\mu_1 \neq \mu_0$ when $\epsilon < E_2$.

By taking $E = \min\{E_1, E_2\}$, we finish showing (4.19). With (4.19), we now have

\[
\text{Ker} \mathcal{F}_R(0, \mu_1) = \text{span}\{\cos(\theta)\},
\]

\[
Y_1 = \text{Im} \mathcal{F}_R(0, \mu_1) = \text{span}\{1, \cos(2\theta), \cos(3\theta), \ldots, \cos(n\theta), \ldots\},
\]

\[
Y_1 \bigoplus \text{Ker} \mathcal{F}_R(0, \mu_1) = Y,
\]

\[
[\mathcal{F}_R(0, \mu_1)] \cos \theta \in \text{span}\{\cos(\theta)\}, \text{ and hence } [\mathcal{F}_R(0, \mu_1)] \cos(\theta) \notin Y_1.
\]

In other words, all the spaces (kernel space, codimension space, non-tangential space) meet the requirements of the Crandall-Rabinowitz theorem, and all the conditions of the theorem are satisfied. Therefore, $\mu = \mu_1$ is a bifurcation point of the system (1.1)–(1.14).

\[\square\]

5 | CONCLUSION

The bifurcation analysis for the plaque formation model explains the asymmetric shapes of plaques. In particular, we have shown that the smallest bifurcation point is $\mu = \mu_1 = O(\epsilon)$. Mathematically, the first bifurcation point often coincides with the change of stability for the system. In fact, it has been proved in Friedman et al.\(^6\) that the radially symmetric plaque would disappear if $\mu < 0$ and remain persistent if $\mu > 0$; hence, it is likely that the stability of the radially symmetric solution would change around $\mu = 0$. More importantly, $\mu = \mu_1 = O(\epsilon)$ is also the most significant bifurcation point biologically, as many arterial plaques are often accumulated more on one side of the artery in reality (see figures in previous studies\(^32-34\)), which resembles the pattern corresponding to the $n = 1$ bifurcation solutions. The bifurcation results can help to understand this phenomenon.

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CONFLICT OF INTEREST

This work does not have any conflicts of interest.

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