Stability analysis of an atherosclerotic plaque formation model with time delay

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Abstract

Atherosclerosis is a chronic inflammatory disease that poses a serious threat to human health. It starts with the buildup of plaque in the artery wall, which results from the accumulation of pro-inflammatory factors and other substances. In this paper, we propose a mathematical model of early atherosclerosis with a free boundary and time delay. The time delay represents the transformation of macrophages into foam cells. We obtain an explicit solution and analyze the stability of the model and the effect of the time delay on plaque size. We show that for non-radial symmetric perturbations, when $n = 0$ or 1, the steady-state solution (M_*, p_*, r_*) is linearly stable; when $n \geq 2$, there exists a critical parameter L_* such that the steady-state solution is linearly stable for $L < L_*$ and unstable for $L > L_*$. Moreover, we find that smaller plaque are associated with the presence of time delay.

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1 Introduction

Human health is significantly threatened by cardiovascular disease, atherosclerosis is one of the most prevalent pathophysiological bases of cardiovascular disease, it occurs when substances such as lipids and cholesterol deposit within the arterial walls, forming plaques. Once the plaque ruptures, it can lead to rapid, lethal conditions like myocardial infarction, which block blood vessels. Based on the most recent data released by the World Health Organization, cardiovascular ailments stand as the foremost global fatality factor ([1]). The mortality rate associated with cardiovascular diseases is disconcerting, with figures surpassing 18.56 million deaths in [20]. In order to treat the cardiovascular disease clinically, it is crucial to understand the mechanisms underlying atherosclerosis formation.

The concise description of the mechanism of atherosclerosis is illustrated in Figure 1. When the intima layer undergoes damage, levels of low-density lipoprotein (LDL) and high-density

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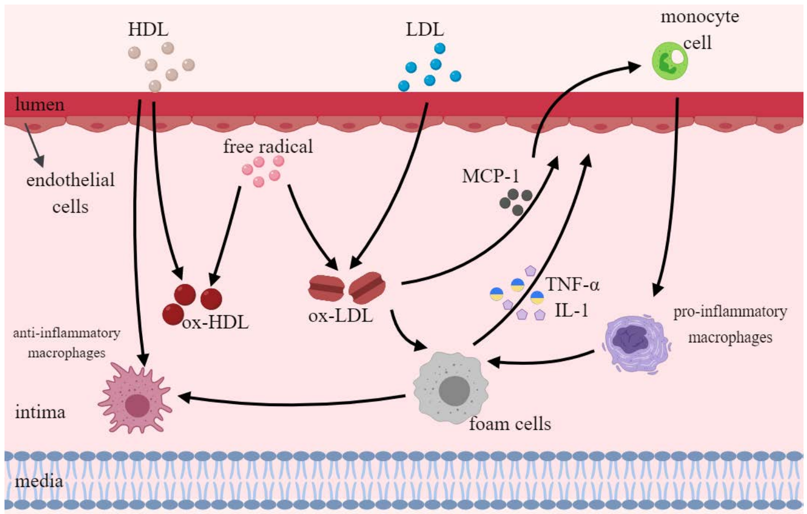

Figure 1: The interaction between HDL, LDL, M_1, M_2, and foam cells involves a dynamic interplay, where the arrowhead symbolizes production or activation.

lipoprotein (HDL) in the blood increase, signifying the beginning of the plaque formation process ([2]). Some LDL and HDL molecules penetrate the endothelial cells and become oxidized by free radicals. Endothelial cells secrete monocyte chemotactic protein (MCP-1) in response to oxidized LDL (ox-LDL), triggering a series of inflammatory processes that lead to the migration of monocytes into the intima. Once monocytes enter the intima, they differentiate into pro-inflammatory macrophages (M_1). When M_1 ingest oxidized LDL, foam cells (F) are formed. These foam cells (F) need to be cleared by the immune system, while simultaneously they trigger a chronic inflammatory response: they secrete proinflammatory cytokines (such as TNF-α, IL-1), increasing the activation of endothelial cells to attract more new monocytes. HDL serves as an antioxidant and plays a role in inhibiting plaque formation. Reverse cholesterol transport (RCT) is the process where HDL molecules bind to foam cells and transport oxidized LDL out of the foam cells and into the liver. Once LDL has been removed from foam cells, they transform back into macrophages, specifically non-inflammatory macrophages (M_2). In order to prevent the oxidation of LDL, HDL and LDL compete with each other for free radicals. Hence, the balance between HDL and LDL is crucial for the development of plaque. (see Figure 1)

In the past few years, there has been a growing emergence of mathematical models aimed at depicting the progressive development of arterial plaque; see [3, 4, 7–9, 11, 15, 18, 19, 21–26] and the reference therein. Among them, [3, 4, 7, 15, 24] are lipid-based models. In particular, Lui and Myerscough [15] proposed an ODE model for lipid dynamics that accounts for the lipid accumulation of macrophages, the formation of apoptotic cells and the formation of necrotic core, and studies the timescales in plaque development. Additionally, there are models that focus on the role of fiber cap (see [23]) and HDL (see [3]). All of these models acknowledge the crucial significance of LDL, commonly known as “bad” cholesterol, and HDL, known as “good” cholesterol, in the determination of plaque growth or regression. These models offer a richer and more comprehensive understanding of plaque growth.

Hao and Friedman ([8,11]) suggested an intricate reaction-diffusion boundary system in the publication. The model includes smooth muscle cells, T cell interactions, MCP-1 (Monocyte Chemoattractant Protein-1), MMP (matrix metalloproteinase), inflammatory macrophages, anti-inflammatory macrophages, foam cells, free radicals, and LDLs, ox-LDLs, and HDLs. This leads to the 17 equations in the system. A good numerical simulation has been performed. Unfortunately, it is not simple to study the reaction-diffusion system, which consists of 17 equations.

In 2015, Friedman [9] considered four aspects of the simplified model, including LDLs, HDLs, macrophage cells (M) and foam cells (F). Theoretically, the simplified free boundary model show that symmetric stationary plaques exist and carry out a careful mathematical analysis to demonstrate that for any H_0 and each small $\varepsilon > 0$, there exists a distinct L_0 such that there exists a unique $\varepsilon - thin$ stationary plaque. It makes sense to have a balance between "good" and "bad" cholesterol. They found the necessary and sufficient conditions to show that the small initial plaque contracted, disappeared or permanently existed.

On the basis of these models, many scholars have also considered bifurcation; see [6,12,13,28,31,32]. Assuming that the plaques have a strict radially symmetrical shape is unreasonable, therefore, Zhao and Hu ([31]) constructed finite branches of symmetry-breaking stationary solutions that bifurcate from the radial symmetric solution. The system involves many highly nonlinear and coupled equations, which prevent explicit solutions and pose great challenges for verifying the Crandall-Rabinowitz theorem. To address this issue, many sharp estimates were developed in [31]. The model has many parameters, to explore the branching phenomenon, they introduced a new parameter μ that represents the balance between HDL and LDL for a stable solution. They showed that for each μ_n ($n \geq 2$), there exists a small ε radially symmetric solution corresponding to the perturbation $\cos(n\theta)$. Moreover, Zhao and Hu [32] further examined [31] by establishing bifurcation points. This study helps to understand why one side of the artery has more plaques than the other. Zhang and Hu [28] also considered the RCT process of HDLs and studied the bifurcation.

Hao and Zheng [12] considered the ingestion of ox-LDL by macrophages and the RCT process of HDL. Assuming that the plaque growth is proportional to the binding rate of LDL and macrophages, they construct the following model and obtain the explicit solution:

$$\begin{cases} \dfrac{\partial M}{\partial t} - D\Delta M = -HM, & x \in \Omega(t), \\ -\Delta P = LM - T, & x \in \Omega(t), \\ \dfrac{\partial P}{\partial n} = 0, \dfrac{\partial M}{\partial n} = -M, & x \in \Gamma_1, \\ M = 1, P = \gamma\kappa, v_n(t) = -\dfrac{\partial P}{\partial n}, & x \in \Gamma_2(t). \end{cases} \tag{1.1}$$

By performing the perturbation analysis on these solutions, they not only established the existence of bifurcation branches, but also analyzed the stability of radial symmetric steady-state solutions.

Combining the aforementioned model and the research on atherosclerotic plaques, it is clear that abnormal proliferation of cells within the plaque directly leads to an increase in arterial wall thickness and plaque formation. This phenomenon inevitably brings to mind the formation and development of tumors in the human body caused by uncontrolled cell proliferation. Similar models have been proposed in tumor research (see [14, 17]), exploring tumor development and bifurcation phenomena (see [16]). Additionally, some studies have considered the impact of time delays on tumor models ([5, 27, 29]). In 1997, Byrne [5] was the first to propose studying the impact of time delay on tumor growth using a mathematical model. The way he introduce time delay in the process of cell proliferation is as follows:

$$S = \mu\sigma(\xi(t-\tau;x,t),t-\tau) - \mu\tilde{\sigma},$$

where $\mu\sigma(\xi(t-\tau;x,t),t-\tau)$ denotes the augmentation of the total volume within a given time period caused by cell proliferation; $\mu\tilde{\sigma}$ denotes the reduction of the total volume during a specific time interval due to natural cell death, and σ denotes the threshold concentration for tissue maintenance; μ is a parameter that quantifies the"intensity" of the proliferative expansion through mitosis. $\xi(s;x,t)$ is the cell position at time s when the cell moves with the velocity field $\mathbf{V}$ and the function $\xi(s;x,t)$ satisfies:

$$\begin{cases} \frac{d\xi}{ds}(s;x,t) = \mathbf{V}(\xi,s), & t-\tau \le s \le t, \\ \xi|_{s=t} = x. \end{cases}$$

Inspired by [5], [29,30] consider time delay into models involving nutrient and pressure dynamics. In [29], the author proved that under non-radially symmetric perturbations, there exists a critical value μ_*, such that while $\mu < \mu_*$, the stationary solution (σ_*, p_*, R_*) is linearly stable; while $\mu > \mu_*$, the stationary solution is unstable. Subsequently, in 2020, Zhao and Hu extended the considerations in [29] by incorporating bifurcations into the model. They established a bifurcation result for all even mode $n \ge 2$, the results encompasses the smallest bifurcation point, which holds utmost significance as it denotes the point of stability changes under specific conditions.

However, in the context of plaque models, time delays have **NOT** been adequately considered. Each process, long or short, is not instantaneous and takes a certain amount of time. Therefore, this paper aims to establish a plaque model that takes into account time delays τ to comprehensively understand the dynamic behavior of cell proliferation within the plaque. By incorporating time delays, we aim to provide a more realistic representation of the biological processes involved in plaque formation. We will build upon existing research (see [29]) and propose a modified model that takes into account the effects of time delays. In this paper, we will study the time delay model based on (1.1) and utilize the time delay formula presented in [5]. By using the explicit solution and the properties of modified Bessel functions, we first construct the radically symmetry stationary solutions, and then we prove that under non-radically symmetry perturbations, both the radius $\rho_n^0(t)$ and perturbation term $\rho_n^1(t)$ have explicit expressions. Therefore, we can determine the influence of time delay on plaques by solving these explicit expressions. Taking into account the effects of parameters, we consider two cases for solving $\rho_n^0(t)$ and $\rho_n^1(t)$: when $n \ge 2$, and when $n = 0$ or 1. By doing so, we obtain the results: when $n = 0$ or 1, the steady-state solution (M_*, p_*, r_*) is linearly stable; when $n \ge 2$, there exists a critical parameter L_* such that the steady-state solution is linearly stable for $L < L_*$ and unstable for $L > L_*$. Moreover, we find that smaller plaque are associated with the presence of time delay.

The rest of this paper is structured as follows. In Sect. 2, we present the mathematical models. In Sect. 3, we briefly explain the existence and uniqueness of radial symmetric steady-state solutions. In Sect. 4, we investigate the linear stability of the model and how the time delay affects plaque size.

2 Mathematical Model

Based on (1.1), we take into consideration the time delay in the formation of early atherosclerotic plaque. Clearly, adding time delay to the atherosclerosis model (1.1) enhances its realism. Due to the presence of the time delay $\tau \in [0, T]$, the size of plaque depends on the initial concentration of macrophages. Thus we can rewrite the equation as

$$-\Delta P = LM(\xi(t-\tau; x, t), t-\tau) - T,$$

where $LM(\xi(t-\tau; x, t), t-\tau)$ is the increase of total volume per unit time interval, and T is the clearance capacity provided by immune system, and $\xi(s; x, t)$ represents the position of the cell at time s and moves at speed $\vec{v}$, hence $\xi(s; x, t)$ satisfies the following ODE:

$$\begin{cases} \dfrac{d\xi}{ds} = \vec{v}(\xi, s), & t-\tau \leq s \leq t, \\ \xi = x, & s = t. \end{cases}$$

For simplicity, we take T as a parameter in the model. We further assume that the plaque texture is a porous medium type and use Darcy's law, to get the model studied in this paper described as:

$$\frac{\partial M}{\partial t} - D\Delta M = -HM, \qquad x \in \Omega(t), t > 0, \tag{2.1}$$

$$-\Delta P = LM(\xi(t-\tau; x, t), t-\tau) - T, \qquad x \in \Omega(t), t > 0, \tag{2.2}$$

$$\begin{cases} \dfrac{d\xi}{ds} = -\nabla p(\xi, s), & t-\tau \leq s \leq t, \\ \xi = x, & s = t, \end{cases} \tag{2.3}$$

$$M = 1, \quad P = \kappa, \quad v_n = -\frac{\partial P}{\partial n}, \qquad x \in \Gamma_2(t), t > 0, \tag{2.4}$$

$$\frac{\partial P}{\partial n} = 0, \quad \frac{\partial M}{\partial n} = -M, \qquad x \in \Gamma_1, \tag{2.5}$$

$$\Omega(t) = \Omega_0, \qquad -\tau \leq t \leq 0, \tag{2.6}$$

$$M(x, t) = M_0, \qquad -\tau \leq t \leq 0, x \in \Omega_0 \tag{2.7}$$

where L and H represents the concentration of LDL and HDL respectively, M represents the density of macrophages, and $\Omega(t)$ represents the intima. The inner surface of the arterial wall, $\Gamma_2(t)$ is a free boundary, at the same time, Γ_1 is a fixed boundary that represents the surface between the intima and media. In addition, we assume that the pressure P is balanced by the surface-tension which is proportional to the mean curvature κ.

3 Radically symmetric case

In the case of radially symmetric, the model of (2.1)-(2.7) becomes

$$\frac{\partial M}{\partial t} - D\Delta M = -HM, \qquad \rho(t) \le r \le R, t > 0, \tag{3.1}$$

$$-\Delta P = LM(\xi(t-\tau; x, t), t-\tau) - T, \qquad \rho(t) \le r \le R, t > 0, \tag{3.2}$$

$$\begin{cases} \dfrac{d\xi}{ds} = -\dfrac{\partial P}{\partial r}(\xi, s), & t-\tau \le \ s \le t, \\ \xi = r, & s = t, \end{cases} \tag{3.3}$$

$$\frac{\partial M}{\partial r}(R,t) = -M(R), \quad M(\rho(t), t) = 1, \tag{3.4}$$

$$\frac{\partial P}{\partial r}(R,t) = 0, \quad P(\rho(t), t) = \frac{1}{\rho(t)}, \tag{3.5}$$

$$\rho(t) = \rho_0, \qquad -\tau \le t \le 0, \tag{3.6}$$

$$M(\rho, t) = M_0, \qquad \rho_0 \le r \le R, -\tau \le t \le 0, \tag{3.7}$$

$$\frac{d\rho}{dt} = -\frac{\partial P}{\partial r}(\rho(t), t). \tag{3.8}$$

Supposed that the radial symmetric steady-state solution of (3.1)-(3.8) is (M_*, P_*, ρ_*), which is on a small ring-region $\Omega_* = \{\rho_* < r < R\}$, then we have

$$D\Delta M_* = HM_*, \qquad \rho_* \le r \le R, \tag{3.9}$$

$$-\Delta P_* = LM_*(\xi(-\tau; r, 0)) - T, \qquad \rho_* \le r \le R, \tag{3.10}$$

$$\begin{cases} \dfrac{d\xi}{ds}(s; r, 0) = -\dfrac{\partial P_*}{\partial r}(\xi(s; r, 0), s), & -\tau \le \ s \le 0, \\ \xi(s; r, 0) = r, & s = 0, \end{cases} \tag{3.11}$$

$$M_* = 1, P_* = \frac{1}{\rho_*}, \qquad r = \rho_*, \tag{3.12}$$

$$\frac{\partial M_*}{\partial r} = -M_*, \frac{\partial P_*}{\partial r}(R,t) = 0, \qquad r = R. \tag{3.13}$$

Theorem 3.1 *For sufficiently small τ, system* (3.9)-(3.13) *admits a unique radically symmetric classical stationary solution (M_*, P_*, ρ_*).*

Proof. The proof is similar to that Lemma 3.1 of [29], so we omit it here. □

Remark 3.1 *Since it is a radially symmetric case, the solution is independent of the angle and only related to the radius. In the case of radial symmetry, the problem becomes one-dimensional. Let r be the radius of the intima, r_2 be the distance from the plaque to the fixed boundary Γ_1, and r_1 be the distance from the lumen center to the plaque. As a consequence, when r_1 exists and is unique, the existence and uniqueness of r_2 is also guaranteed. So we can quote Lemma 3.1 of [29] to prove the existence of r_1.*

4 Linear stability

In this section, we consider the stability of (2.1)-(2.5). For a small enough ε, in order to linearize (2.1)-(2.5), we let

$$\partial\Omega(t) : r = \rho_* + \varepsilon\rho_1(\theta,t) + O(\varepsilon^2), \tag{4.1}$$

$$M(r,\theta,t) = M_*(r) + \varepsilon M_1(r,\theta,t) + O(\varepsilon^2), \tag{4.2}$$

$$P(r,\theta,t) = P_*(r) + \varepsilon P_1(r,\theta,t) + O(\varepsilon^2). \tag{4.3}$$

In polar coordinate system, $\xi(s;r,\theta,t)$ in formula (2.3) can be expressed as $(\xi_1(s;r,\theta,t), \xi_2(s;r,\theta,t))$, where ξ_1 represents radius and ξ_2 represents angle. We expand ξ_1, ξ_2 in ε as

$$\begin{cases} \xi_1 = \xi_{10} + \varepsilon\xi_{11} + O(\varepsilon^2), \\ \xi_2 = \xi_{20} + \varepsilon\xi_{21} + O(\varepsilon^2), \end{cases}$$

where ξ_{ij} $(i = 1,2;\ j = 0,1)$ is calculated in [29] as follows.

$$\begin{cases} \frac{d\xi_{10}}{ds} = -\frac{\partial p_*}{\partial r}(\xi_{10}), \quad t-\tau \le s \le t, \\ \xi_{10}|_{s=t} = r; \end{cases} \qquad \begin{cases} \frac{d\xi_{11}}{ds} = -\frac{\partial^2 p_*}{\partial r^2}(\xi_{10})\xi_{11} - \frac{\partial q}{\partial r}(\xi_{10},\xi_{20},s),\ t-\tau \le s \le t, \\ \xi_{11}|_{s=t} = 0; \end{cases} \tag{4.4}$$

$$\begin{cases} \frac{d\xi_{20}}{ds} = 0, \quad t-\tau \le s \le t, \\ \xi_{20}|_{s=t} = \theta; \end{cases} \qquad \begin{cases} \frac{d\xi_{21}}{ds} = -\frac{\partial 1}{\partial(\xi_{10})^2}\frac{\partial q}{\partial\theta}(\xi_{10},\xi_{20},s), \quad t-\tau \le s \le t, \\ \xi_{21}|_{s=t} = 0; \end{cases} \tag{4.5}$$

then we substitute (4.1)-(4.5) into (2.1)-(2.5). We collect only the linear terms in ε, so we obtain the equation satisfied by the first order term of ε, namely,

$$\Delta M_1 = \frac{H}{D}M_1, \tag{4.6}$$

$$M_1(\rho_*,\theta,t) = -\frac{\partial M_*(\rho_*)}{\partial r}\rho_1(\theta,t), \tag{4.7}$$

$$\frac{\partial M_1(R)}{\partial r} = -M_1(R), \tag{4.8}$$

$$-\Delta P_1(r,\theta,t) = L\frac{\partial M_*(\xi_{10})}{\partial r}\xi_{11}(t-\tau;r,\theta,t) + LM_1(\xi_{10},t-\tau), \tag{4.9}$$

$$P_1(\rho_*,\theta,t) = -\frac{1}{\rho_*^2}\left(\rho_1(\theta,t) + \rho_{1\theta\theta}(\theta,t)\right), \tag{4.10}$$

$$\frac{\partial P_1(R)}{\partial r} = 0, \tag{4.11}$$

$$\frac{d\rho_1}{dt} = -\frac{\partial^2 P_*(\rho_*)}{\partial r^2}\rho_1(\theta,t) - \frac{\partial P_1(\rho_*)}{\partial r}. \tag{4.12}$$

In what follows, we seek solutions of the form

$$\begin{aligned} M_1(r,\theta,t) &= M_{1n}(r,t)\cos(n\theta), \\ P_1(r,\theta,t) &= P_{1n}(r,t)\cos(n\theta), \\ \rho_1(\theta,t) &= \rho_{1n}(r,t)\cos(n\theta), \\ \xi_{11}(s;r,\theta,t) &= \varphi_n(s;r,t)\cos(n\theta). \end{aligned} \tag{4.13}$$

Substituting (4.13) into (4.6)-(4.12), and using the relation $\Delta = \partial_{rr} + \frac{1}{r}\partial_r + \frac{1}{r^2}\partial_{\theta\theta}$, we obtain the following system:

$$-\frac{\partial^2 M_{1n}(r,t)}{\partial r^2} - \frac{1}{r}\frac{\partial M_{1n}(r,t)}{\partial r} + \left(\frac{n^2}{r^2} + \frac{H}{D}\right) M_{1n}(r,t) = 0, \tag{4.14}$$

$$M_{1n}(\rho_*, \theta, t) = -\frac{\partial M_*(\rho_*)}{\partial r}\rho_{1n}(\theta, t), \tag{4.15}$$

$$\frac{\partial M_{1n}(R)}{\partial r} = -M_{1n}(R), \tag{4.16}$$

$$\begin{aligned} -\frac{\partial^2 P_{1n}(r,t)}{\partial r^2} - \frac{1}{r}\frac{\partial P_{1n}(r,t)}{\partial r} + \frac{n^2}{r^2}P_{1n}(r,t) = LM_{1n}(\xi_{10}(t-\tau), t-\tau) \\ + L\frac{\partial M_*}{\partial r}(\xi_{10}(t-\tau), t-\tau)\varphi_n(t-\tau;), \end{aligned} \tag{4.17}$$

$$P_{1n}(\rho_*, t) = \frac{n^2-1}{\rho_*^2}\rho_{1n}(t), \tag{4.18}$$

$$\frac{\partial P_{1n}(R)}{\partial r} = 0, \tag{4.19}$$

$$\frac{d\rho_{1n}(t)}{dt} = -\frac{\partial^2 P_*(\rho_*)}{\partial r^2}\rho_{1n}(t) - \frac{\partial P_{1n}(\rho_*)}{\partial r}, \tag{4.20}$$

where φ_n satisfies (see [29])

$$\begin{cases} \frac{\partial \varphi_n(s;r,t)}{\partial s} = -\frac{\partial^2 P_*(\xi_{10})}{\partial r^2}\varphi_n(s;r,t) - \frac{\partial P_{1n}(\xi_{10}, s)}{\partial r}, t-\tau \le s \le t, \\ \varphi_n \mid_{s=t} = 0. \end{cases}$$

By combining the above formulas, we can derive the following theorem:

Theorem 4.1 *When $n = 0, 1$, for any $L > 0$, there exists $\delta > 0$ such that $\left|\rho_n^0(t)\right| < Ce^{-\delta t}$, $\left|\rho_{1n}^1(t)\right| < Ce^{-\delta t}$; when $n \ge 2$ and $L < L_*$, there exists $\delta > 0$ such that $\left|\rho_n^0(t)\right| < Ce^{-\delta t}$, $\left|\rho_{1n}^1(t)\right| < Ce^{-\delta t}$, for all $t > 0$, where δ is independent of n; otherwise, the stationary solution is linearly unstable.*

In order to get Theorem 4.1, we should look for the expansion in τ.

4.1 Expansion in τ

We now study the impact of τ on this system. Since the time delay τ is actually very small, we look for the expansion in τ. Let us denote

$$\begin{aligned} &\rho_* = \rho_*^0 + \tau\rho_*^1 + O(\tau^2), && M_* = M_*^0 + \tau M_*^1 + O(\tau^2), \\ &P_* = P_*^0 + \tau P_*^1 + O(\tau^2), && M_{1n} = M_{1n}^0 + \tau M_{1n}^1 + O(\tau^2), \\ &P_{1n} = P_{1n}^0 + \tau P_{1n}^1 + O(\tau^2), && \rho_{1n} = \rho_{1n}^0 + \tau\rho_{1n}^1 + O(\tau^2). \end{aligned} \tag{4.21}$$

Combining (3.9), (3.12), (3.13), then we have

$$\begin{cases} \frac{\partial^2 M_*}{\partial r^2} + \frac{1}{r}\frac{\partial M_*}{\partial r} = \frac{H}{D}M_*, & \rho_* \le r \le R, \\ M_* = 1, & r = \rho_*, \\ \frac{\partial M_*}{\partial r} = -M_*, & r = R. \end{cases}$$

Denoting $z_r = \sqrt{\frac{H}{D}}r$, we get

$$M_*(r) = C_1 I_0(z_r) + C_2 K_0(z_r),$$

where $I_0(z_r)$ is Hankel function of the first kind, and $K_0(z_r)$ is Hankel function of the second kind (see [10, 12]), and

$$C_1 = \frac{A_1}{A_1 I_0(z_{\rho_*}) + A_2 K_0(z_{\rho_*})}, \quad C_2 = \frac{A_2}{A_1 I_0(z_{\rho_*}) + A_2 K_0(z_{\rho_*})},$$

with

$$A_1 = \sqrt{\frac{H}{D}} K_1(z_R) - K_0(z_R), \quad A_2 = \sqrt{\frac{H}{D}} I_1(z_R) + I_0(z_R),$$

so we conclude

$$\begin{aligned}
M_*(r) =& \frac{A_1 I_0(z_r) + A_2 K_0(z_r)}{A_1 I_0(z_{\rho_*}) + A_2 K_0(z_{\rho_*})} = \frac{A_1 I_0(z_r) + A_2 K_0(z_r)}{A_1 I_0(z_{\rho_*^0} + \tau z_{\rho_*^1}) + A_2 K_0(z_{\rho_*^0} + \tau z_{\rho_*^1})} \\
=& \frac{A_1 I_0(z_r) + A_2 K_0(z_r)}{A_1 \left[I_0(z_{\rho_*^0}) + \tau \frac{\partial I_0(z_{\rho_*^0})}{\partial r} z_{\rho_*^1} \right] + A_2 \left[K_0(z_{\rho_*^0}) + \tau \frac{\partial K_0(z_{\rho_*^0})}{\partial r} z_{\rho_*^1} \right]} \\
=& \frac{A_1 I_0(z_r) + A_2 K_0(z_r)}{A_1 I_0(z_{\rho_*^0}) + A_2 K_0(z_{\rho_*^0}) + \tau \left[A_1 \frac{\partial I_0(z_{\rho_*^0})}{\partial r} z_{\rho_*^1} + A_2 \frac{\partial K_0(z_{\rho_*^0})}{\partial r} z_{\rho_*^1} \right]} \\
=& \frac{A_1 I_0(z_r) + A_2 K_0(z_r)}{A_1 I_0(z_{\rho_*^0}) + A_2 K_0(z_{\rho_*^0})} - \tau \frac{\left[A_1 I_1(z_{\rho_*^0}) - A_2 K_1(z_{\rho_*^0}) \right] \left[A_1 I_0(z_r) + A_2 K_0(z_r) \right]}{\left[A_1 I_0(z_{\rho_*^0}) + A_2 K_0(z_{\rho_*^0}) \right]^2} z_{\rho_*^1} + O(\tau^2) \\
=& M_*^0(r) + \tau M_*^1(r),
\end{aligned}$$

thereby

$$M_*^0(r) = M_*(r; \rho_*^0) = \frac{A_1 I_0(z_r) + A_2 K_0(z_r)}{A_1 I_0(z_{\rho_*^0}) + A_2 K_0(z_{\rho_*^0})}, \tag{4.22}$$

$$M_*^1(r) = -\frac{\left[A_1 I_1(z_{\rho_*^0}) - A_2 K_1(z_{\rho_*^0}) \right] \left[A_1 I_0(z_r) + A_2 K_0(z_r) \right]}{\left[A_1 I_0 z_{\rho_*^0} + A_2 K_0 z_{\rho_*^0} \right]^2} z_{\rho_*^1}. \tag{4.23}$$

In what follows, we calculate P_*. For equation (3.11), integrating from $-\tau$ to 0 on both sides, then we get

$$r - \xi(-\tau; r, 0) = \int_{-\tau}^{0} \left(-\frac{\partial P_*(\xi(s; r, 0))}{\partial r} \right) ds,$$

so

$$M_*(\xi(-\tau; r, 0)) = M_*^0(r) + \tau \left(\frac{\partial M_*^0(r)}{\partial r} \frac{\partial P_*^0(r)}{\partial r} + M_*^1(r) \right) + O(\tau^2). \tag{4.24}$$

From (3.10), we know

$$-\Delta(P_*^0+\tau P_*^1) = L\left[M_*^0(\xi(s;r,0))+\tau M_*^1(\xi(s;r,0))\right]-T.$$

We then derive the equation for P_*^0 and P_*^1,

$$-\frac{\partial^2 P_*^0}{\partial r^2}-\frac{1}{r}\frac{\partial P_*^0}{\partial r} = LM_*^0(r)-T, \tag{4.25}$$

$$-\frac{\partial^2 P_*^1}{\partial r}-\frac{1}{r}\frac{\partial P_*^1}{\partial r} = L\left[\frac{\partial M_*^0(r)}{\partial r}\frac{\partial P_*^0(r)}{\partial r}+M_*^1(r)\right], \tag{4.26}$$

with the boundary condition

$$P_*^0(\rho_*^0)=\frac{1}{\rho_*^0},\, P_*^1(\rho_*^0)=-\frac{\rho_*^1}{(\rho_*^0)^2}-\frac{\partial P_*^0(\rho_*^0)}{\partial r}\rho_*^1, \tag{4.27}$$

$$\frac{\partial P_*^0}{\partial r}(R,t)=0,\, \frac{\partial P_*^1}{\partial r}(R,t)=0. \tag{4.28}$$

Similarly, by substituting the expression of M_{1n} into (4.14), we get that M_{1n}^0, M_{1n}^1 and (4.14) satisfy the same formula. We then expand (4.15) to get

$$M_{1n}^0(\rho_*^0+\tau\rho_*^1,t)+\tau M_{1n}^1(\rho_*^0,t) = -\left(\frac{\partial M_*^0}{\partial r}(\rho_*^0+\tau\rho_*^1)+\tau\frac{\partial M_*^1}{\partial r}(\rho_*^1)\right)(\rho_{1n}^0(t)+\tau\rho_{1n}^1(t))+O(\tau^2), \tag{4.29}$$

so we can obtain that M_{1n}^0 and M_{1n}^1, respectively, satisfy

$$M_{1n}^0(\rho_*^0,t) = -\frac{\partial M_*^0}{\partial r}(\rho_*^0)\rho_{1n}^0(t), \tag{4.30}$$

$$M_{1n}^1(\rho_*^0,t) = -\frac{\partial M_{1n}^1(\rho_*^0)(\rho_*^0)}{\partial r}\rho_*^1-\frac{\partial M_*^0(\rho_*^0)}{\partial r}\rho_{1n}^1(t)-\frac{\partial^2 M_*^0(\rho_*^0)}{\partial r^2}\rho_*^1\rho_{1n}^0-\frac{\partial M_*^1(\rho_*^0)}{\partial r}\rho_{1n}^0(t). \tag{4.31}$$

Similarly, expanding (4.16), we find

$$\frac{\partial M_{1n}^0(R)}{\partial r} = -M_{1n}^0(R), \tag{4.32}$$

$$\frac{\partial M_{1n}^1(R)}{\partial r} = -M_{1n}^1(R). \tag{4.33}$$

Noting that (see [29])

$$\varphi_n(t-\tau;r,t) = \varphi_n(t;r,t)+\frac{\partial\varphi_n}{\partial s}(t;r,t)(-\tau)+O(\tau^2) = \tau\frac{\partial P_{1n}^0}{\partial r}(r,t)+O(\tau^2), \tag{4.34}$$

and using (4.24),

$$\begin{aligned}\frac{\partial M_*}{\partial r}\left(\xi_{10}(t-\tau;r,t),t-\tau\right)\varphi_n(t-\tau;r,t) &= \left(\frac{\partial M_*(r)}{\partial r}+O(\tau)\right)\left(\tau\frac{\partial P_{1n}^0}{\partial r}(r,t)+O(\tau^2)\right)\\ &= \tau\frac{\partial M_*}{\partial r}(r)\frac{\partial P_{1n}^0}{\partial r}(r,t)+O(\tau^2),\end{aligned} \tag{4.35}$$

we deduce,

$$
\begin{aligned}
&M_{1n}^0(\xi_{10}(t-\tau;r,t),t-\tau)\\
=&M_{1n}^0(\xi_{10}(t-\tau;r,t),t-\tau)+\tau M_{1n}^1(r,t)+O(\tau^2)\\
=&M_{1n}^0\left(r+\int_{t-\tau}^t\frac{\partial P_*}{\partial r}(\xi_{10}(s;r,t))ds,t-\tau\right)+\tau M_{1n}^1(r,t)+O(\tau^2)\\
=&M_{1n}^0(r,t)+\tau\left[\frac{\partial M_{1n}^0(r,t)}{\partial r}\frac{\partial P_*(r)}{\partial r}-\frac{\partial M_{1n}^0}{\partial t}(r,t)+M_{1n}^1(r,t)\right]+O(\tau^2).
\end{aligned}
\tag{4.36}
$$

By substituting equations (4.34)-(4.36) into equation (4.17), we drive equations for P_{1n}^0 and P_{1n}^1, respectively,

$$
-\frac{\partial^2 P_{1n}^0}{\partial r^2}-\frac{1}{r}\frac{\partial P_{1n}^0}{\partial r}+\frac{n^2}{r^2}P_{1n}^0=LM_{1n}^0, \tag{4.37}
$$

$$
-\frac{\partial^2 P_{1n}^1}{\partial r^2}-\frac{1}{r}\frac{\partial P_{1n}^1}{\partial r}+\frac{n^2}{r^2}P_{1n}^1=L\frac{\partial M_*^0}{\partial r}\frac{\partial P_{1n}^0}{\partial r}+L\frac{\partial M_{1n}^0}{\partial r}\frac{\partial P_*^0}{\partial r}-L\frac{\partial M_{1n}^0}{\partial t}+LM_{1n}^1, \tag{4.38}
$$

with boundary condition from (4.18) and (4.19), we have

$$
P_{1n}^0(\rho_*^0,t)=\frac{n^2-1}{(\rho_*^0)^2}\rho_{1n}^0(t), \tag{4.39}
$$

$$
P_{1n}^1(\rho_*^0,t)=-\frac{\partial P_{1n}^0}{\partial r}(\rho_*^0,t)\rho_*^1+\frac{n^2-1}{(\rho_*^0)^2}\rho_{1n}^1(t)-\frac{2(n^2-1)\rho_*^1}{(\rho_*^0)^3}\rho_{1n}^0(t), \tag{4.40}
$$

$$
\frac{\partial P_{1n}^0(R)}{\partial r}=0, \tag{4.41}
$$

$$
\frac{\partial P_{1n}^1(R)}{\partial r}=0. \tag{4.42}
$$

Next, we substitute (4.21) into (4.20) to get

$$
\begin{aligned}
\frac{d(\rho_{1n}^0+\tau\rho_{1n}^1)}{dt}=&-\frac{\partial^2\left[P_*^0(\rho_*^0+\tau\rho_*^1)+\tau P_*^1(\rho_*^0+\tau\rho_*^1)\right]}{\partial r^2}\left[\rho_{1n}^0(t)+\tau\rho_{1n}^1(t)\right]\\
&-\frac{\partial\left[P_{1n}^0(\rho_*^0+\tau\rho_*^1)+\tau P_{1n}^1(\rho_*^0+\tau\rho_*^1)\right]}{\partial r},
\end{aligned}
$$

which implies that

$$
\frac{d\rho_{1n}^0(t)}{dt}=-\frac{\partial^2 P_*^0(\rho_*^0)}{\partial r^2}\rho_{1n}^0(t)-\frac{\partial P_{1n}^0}{\partial r}(\rho_*^0,t), \tag{4.43}
$$

$$
\begin{aligned}
\frac{d\rho_{1n}^1(t)}{dt}=&-\frac{\partial^2 P_*^0(\rho_*^0)}{\partial r^2}\rho_{1n}^1(t)-\frac{\partial^3 P_*^0(\rho_*^0)}{\partial r^3}\rho_*^1\rho_{1n}^0(t)-\frac{\partial^2 P_*^1(\rho_*^0)}{\partial r}\rho_{1n}^0(t)\\
&-\frac{\partial^2 P_{1n}^0}{\partial r^2}(\rho_*^0,t)\rho_*^1-\frac{\partial P_{1n}^1}{\partial r}(\rho_*^0,t).
\end{aligned}
\tag{4.44}
$$

4.2 Zeroth-order terms in τ

Combining with formula (4.22), (4.25), (4.27), (4.28), (4.30), (4.32), (4.37), (4.39), (4.41) and (4.43), we obtain the zeroth-order term system of τ

$$
\Delta M_*^0=\frac{H}{D}M_*^0,\quad M_*^0(\rho_*^0)=1,\quad \frac{\partial M_*^0(R)}{\partial r}=M_*^0, \tag{4.45}
$$

$$-\frac{\partial^2 P_*^0}{\partial r^2}-\frac{1}{r}\frac{\partial P_*^0}{\partial r}=LM_*^0(r)-T,\quad P_*^0(\rho_*^0)=\frac{1}{\rho_*^0},\quad \frac{\partial P_*^0(R)}{\partial r}=0, \tag{4.46}$$

$$\begin{cases}-\dfrac{\partial^2 M_{1n}^0}{\partial r^2}-\dfrac{1}{r}\dfrac{\partial M_{1n}^0}{\partial r}+\left(\dfrac{n^2}{r^2}+\dfrac{H}{D}\right)M_{1n}^0=0,\\ M_{1n}^0(\rho_*^0,t)=-\dfrac{\partial M_*^0}{\partial r}(\rho_*)\rho_{1n}^0(t),\quad \dfrac{\partial M_{1n}^0(R,t)}{\partial r}=-M_{1n}^0(R,t),\end{cases} \tag{4.47}$$

$$-\frac{\partial^2 P_{1n}^0}{\partial r^2}-\frac{1}{r}\frac{\partial P_{1n}^0}{\partial r}+\frac{n^2}{r^2}P_{1n}^0=LM_{1n}^0,\quad P_{1n}^0(\rho_*^0,t)=\frac{n^2-1}{(\rho_*^0)^2}\rho_{1n}^0(t),\quad \frac{\partial P_{1n}^0(R)}{\partial r}=0, \tag{4.48}$$

$$\frac{d\rho_{1n}^0(t)}{dt}=-\frac{\partial^2 P_*^0(\rho_*^0)}{\partial r^2}\rho_{1n}^0(t)-\frac{\partial P_{1n}^0}{\partial r}(\rho_*^0,t). \tag{4.49}$$

From (4.45), (4.46), we know

$$M_*^0(r)=\frac{A_1I_0(z_r)+A_2K_0(z_r)}{A_1I_0(z_{\rho_*^0})+A_2K_0(z_{\rho_*^0})},$$

$$P_*^0(r)=-\frac{DL}{H}M_*^0(r)+A_3\ln r+A_4+\frac{1}{4}Tr^2,$$

where (see [12])

$$\begin{aligned}A_3&=\frac{DL}{H}\frac{R^2(\rho_*^0)^2}{R^2-(\rho_*^0)^2}\left(\frac{(M_*^0(\rho_*^0))'}{\rho_*^0}+\frac{M_*^0(R)}{R}\right),\\ A_4&=\frac{1}{\rho_*^0}+\frac{DL}{H}-A_3\ln\rho_*^0-\frac{1}{4}T(\rho_*^0)^2,\\ T&=-\frac{DL}{H}\frac{2}{R^2-(\rho_*^0)^2}(RM_*^0(R)+\rho_*^0(M_*^0(\rho_*^0))').\end{aligned}$$

Our mean calculation is the formula of (4.49). In fact, from (4.46), we have

$$-\frac{\partial^2 P_*^0(\rho_*^0+\tau\rho_*^1)}{\partial r^2}-\frac{1}{r}\frac{\partial P_*^0(\rho_*^0+\tau\rho_*^1)}{\partial r}=LM_*^0(\rho_*^0+\tau\rho_*^1)-T,$$

so

$$-\frac{\partial^2 P_*^0(\rho_*^0)}{\partial r^2}=LM_*^0(\rho_*^0)-T$$

i.e.

$$\frac{\partial^2 P_*^0(\rho_*^0)}{\partial r^2}=T(L)-L. \tag{4.50}$$

In what follows, we calculate $\dfrac{\partial P_{1n}^0(\rho_*^0,t)}{\partial r}$. Let

$$\eta_n^0=P_{1n}^0+\frac{DL}{H}M_{1n}^0,$$

then

$$P_{1n}^0 = \eta_n^0 - \frac{DL}{H} M_{1n}^0, \tag{4.51}$$

$$-\frac{\partial^2 \eta_n^0}{\partial r^2} - \frac{1}{r}\frac{\partial \eta_n^0}{\partial r} + \frac{n^2}{r^2}\eta_n^0 = 0,$$

we get

$$\eta_n^0 = C_1(t) r^n + C_2(t) r^{-n}.$$

Substituting boundary condition, we obtain

$$\begin{aligned} P_{1n}^0(\rho_*^0, t) &= \frac{n^2-1}{(\rho_*^0)^2}\rho_{1n}^0(t), \\ \frac{\partial P_{1n}^0(R)}{\partial r} &= 0, \end{aligned}$$

so

$$C_1(t)(\rho_*^0)^n + C_2(t)(\rho_*^0)^{-n} - \frac{DL}{H} M_{1n}^0(\rho_*^0) = \frac{n^2-1}{(\rho_*^0)^2}\rho_{1n}^0(t), \tag{4.52}$$

$$C_1(t) n R^{n-1} - C_2(t) n R^{-n-1} - \frac{DL}{H}\frac{\partial M_{1n}^0(R)}{\partial r} = 0. \tag{4.53}$$

In order to get $C_1(t)$ and $C_2(t)$ from (4.52), (4.53), we first calculate $\dfrac{\partial M_{1n}^0(R)}{\partial r}$, and then calculate M_{1n}^0 from (4.47), it follows that

$$-\frac{\partial^2 M_{1n}^0}{\partial r^2} - \frac{1}{r}\frac{\partial M_{1n}^0}{\partial r} + \left(\frac{n^2}{r^2} + \frac{H}{D}\right) M_{1n}^0 = 0,$$

that means

$$M_{1n}^0 = B_1 I_n(z_r) + B_2 K_n(z_r).$$

Substituting boundary conditions, then

$$\begin{aligned} M_{1n}^0(\rho_*^0, t) &= -\frac{\partial M_*^0(\rho_*^0)}{\partial r}\rho_{1n}^0(t), \\ \frac{\partial M_{1n}^0(R,t)}{\partial r} &= -M_{1n}^0(R,t). \end{aligned}$$

In consequence

$$B_1 I_n(z_{\rho_*^0}) + B_2 K_n(z_{\rho_*^0}) = -\left[M_*^0(\rho_*^0)\right]\rho_{1n}^0(t), \tag{4.54}$$

$$B_1 I_n(z_R) + B_2 K_n(z_R) = -B_1 I_n'(z_R) - B_2 K_n'(z_R). \tag{4.55}$$

Combine (4.54), (4.55), we get

$$B_1 = -\frac{[M_*^0(\rho_*^0)]'}{I_n z(\rho_*^0) + K K_n(z_{\rho_*^0})}\rho_{1n}^0(t) = \tilde{B}_1 \rho_{1n}^0(t),$$

$$B_2 = -\frac{K[M_*^0(\rho_*^0)]'}{I_n z(\rho_*^0) + KK_n(z_{\rho_*^0})}\rho_{1n}^0(t) = \tilde{B}_2\rho_{1n}^0(t),$$

where

$$K = -\frac{I_n(z_R) + I_n'(z_R)}{K_n(z_R) + K_n'(z_R)}, \tag{4.56}$$

as a result

$$M_{1n}^0(r) = [\tilde{B}_1 I_n(z_r) + \tilde{B}_2 K_n(z_r)]\rho_{1n}^0(t) = Q_n(r)\rho_{1n}^0(t). \tag{4.57}$$

Next, we go back to (4.52) and (4.53) to obtain

$$\begin{cases} C_1(t)nR^{-n-1}(\rho_*^0)^n + C_2(t)nR^{-n-1}(\rho_*^0)^{-n} - \frac{DL}{H}M_{1n}^0(\rho_*^0)nR^{-n-1} = \frac{n^2-1}{(\rho_*^0)^2}nR^{-n-1}\rho_{1n}^0(t), \\ C_1(t)nR^{n-1}(\rho_*^0)^{-n} - C_2(t)nR^{-n-1}(\rho_*^0)^{-n} - \frac{DL}{H}(\rho_*^0)^{-n}\frac{\partial M_{1n}^0(R)}{\partial r} = 0. \end{cases}$$

Adding two equations and then

$$C_1(t) = \frac{n(n^2-1)(\rho_*^0)^{n-2} - \frac{DL}{H}\left[Q_n(R)R^{n+1} - Q_n(\rho_*^0)n(\rho_*^0)^n\right]}{n\left[(\rho_*^0)^{2n} + R^{2n}\right]}\rho_{1n}^0(t), \tag{4.58}$$

$$C_2(t) = \left[C_1(t)R^{2n} + \frac{DL}{H}Q_n(R)\frac{R^{n+1}}{n}\right]\rho_{1n}^0(t). \tag{4.59}$$

We mark the right hand of (4.58) and (4.59) as $\tilde{C}_1\rho_{1n}^0(t)$ and $\tilde{C}_2\rho_{1n}^0(t)$ respectively. From (4.51), we get

$$P_{1n}^0(r) = C_1(t)r^n + C_2(t)r^{-n} - \frac{DL}{H}M_{1n}^0. \tag{4.60}$$

Now, we take derivation of (4.60),

$$\frac{\partial P_{1n}^0}{\partial r} = nC_1(t)r^{n-1} - nC_2(t)r^{-n-1} - \frac{DL}{H}\frac{\partial M_{1n}^0}{\partial r},$$

thus

$$\frac{\partial P_{1n}^0(\rho_*^0, t)}{\partial r} = \left[n\tilde{C}_1(\rho_*^0)^{n-1} - n\tilde{C}_2(\rho_*^0)^{-n-1} - \frac{DL}{H}\frac{\partial Q_n(\rho_*^0)}{\partial r}\right]\rho_{1n}^0(t).$$

Substituting formula (4.50), (4.51) into formula (4.49), then we obtain

$$\begin{aligned} \frac{d\rho_{1n}^0(t)}{dt} &= -\frac{\partial^2 P_*^0(\rho_*^0)}{\partial r^2}\rho_{1n}^0(\rho_*^0, t) - \frac{\partial P_{1n}^0(\rho_*^0, t)}{\partial r} \\ &= \left(-[T(L) - L] - \left(n\tilde{C}_1(\rho_*^0)^{n-1} - n\tilde{C}_2(\rho_*^0)^{-n-1} - \frac{DL}{H}\frac{\partial Q_n(\rho_*^0)}{\partial r}\right)\right)\rho_{1n}^0(t) \\ &= \left(L - T + \frac{DL}{H}\frac{\partial Q_n(\rho_*^0)}{\partial r} - n\tilde{C}_1(\rho_*^0)^{n-1} + n\tilde{C}_2(\rho_*^0)^{-n-1}\right)\rho_{1n}^0(t), \end{aligned}$$

hence

$$\rho_{1n}^0(t) = \rho_{1n}^0(0)e^{\left(L - T + \frac{DL}{H}\frac{\partial Q_n(\rho_*^0)}{\partial r} - n\tilde{C}_1(\rho_*^0)^{n-1} + n\tilde{C}_2(\rho_*^0)^{-n-1}\right)t}. \tag{4.61}$$

Lemma 4.1 *([12]) For given $R > 0$, ρ is a neighbor of R, namely, $\rho = R - \varepsilon$ for a small $\varepsilon, C_2(n, \rho, R) > 0$ is decreasing with respect to n.*

We study the properties of the index part of (4.61) below.

$$
\begin{aligned}
& L - T + \frac{DL}{H}\frac{\partial Q_n(\rho_*^0)}{\partial r} - n\tilde{C}_1(\rho_*^0)^{n-1} + n\tilde{C}_2(\rho_*^0)^{-n-1} \\
=& \frac{DL}{H}\frac{2}{R^2-(\rho_*^0)^2}\left(RM_*(R) + \rho_*^0[M_*(\rho_*^0)]'\right) + L + \frac{DL}{H}Q_n'(\rho_*^0) + 2\frac{\frac{DL}{H}Q_n(R)R^{n+1}}{(\rho_*^0)^{2n}+R^{2n}}\rho^{n-1} \\
& - \frac{(n^3-n)(\rho^{2n}-R^{2n})}{(\rho_*^0)^3[(\rho_*^0)^{2n}+R^{2n}]} - n\frac{DL}{H}\frac{(\rho_*^0)^{2n}-R^{2n}}{\rho_*^0[(\rho_*^0)^{2n}+R^{2n}]}Q_n(\rho),
\end{aligned}
$$

when $n=0$, remember $E(n,\rho_*^0,R,L) = C_2(n,\rho_*^0,R)L$

$$
\left[\frac{D}{H}\frac{2}{R^2-(\rho_*^0)^2}(RM_*(R)) + \rho_*^0[M_*(\rho_*^0)]' + 1 + \frac{D}{H}Q_n'(\rho_*^0) + \frac{D}{H}\frac{2R^{n+1}(\rho_*^0)^nQ_n(R) + n(R^{2n}-(\rho_*^0)^{2n})}{\rho_*^0[(\rho_*^0)^{2n}+R^{2n}]}\right]L.
$$

From Lemma 4.1, it is easy to know $C_2(n,\rho_*^0,R)<0$ and that $C_2(n,\rho_*^0,R)$ is monotonically decreasing with respect to n. Therefore $E(n,\rho_*^0,R,L)<0$ is decreasing with respect to n as well, as a result when $n=0$, we get

$$
\rho_{10}^0(t) = \rho_{10}^0(0)e^{E(0,\rho_*^0,R,L)t} \to 0.
$$

Similarly, when $n=1$,

$$
\rho_{11}^0(t) = \rho_{11}^0(0)e^{E(1,\rho_*^0,R,L)t} \to 0.
$$

When $n \geq 2$, we define L_n as the solution of the following formula

$$
E(n,\rho,R,L) - \frac{(n^3-n)((\rho_*^0)^{2n}-R^{2n})}{(\rho_*^0)^3[(\rho_*^0)^{2n}+R^{2n}]} = 0,
$$

as a consequence

$$
L_n = \frac{\frac{n(n^2-1)[(\rho_*^0)^{2n}-R^{2n}]}{(\rho_*^0)^3[(\rho_*^0)^{2n}+R^{2n}]}}{C_2(n,\rho_*^0,R)},
$$

when $n\geq 2$, $L_n>0$ and on monotonic increasing of n, i.e. $L_2<L_3<...<L_n$. Since $n=0,1$ is true for all L, we define $L_0=L_1=\infty$, and let $L_* = \min\{L_0,L_1,L_2,L_3,...\}$, it is easy to know $L_*=L_2$. As for $n\leq 2$, and $L<L_*$, we have

$$
\exists\,\delta>0\,,\ s.t. \left|\rho_{1n}^0(t)\right| \leq \left|\rho_{1n}^0\right| e^{-\delta n^3 t}, \quad for\ all\ t>0,
$$

$$
L\,C_2(n,\rho_*^0,R) - \frac{n(n^2-1)[(\rho_*^0)^{2n}-R^{2n}]}{(\rho_*^0)^3[(\rho_*^0)^{2n}+R^{2n}]} < -\delta_1 n^3.
$$

For sufficiently large n, there exists the corresponding $\delta_n n^3>0$, for each $n\in[2,n_0]$, s.t.

$$
L\,C_2(n,\rho_*^0,R) - \frac{n(n^2-1)[(\rho_*^2)^2-R^{2n}]}{(\rho_*^0)^3[(\rho_*^0)^{2n}+R^{2n}]} < -\delta_n n^3.
$$

Let $0<\delta<\min\{\delta_1,\delta_2,...\delta_{n_0}\}$, as a result we have

$$
\left|\rho_n^0(t)\right| \leq \left|\rho_n^0\right| e^{-\delta n^3 t}, \quad t>0.
$$

So far, we have completed the proof of the first part of Theorem 4.1.

4.3 Calculate of ρ_*^1

Since $\rho_* = \rho_*^0 + \tau\rho_*^1 + O(\tau^2)$, we would like to know how the time delay τ affects the size of the tumor ρ_*, thus we are interested in the sign of ρ_*^1.

Theorem 4.2 *$\rho_*^1 > 0$, which means adding the time delay in the model would result in a smaller stationary tumor.*

Proof. From (3.10) $-\Delta P = f$, multiplying r on both sides and then integrating, we get

$$\frac{\partial P_*(R)}{\partial r}R - \frac{\partial P_*(\rho_*)}{\partial r}\rho_* = -\int_{\rho_*}^{R}(LM_*(\xi(-\tau;r,0)) - T)rdr. \tag{4.62}$$

From the boundary condition (3.13), we get $\frac{\partial P_*(R)}{\partial r}R - \frac{\partial P_*(\rho_*)}{\partial r}\rho_* = 0$, so (4.62) becomes

$$\int_{\rho_*}^{R}(LM_*(\xi(-\tau;r,0)) - T)rdr = 0, \tag{4.63}$$

Because

$$\begin{aligned} M_*(\xi(-\tau;r,0)) &= M_*\left(r + \tau\frac{\partial P_*^0}{\partial r} + O(\tau^2)\right) \\ &= M_*^0\left(r + \tau\frac{\partial P_*^0}{\partial r}\right) + \tau M_*^1\left(r + \tau\frac{\partial P_*^0}{\partial r}\right) \\ &= M_*^0(r) + \tau\left(\frac{\partial M_*^0(r)}{\partial r}\frac{\partial P_*^0(r)}{\partial r} + M_*^1(r)\right), \end{aligned}$$

so

$$M_*(\xi(-\tau;r,0)) = M_*^0(r) + \tau\left(\frac{\partial M_*^0(r)}{\partial r}\frac{\partial P_*^0(r)}{\partial r} + M_*^1(r)\right). \tag{4.64}$$

Substituting (4.64) into (4.63), we get

$$\int_{\rho_*}^{R} L\left[M_*^0(r) + \tau\left(\frac{\partial M_*^0(r)}{\partial r}\frac{\partial P_*^0(r)}{\partial r}\right) + O(\tau^2)\right]rdr - \frac{1}{2}T[R^2 - (\rho_*)^2] = 0. \tag{4.65}$$

For the first term of (4.65), substituting (4.22) into it, then we get

$$\begin{aligned} \int_{\rho_*}^{R} LM_*^0(r)rdr &= \frac{L}{A_1I_0(z_{\rho_*^0}) + A_2K_0(z_{\rho_*^0})}\int_{\rho_*}^{R}\left[A_1I_0(z_r) + A_2K_0(z_r)\right]rdr \\ &= \frac{L}{A_1I_0(z_{\rho_*^0}) + A_2K_0(z_{\rho_*^0})}\frac{D}{H}\int_{\rho_*}^{R}[A_1I_0(z_r) + A_2K_0(z_r)]z_rdz_r. \end{aligned} \tag{4.66}$$

Owing to

$$xI_0(x) = \frac{d}{dx}\left[xI_1(x)\right], \qquad xK_0(x) = \frac{d}{dx}\left[-xK_1(x)\right]. \tag{4.67}$$

Substituting (4.67) into (4.66), we get

$$\int_{\rho_*}^{R} LM_*^0(r)rdr = \frac{DL}{H}\frac{z_R[A_1I_1(z_R) - A_2K_1(z_R)]}{A_1I_0(z_{\rho_*^0}) + A_2K_0(z_{\rho_*^0})} - \frac{DL}{H}\frac{z_{\rho_*}[A_1I_1(z_{\rho_*}) - A_2K_1(z_{\rho_*})]}{A_1I_0(z_{\rho_*^0}) + A_2K_0(z_{\rho_*^0})}$$

$$=\frac{DLR}{H}\frac{\partial M_*^0(R)}{\partial r}-\frac{DL}{H}\frac{(z_{\rho_*^0}+\tau z_{\rho_*^1})[A_1I_1(z_{\rho_*^0}+\tau z_{\rho_*^0})-A_2K_1(z_{\rho_*^0}+\tau z_{\rho_*^0})]}{A_1I_1(z_{\rho_*^0})+A_2K_1(z_{\rho_*^0})}$$

$$=\frac{DLR}{H}\frac{\partial M_*^0(R)}{\partial r}-\frac{DL}{H}\frac{(z_{\rho_*^0}+\tau z_{\rho_*^1})\left[\left(A_1I_1(z_{\rho_*^0})+\tau A_1\frac{\partial I_1(z_{\rho_*^0})}{\partial r}z_{\rho_*^1}\right)-\left(A_2K_1(z_{\rho_*^0})+\tau A_2\frac{\partial K_1(z_{\rho_*^0})}{\partial r}z_{\rho_*^1}\right)\right]}{A_1I_0(z_{\rho_*^0})+A_2K_0(z_{\rho_*^0})}$$

$$=\frac{DLR}{H}\frac{\partial M_*^0(R)}{\partial r}-\frac{DL}{H}\frac{(z_{\rho_*^0}+\tau z_{\rho_*^1})\left(A_1I_1(z_{\rho_*^0})-A_2K_1(z_{\rho_*^0})+\tau z_{\rho_*^1}\left[A_1\frac{\partial I_1(z_{\rho_*^0})}{\partial r}-A_2\frac{\partial K_1(z_{\rho_*^0})}{\partial r}\right]\right)}{A_1I_0(z_{\rho_*^0})+A_2K_0(z_{\rho_*^0})}$$

$$=\frac{DLR}{H}\frac{\partial M_*^0(R)}{\partial r}-\frac{DL}{H}\frac{z_{\rho_*^0}\left[A_1I_1(z_{\rho_*^0})-A_2K_1(z_{\rho_*^0})\right]}{A_1I_0(z_{\rho_*^0})+A_2K_0(z_{\rho_*^0})}+\tau\frac{\left[z_{\rho_*^0}z_{\rho_*^1}\left(A_1\frac{\partial I_1(z_{\rho_*^0})}{\partial r}-A_2\frac{\partial K_1(z_{\rho_*^0})}{\partial r}\right)\right]}{A_1I_0(z_{\rho_*^0})+A_2K_0(z_{\rho_*^0})}$$

$$+\tau\frac{\left[z_{\rho_*^1}(A_1I_1(z_{\rho_*^0})-A_2K_1(z_{\rho_*^0}))\right]}{A_1I_0(z_{\rho_*^0})+A_2K_0(z_{\rho_*^0})}.$$

Therefore, the above formula is

$$\begin{aligned}\int_{\rho_*}^{R}LM_*^0(r)rdr=&\frac{DLR}{H}\frac{\partial M_*^0(R)}{\partial r}-\frac{DL\rho_*^0}{H}\frac{\partial M_*^0(\rho_*^0)}{\partial r}\\&+\tau\frac{DL}{H}\rho_*^1\left[\frac{\frac{H}{D}\rho_*^0\left(A_1\frac{\partial I_1(z_{\rho_*^0})}{\partial r}-A_2\frac{\partial K_1(z_{\rho_*^0})}{\partial r}\right)+\sqrt{\frac{H}{D}}\left(A_1I_1(z_{\rho_*^0})-A_2K_1(z_{\rho_*^0})\right)}{A_1I_0(z_{\rho_*^0})+A_2K_0(z_{\rho_*^0})}\right]\\=&\frac{DL}{H}R\frac{\partial M_*^0(R)}{\partial r}-\frac{DL}{H}\rho_*^0\frac{\partial M_*^0(\rho_*^0)}{\partial r}+\tau\frac{DL}{H}z_{\rho_*^1}\left\{\rho_*^0\left[\frac{\partial M_*^0(\rho_*^0)}{\partial r}\right]'+\left[\frac{\partial M_*^0(\rho_*^0)}{\partial r}\right]\right\}.\end{aligned}\tag{4.68}$$

Substituting (4.68) into (4.65), we have

$$\begin{aligned}&\frac{DL}{H}R\frac{\partial M_*^0}{\partial r}-\frac{DL}{H}\rho_*^0\frac{\partial M_*^0(\rho_*^0)}{\partial r}+\tau\left\{\frac{DL}{H}\rho_*^1\left[\rho_*^0\left(\frac{\partial M_*^0(\rho_*^0)}{\partial r}\right)'+\left(\frac{\partial M_*^0(\rho_*^0)}{\partial r}\right)\right]\right.\\&\left.+\int_{\rho_*}^{R}\left(\frac{\partial M_*^0(r)}{\partial r}\frac{\partial P_*^0(r)}{\partial r}+M_*^1(r)\right)rdr\right\}-\frac{1}{2}T[R^2-(\rho_*)^2]=0.\end{aligned}\tag{4.69}$$

Expanding the fourth item in (4.69), we get

$$\frac{1}{2}T[R^2-(\rho_*)^2]=\frac{1}{2}T[R^2-(\rho_*^0+\tau\rho_*^1)^2]=\frac{1}{2}T[R^2-(\rho_*^0)^2-2\tau\rho_*^0\rho_*^1+O(\tau^2)].\tag{4.70}$$

Substituting formula (4.70) into formula (4.69), we get

$$
\begin{aligned}
&\frac{DL}{H}R\frac{\partial M_*^0}{\partial r} - \frac{DL}{H}\rho_*^0\frac{\partial M_*^0(\rho_*^0)}{\partial r} + \tau\left\{\frac{DL}{H}\rho_*^1\left[\rho_*^0\left(\frac{\partial M_*^0(\rho_*^0)}{\partial r}\right)' + \left(\frac{\partial M_*^0(\rho_*^0)}{\partial r}\right)\right]\right. \\
&\left. + \int_{\rho_*}^{R}\left(\frac{\partial M_*^0(r)}{\partial r}\frac{\partial P_*^0(r)}{\partial r} + M_*^1(r)\right)rdr + T\rho_*^0\rho_*^1\right\} - \frac{1}{2}T[R^2 - (\rho_*^0)^2] = 0.
\end{aligned}
\tag{4.71}
$$

In the formula of (4.71), the zero-order term of τ and the first-order term of τ, respectively, meets

$$
\frac{DL}{H}R\frac{\partial M_*^0(R)}{\partial r} - \frac{DL}{H}\rho_*^0\frac{\partial M_*^0(\rho_*^0)}{\partial r} = \frac{1}{2}T[R^2 - (\rho_*^0)^2],
$$

$$
\frac{DL}{H}\rho_*^1\left\{\rho_*^0\left(\frac{\partial M_*^0(\rho_*^0)}{\partial r}\right)' + \left(\frac{\partial M_*^0(\rho_*^0)}{\partial r}\right)\right\} + \int_{\rho_*}^{R}\left(\frac{\partial M_*^0(r)}{\partial r}\frac{\partial P_*^0(r)}{\partial r} + M_*^1(r)\right)rdr + T\rho_*^0\rho_*^1 = 0.
\tag{4.72}
$$

As for the first item of (4.72), we have

$$
\frac{DL}{H}\rho_*^1\left\{\rho_*^0\left[\frac{\partial M_*^0(\rho_*^0)}{\partial r}\right]' + \left[\frac{\partial M_*^0(\rho_*^0)}{\partial r}\right]\right\} = \frac{DL}{H}\rho_*^1\left[r\frac{\partial M_*^0(r)}{\partial r}\right]'\Bigg|_{\rho_*^0}. \tag{4.73}
$$

In the second item of (4.72), we substitute into formula (4.22), (4.46) then

$$
\begin{aligned}
&\int_{\rho_*}^{R}\left(\frac{\partial M_*^0(r)}{\partial r}\frac{\partial P_*^0(r)}{\partial r} + M_*^1(r)\right)rdr = \int_{\rho_*}^{R}\left[\frac{\partial M_*^0(r)}{\partial r}\left(-\frac{DL}{H}\frac{\partial M_*^0(r)}{\partial r} + \frac{A_3}{r} + \frac{1}{2}Tr\right) + M_*^1(r)\right]rdr \\
&= \int_{\rho_*}^{R}\left[-\frac{DL}{H}\left(\frac{\partial M_*^0(r)}{\partial r}\right)^2 + \frac{A_3}{r}\frac{\partial M_*^0(r)}{\partial r} + \frac{1}{2}Tr\frac{\partial M_*^0(r)}{\partial r} + M_*^1(r)\right]rdr \qquad (4.74) \\
&= \int_{\rho_*}^{R} -\frac{DL}{H}\left(\frac{\partial M_*^0(r)}{\partial r}\right)^2 rdr + A_3[M_*^0(R) - M_*^0(\rho_*)] + \frac{1}{2}T\int_{\rho_*}^{R} r^2\frac{\partial M_*^0(r)}{\partial r}dr + \int_{\rho_*}^{R} M_*^1(r)rdr.
\end{aligned}
$$

Substituting (4.74) into formula (4.68), since equation (4.72) itself is a first-order term of τ, we can ignore the first-order term of τ in equation (4.68) Thanks to

$$
\left[\frac{\partial M_*^0(r)}{\partial r}\right]^2 r > 0,
$$

so

$$
\int_{\rho_*}^{R} -\frac{DL}{H}\left(\frac{\partial M_*^0(r)}{\partial r}\right)^2 rdr < 0. \tag{4.75}
$$

We then deal with the second item of the right hand side in (4.74), and it follows that

$$
A_3\left[M_*^0(R) - M_*^0(\rho_*)\right] = A_3\left[M_*^0(R) - M_*^0(\rho_*^0 + \tau\rho_*^1)\right]
$$

$$= A_3 \left[M_*^0(R) - M_*^0(\rho_*^0) - \tau \frac{\partial M_*^0(\rho_*^0)}{\partial r}\rho_*^1\right].$$

We ignore $O(\tau^2)$ item, then

$$A_3\,[M_*^0(R) - M_*^0(\rho_*)] = A_3\,[M_*^0(R) - M_*^0(\rho_*^0)]. \tag{4.76}$$

Utilizing the third item of the right hand side in (4.74), and combining with the properties of Bessel function and Hankel function of virtual argument, we arrive at

$$\frac{d}{dr}(r^2 I_2(r)) = r^2 I_1(r), \qquad \frac{d}{dr}(r^2 K_2(r)) = -r^2 K_1(r).$$

Hence

$$\begin{aligned}
&\frac{1}{2}T\int_{\rho_*}^{R} r^2 \frac{\partial M_*^0(r)}{\partial r}dr\\
=&\frac{1}{2}T\int_{\rho_*}^{R} r^2 \frac{A_1 I_1(z_r) - A_2 K_(z_r)}{A_1 I_0(z_{\rho_*^0}) + A_2 K_0(z_{\rho_*^0})}dr\\
=&\frac{1}{2}T\frac{1}{A_1 I_0(z_{\rho_*^0}) + A_2 K_0(z_{\rho_*^0})}\left[\int_{\rho_*}^{R} r^2 A_1 I_1(z_r)dr - \int_{\rho_*}^{R} r^2 A_2 K_1(z_r)dr\right]\\
=&\frac{T(\frac{D}{H})^{\frac{3}{2}}}{2(A_1 I_0(z_{\rho_*^0}) + A_2 K_0(z_{\rho_*^0}))}[A_1(z_R)^2 I_2(z_R) + A_2(z_R)^2 K_2(z_R) - A_1(z_{\rho_*^0})^2 I_2(z_{\rho_*^0}) - A_2(z_{\rho_*^0})^2 K_2(z_{\rho_*^0})].
\end{aligned} \tag{4.77}$$

As for the fourth item of the right hand side of (4.74), we have

$$\int_{\rho_*}^{R} M_*^1(r) r dr = -\frac{\partial M_*^0(\rho_*^0)}{\partial r}\rho_*^1 \int_{\rho_*}^{R} M_*^0(r) r dr. \tag{4.78}$$

We substitute formula (4.73)-(4.78) into formula (4.72) to get:

$$\begin{aligned}
&\frac{DL}{H}\rho_*^1 \left[r\frac{\partial M_*^0(r)}{\partial r}\right]'\Bigg|_{\rho_*^0} - \frac{DL}{H}\int_{\rho_*}^{R}\left(\frac{\partial M_*^0(r)}{\partial r}\right)^2 r dr + A_3[M_*^0(R) - M_*^0(\rho_*^0)] + T\rho_*^0\rho_*^1\\
&+\frac{1}{2}T\left(\frac{D}{H}\right)^{\frac{3}{2}} \frac{\left[A_1(z_R)^2 I_2(z_R) + A_2(z_R)^2 K_2(z_R) - (A_1(z_{\rho_*^0})^2 I_2(z_{\rho_*^0}) + A_2(z_{\rho_*^0})^2 K_2(z_{\rho_*^0}))\right]}{A_1 I_0(z_{\rho_*^0}) + A_2 K_0(z_{\rho_*^0})}\\
&-\frac{\partial M_*^0(\rho_*^0)}{\partial r}\rho_*^1 \int_{\rho_*}^{R} M_*^0(r) r dr = 0.
\end{aligned} \tag{4.79}$$

To simplify (4.79), as for $\frac{DL}{H}\rho_*^1 \left[r\frac{\partial M_*^0(r)}{\partial r}\right]'\Big|_{\rho_*^0}$, we let $f(r) = r\left(M_*^0(r)\right)'$, then $f'(r) = r\left(M_*^0(r)\right)'' + \left(M_*^0(r)\right)' = \frac{H}{D} r M_*^0(r) \geq 0$, so $f'(r) \geq 0$, thus $\left[z_r \frac{\partial M_*^0(r)}{\partial r}\right]'\Big|_{\rho_*^0} \geq 0$.

As for $-\frac{DL}{H}\left[z_R\frac{\partial M_*^0(R)}{\partial r} - z_{\rho_*^0}\frac{\partial M_*^0(z_{\rho_*^0})}{\partial r}\right]$, due to the fact that f is increasing, we get

$$z_R\frac{\partial M_*^0(R)}{\partial r} - z_{\rho_*^0}\frac{\partial M_*^0(z_{\rho_*^0})}{\partial r} > 0.$$

By the maximum principle, we know that $M_*(r) \geq 0, for\, \rho_*^0 \leq r \leq R, M_*'(\rho_*^0) < 0, M_*'(R) < 0$, thus

$$A_3\left[M_*^0(R) - M_*^0(\rho_*^0)\right] < 0.$$

As

$$\frac{1}{2}T\frac{\left(\frac{D}{H}\right)^{\frac{3}{2}}}{A_1 I_0(z_{\rho_*^0}) + A_2 K_0(z_{\rho_*^0})}[A_1(z_R)^2 I_2(z_R) + A_2(z_R)^2 K_2(z_R) - (A_1(z_{\rho_*^0})^2 I_2(z_{\rho_*^0}) + A_2(z_{\rho_*^0})^2 K_2(z_{\rho_*^0}))],$$

let $g(r) = A_1\, r^2 I_2(r) + A_2\, r^2 K_2(r)$, then $g(r)' = 2A_1\, r I_2(r) + A_1\, r^2 I_2'(r) + 2A_2\, r K_2(r) + A_2\, r^2 K_2'(r)$. On account of $I_\nu'(x) + \frac{\nu}{x}I_\nu(x) = I_{\nu-1}(x)$, and $K_\nu'(x) = -\frac{\nu}{x}K_\nu(x) - K_{\nu-1}(x)$, we have

$$\begin{aligned} g'(r) &= 2A_1 r I_2(r) + A_1 r^2\left[I_1(r) - \frac{2}{r}I_2(r)\right] + 2A_2 r K_2(r) + A_2 r^2\left[-K_1(r) - \frac{2}{r}K_2(r)\right] \\ &= A_1 r^2 I_1(r) - A_2 r^2 K_1(r). \end{aligned}$$

Comparing $\frac{A_1\, r^2\, I_1(r)}{A_2\, r^2\, K_1(r)}$, and transferring the values of A_1, A_2, we get

$$\frac{\left[\sqrt{\frac{H}{D}}K_1(z_R) - K_0(z_R)\right] I_1(r)}{\left[\sqrt{\frac{H}{D}}I_1(z_R) + I_0(z_R)\right] K_1(r)}. \tag{4.80}$$

If $\sqrt{\frac{H}{D}}$ is near 1, then (4.80) < 1, so we can get $g'(r) < 0$, and g monotonically decreases. In summary,

$$\begin{aligned} \int_{\rho_*}^R \left(\frac{\partial M_*^0(r)}{\partial r}\frac{\partial P_*^0(r)}{\partial r} + M_*^1(r)\right) r dr &= \int_{\rho_*}^R -\frac{DL}{H}\left(\frac{\partial M_*^0(r)}{\partial r}\right)^2 r dr \\ + A_3[M_*^0(R) - M_*^0(\rho_*^0)] &+ \frac{T\left(\frac{D}{H}\right)^{\frac{3}{2}}(g(z_R) - g(z_{\rho_*^0}))}{2(A_1 I_0(z_{\rho_*^0}) + A_2 K_0(z_{\rho_*^0}))} - \frac{\partial M_*^0(\rho_*^0)}{\partial r}\rho_*^1\int_{\rho_*}^R M_*^0(r) r dr. \end{aligned} \tag{4.81}$$

Therefore, (4.79) can be simplified as

$$\begin{aligned} &\left\{\frac{DL}{H}\left[r\frac{\partial M_*^0(r)}{\partial r}\right]'\Bigg|_{\rho_*^0} + T\rho_*^0 - \frac{\partial M_*^0(\rho_*^0)}{\partial r}\int_{\rho_*}^R M_*^0(r) r dr\right\}\rho_*^1 \\ =&\frac{DL}{H}\int_{\rho_*}^R\left(\frac{\partial M_*^0(r)}{\partial r}\right)^2 r dr - A_3[M_*^0(R) - M_*^0(\rho_*^0)] + \frac{T\left(\frac{D}{H}\right)^{\frac{3}{2}}}{2}\frac{g(z_R) - g(z_{\rho_*^0})}{A_1 I_0(z_{\rho_*^0}) + A_2 K_0(z_{\rho_*^0})}, \end{aligned}$$

then

$$\rho_*^1 = \frac{\frac{DL}{H}\int_{\rho_*}^R \left(\frac{\partial M_*^0(r)}{\partial r}\right)^2 rdr - A_3[M_*^0(R) - M_*^0(\rho_*^0)] + \frac{T\left(\frac{D}{H}\right)^{\frac{3}{2}}}{2}\frac{g(z_R)-g(z_{\rho_*^0})}{A_1 I_0(z_{\rho_*^0})+A_2 K_0(z_{\rho_*^0})}}{\frac{DL}{H}\left[r\frac{\partial M_*^0(r)}{\partial r}\right]'\Big|_{\rho_*^0} + T\rho_*^0 - \frac{\partial M_*^0(\rho_*^0)}{\partial r}\int_{\rho_*}^R M_*^0(r) rdr} > 0,$$

which means $\rho_*^1 > 0$. $\square$

Remark 4.1 *Compared with models without time delays, Theorem 4.2 indicates that the size of stationary solution with time delay is smaller. It is reasonable because there is more time for the combination of macrophages and ox-LDLs to turn into foam cells, which gives the plaque a chance to grow slowly.*

4.4 First-order terms in τ

In what follows, we will prove the second part of Theorem 4.1. We are going to tackle the system involving all the first-order terms in τ. Noting that:

$$M_*^0(\rho_*^0 + \tau\rho_*^1) + \tau M_*^1(\rho_*^0 + \tau\rho_*^1) = 1,$$

as a consequence

$$M_*^0(\rho_*^0) + \tau\left[\frac{\partial M_*^0(\rho_*^0)}{\partial r}\rho_*^1 + M_*^1(\rho_*^0)\right] = 1,$$

i.e.

$$\begin{cases} M_*^0(\rho_*^0) = 1, \\ \dfrac{\partial M_*^0(\rho_*^0)}{\partial r}\rho_*^1 + M_*^1(\rho_*^0) = 0. \end{cases}$$

We now collect first-order equations and their respective boundary conditions from (4.23), (4.26), (4.29), (4.31), (4.33), (4.38), (4.40), (4.42) and (4.44):

$$M_*^1(r) = -\frac{\left[A_1 I_1(z_{\rho_*^0}) - A_2 K_1(z_{\rho_*^1})\right]\left[A_1 I_0(z_r) + A_2 K_0(z_r)\right]}{[A_1 I_0(z_{\rho_*^0}) + A_2 K_0(z_{\rho_*^0})]^2} z_{\rho_*^1}, \tag{4.82}$$

$$-\frac{\partial^2 P_*^1(r)}{\partial r^2} - \frac{1}{r}\frac{\partial P_*^1}{\partial r} = L\left[\frac{\partial M_*^0(r)}{\partial r}\frac{\partial P_*^0}{\partial r} + M_*^1(r)\right], \tag{4.83}$$

$$P_*^1(\rho_*^0) = -\frac{\rho_*^1}{(\rho_*^0)^2} - \frac{\partial P_*^0}{\partial r}\rho_*^1, \tag{4.84}$$

$$-\frac{\partial^2 M_{1n}^1(\rho_*^0)}{\partial r^2} - \frac{1}{r}\frac{\partial M_{1n}^1}{\partial r} + \left(\frac{n^2}{r^2} + \frac{H}{D}\right) M_{1n}^1 = 0, \tag{4.85}$$

$$M_{1n}^1(\rho_*^0, t) = -\frac{\partial M_{1n}^1(\rho_*^0)}{\partial r}\rho_*^1 - \frac{\partial M_*^0(\rho_*^0)}{\partial r}\rho_{1n}^1(t) - \frac{\partial^2 M_*^0(\rho_*^0)}{\partial r^2}\rho_*^1\rho_{1n}^0 - \frac{\partial M_*^1(\rho_*^0)}{\partial r}\rho_{1n}^0(t), \tag{4.86}$$

$$\frac{\partial^2 P_{1n}^1}{\partial r^2}-\frac{1}{r}\frac{\partial P_{1n}^1}{\partial r}+\frac{n^2}{r^2}P_{1n}^1=L\frac{\partial M_*^0}{\partial r}\frac{\partial P_{1n}^0}{\partial r}+L\frac{\partial M_{1n}^0}{\partial r}\frac{\partial P_*^0}{\partial r}-L\frac{\partial M_{1n}^0}{\partial t}+LM_{1n}^1, \tag{4.87}$$

$$P_{1n}^1(\rho_*^0,t)=-\frac{\partial P_{1n}^0}{\partial r}(\rho_*^0,t)\rho_*^1+\frac{n^2-1}{(\rho_*^0)^2}\rho_{1n}^1(t)-\frac{2(n^2-1)\rho_*^1}{(\rho_*^0)^3}, \tag{4.88}$$

$$\frac{d\rho_{1n}^1(t)}{dt}=-\frac{\partial^2 P_*^0(\rho_*^0)}{\partial r^2}\rho_{1n}^1(t)-\frac{\partial^3 P_*^0(\rho_*^0)}{\partial r^3}\rho_*^1\rho_{1n}^0(t)-\frac{\partial^2 P_*^1(\rho_*^0)}{\partial r}\rho_{1n}^0(t)-\frac{\partial^2 P_{1n}^0}{\partial r^2}(\rho_*^0,t)\rho_*^1-\frac{\partial P_{1n}^1}{\partial r}(\rho_*^0,t), \tag{4.89}$$

$$\frac{\partial M_*^0(\rho_*^0)}{\partial r}\rho_*^1+M_*^1(\rho_*^0)=0, \frac{\partial P_{1n}^1(R)}{\partial r}=0, \frac{\partial M_{1n}^1(R)}{\partial r}=-M_{1n}^1(R). \tag{4.90}$$

In formula (4.89), $\frac{\partial^2 P_*^0(\rho_*^0)}{\partial r^2}$ has been calculated in formula (4.50), we will next calculate $\frac{\partial^3 P_*^0(\rho_*^0)}{\partial r^3}$. Taking the derivative of r on both sides of equation (4.46) simultaneously, we get

$$\frac{\partial^3 P_*^0}{\partial r^3}+\frac{1}{r^2}\frac{\partial P_*^0}{\partial r}-\frac{1}{r}\frac{\partial^2 P_*^0}{\partial r^2}=L\frac{\partial M_*^0}{\partial r}.$$

Consequently, we have

$$\frac{\partial^3 P_*^0(\rho_*^0+\tau\rho_*^1)}{\partial r^3}-\frac{1}{\rho_*^0+\tau\rho_*^1}\left(\frac{\partial^2 P_*^0(\rho_*^0+\tau\rho_*^1)}{\partial r^2}-\frac{1}{r}\frac{\partial P_*^0}{\partial r}\right)=L\frac{\partial M_*^0}{\partial r}.$$

Substituting formula (4.46), we get

$$\frac{\partial^3 P_*^0(\rho_*^0+\tau\rho_*^1)}{\partial r^3}=\frac{1}{\rho_*^0+\tau\rho_*^1}[LM_*^0(\rho_*^0+\tau\rho_*^1)-T]+L\frac{\partial M_*^0}{\partial r}, \tag{4.91}$$

where

$$\frac{\partial^3 P_*^0(\rho_*^0+\tau\rho_*^1)}{\partial r^3}=\frac{\partial^3 P_*^0(\rho_*^0)}{\partial r^3}+\tau\rho_*^1\frac{\partial^4 P_*^0}{\partial r^4}.$$

It is easy to know that the first item of the right hand of (4.91) can be calculated as

$$\frac{1}{\rho_*^0+\tau\rho_*^1}=\frac{1}{\rho_*^0}+\frac{1}{\rho_*^0+\tau\rho_*^1}-\frac{1}{\rho_*^0}=\frac{1}{\rho_*^0}+\frac{-\tau\rho_*^1}{\rho_*^0(\rho_*^0+\tau\rho_*^1)}=\frac{1}{\rho_*^0}+O(\tau),$$

$$LM_*^0(\rho_*^0+\tau\rho_*^1)-T=LM_*^0(\rho_*^0)+L\tau\rho_*^1\frac{\partial M_*^0(\rho_*^0)}{\partial r}-T,$$

Therefore, (4.91) is transformed into

$$\frac{\partial^3 P_*^0}{\partial r^3}=\frac{1}{\rho_*^0}LM_*^0(\rho_*^0)+L\left(-\frac{M_*^1(\rho_*^0)}{\rho_*^1}\right)-\frac{T}{\rho_*^0}. \tag{4.92}$$

Next, we calculate $\frac{\partial^2 P_{1n}^0(\rho_*^0,t)}{\partial r^2}$. According to formula (4.60), we get

$$\frac{\partial P_{1n}^0}{\partial r}=nC_1(t)r^{n-1}-nC_2(t)r^{-n-1}-\frac{DL}{H}\frac{\partial M_{1n}^0}{\partial r},$$

$$\frac{\partial^2 P_{1n}^0}{\partial r^2} = n(n-1)C_1(t)r^{n-2} + n(n+1)C_2(t)r^{-n-2} - \frac{DL}{H}\frac{\partial^2 M_{1n}^0}{\partial r^2}.$$

Accordingly

$$\frac{\partial^2 P_{1n}^0(\rho_*^0, t)}{\partial r^2} = \left[n(n-1)\tilde{C}_1(\rho_*^0)^{n-2} + n(n+1)\tilde{C}_2(\rho_*^0)^{-n-2} - \frac{DL}{H}\frac{\partial^2 Q_n^0}{\partial r^2}\right]\rho_{1n}^0(t). \tag{4.93}$$

We then calculate $\frac{\partial^2 P_*^1(\rho_*^0)}{\partial r^2}$, from (4.26), we know

$$\frac{\partial^2 P_*^1(r)}{\partial r^2} = -\frac{1}{r}\frac{\partial P_*^1}{\partial r} - L\left[\frac{\partial M_*^0(r)}{\partial r}\frac{\partial P_*^0(r)}{\partial r} + M_*^1(r)\right]. \tag{4.94}$$

From (4.84), we multiply r in both sides and integrate to get

$$\frac{\partial P_*^1}{\partial r} = -\frac{L}{r}\int_r^R \left(\frac{\partial M_*^0(y)}{\partial r}\frac{\partial P_*^0(y)}{\partial r} + M_*^1(y)\right) ydy. \tag{4.95}$$

Substituting (4.95) into (4.94), we know

$$\frac{\partial^2 P_*^1}{\partial r^2} = -\frac{1}{r}\left\{-\frac{L}{r}\int_r^R \left[\frac{\partial M_*^0(y)}{\partial r}\frac{\partial P_*^0(y)}{\partial r} + M_*^1(y)\right] ydy\right\} - L\left[\frac{\partial M_*^0(r)}{\partial r}\frac{\partial P_*^0(r)}{\partial r} + M_*^1(r)\right]. \tag{4.96}$$

Let $h(y) = \frac{\partial M_*^0(y)}{\partial r}\frac{\partial P_*^0(y)}{\partial r} + M_*^1(y)dy$, thus (4.96) becomes

$$\frac{\partial^2 P_*^1(r)}{\partial r^2} = \frac{L}{r^2}\int_r^R h(y)ydy - Lh(r). \tag{4.97}$$

Substituting ρ_*^0 into (4.97), we get

$$\frac{\partial^2 P_*^1(\rho_*^0)}{\partial r^2} = \frac{L}{(\rho_*^0)^2}\int_{\rho_*^0}^R h(y)ydy - Lh(\rho_*^0). \tag{4.98}$$

Because τ is small enough, from (4.81), we know

$$\begin{aligned}\int_{\rho_*^0}^R h(r)rdr = &\int_{\rho_*^0}^R -\frac{DL}{H}\left(\frac{\partial M_*^0(r)}{\partial r}\right)^2 rdr + A_3[M_*^0(R) - M_*^0(\rho_*^0)] \\ &+ \frac{T(\frac{D}{H})^{\frac{3}{2}}(g(z_R) - g(z_{\rho_*^0}))}{2(A_1 I_0(z_{\rho_*^0}) + A_2 K_0(z_{\rho_*^0}))} - \frac{\partial M_*^0(\rho_*^0)}{\partial r}\rho_*^1\int_{\rho_*^0}^R M_*^0(r)rdr,\end{aligned} \tag{4.99}$$

Substituting (4.99) into (4.98), we get

$$\begin{aligned}\frac{\partial^2 P_*^1(\rho_*^0)}{\partial r^2} = &\frac{L}{(\rho_*^0)^2}\left\{\int_{\rho_*^0}^R -\frac{DL}{H}\left(\frac{\partial M_*^0(r)}{\partial r}\right)^2 rdr + A_3[M_*^0(R) - M_*^0(\rho_*^0)]\right. \\ &\left.+\frac{T\left(\frac{D}{H}\right)^{\frac{3}{2}}(g(z_R) - g(z_{\rho_*^0}))}{2(A_1 I_0(z_{\rho_*^0}) + A_2 K_0(z_{\rho_*^0}))} - \frac{\partial M_*^0(\rho_*^0)}{\partial r}\rho_*^1\int_{\rho_*^0}^R M_*^0(r)rdr\right\} - Lh(\rho_*^0).\end{aligned} \tag{4.100}$$

So far, $\frac{\partial^2 P_*^1(\rho_*^0)}{\partial r^2}$ has been found.

Moreover, we need to calculate $\frac{\partial P_{1n}^1}{\partial r}(\rho_*^0, t)$, based on

$$\begin{cases} -\dfrac{\partial^2 M_{1n}^1}{\partial r^2} - \dfrac{1}{r}\dfrac{\partial M_{1n}^1}{\partial r} + \left(\dfrac{n^2}{r^2} + \dfrac{H^2}{D^2}\right) M_{1n}^1 = 0, \\ M_{1n}^1(\rho_*^0, t) = -\dfrac{\partial M_{1n}^1(\rho_*^0)(\rho_*^0)}{\partial r}\rho_*^1 - \dfrac{\partial M_*^0(\rho_*^0)}{\partial r}\rho_{1n}^1(t) - \dfrac{\partial^2 M_*^0(\rho_*^0)}{\partial r^2}\rho_*^1\rho_{1n}^0 - \dfrac{\partial M_*^1(\rho_*^0)}{\partial r}\rho_{1n}^0(t), \\ \dfrac{\partial M_{1n}^1(R)}{\partial r} = -M_{1n}^1(R), \end{cases}$$

therefore

$$M_{1n}^1(r) = E_1 I_n(z_r) + E_2 K_n(z_r),$$

Let

$$\eta_n^1 = P_{1n}^1 + \frac{DL}{H}M_{1n}^1,$$

so

$$-\frac{\partial^2 \eta_n^1}{\partial r^2} - \frac{1}{r}\frac{\partial \eta_n^1}{\partial r} + \frac{n^2}{r^2}\eta_n^1 = L\frac{\partial M_*^0}{\partial r}\frac{\partial P_{1n}^0}{\partial r} + L\frac{\partial M_{1n}^0}{\partial r}\frac{\partial P_*^0}{\partial r} - L\frac{\partial M_{1n}^0}{\partial t}. \tag{4.101}$$

From (4.22), (4.60), (4.57), we know

$$\frac{\partial M_*^0}{\partial r} = \sqrt{\frac{H}{D}}\frac{A_1 I_0'(z_r) + A_2 K_0'(z_r)}{A_1 I_0(z_{\rho_*^0}) + A_2 K_0(z_{\rho_*^0})}, \tag{4.102}$$

$$\frac{\partial P_{1n}^0}{\partial r} = nC_1(t)r^{n-1} - nC_2(t)r^{-n-1} - \frac{DL}{H}\frac{\partial M_{1n}^0}{\partial r}, \tag{4.103}$$

$$\frac{\partial M_{1n}^0}{\partial r} = \frac{\partial Q_n(r)}{\partial r}\rho_{1n}^0(t), \tag{4.104}$$

we further deduce

$$\frac{\partial M_{1n}^0}{\partial t} = Q_n(r)\frac{d\rho_{1n}^0(t)}{dt}. \tag{4.105}$$

Then we get the following formula from (4.46),

$$\frac{\partial P_*^0}{\partial r} = -\frac{DL}{H}\frac{\partial M_*^0}{\partial r} + A_3\frac{1}{r} + \frac{1}{2}Tr. \tag{4.106}$$

Substituting (4.102) - (4.106) into (4.101), we get

$$\begin{aligned} -\frac{\partial^2 \eta_n^1}{\partial r} - \frac{1}{r}\frac{\partial \eta_n^1}{\partial r} + \frac{n^2}{r^2}\eta_n^1 =& L\frac{\partial M_*^0}{\partial r}\left[n\tilde{C}_1 r^{n-1} - n\tilde{C}_2 r^{-n-1} - \frac{DL}{H}\frac{\partial Q_n(r)}{\partial r}\right]\rho_{1n}^0(t) \\ &+ L\frac{\partial Q_n(r)}{\partial r}\left(-\frac{DL}{H}\frac{\partial M_*^0}{\partial r} + A_3\frac{1}{r} + \frac{1}{2}Tr\right)\rho_{1n}^0(t) - LQ_n(r)\frac{d\rho_{1n}^0(t)}{dt} \\ =& \Bigg[L\frac{\partial M_*^0(r)}{\partial r}n\tilde{C}_1 r^{n-1} - L\frac{\partial M_*^0}{\partial r}n\tilde{C}_2 r^{-n-1} - 2L\frac{\partial M_*^0}{\partial r} \\ &+ L\left(\frac{\partial Q_n(R)}{\partial r}\right)^2 A_3\frac{1}{r} + \frac{1}{2}LTr\frac{\partial Q_n}{\partial r}\Bigg]\rho_{1n}^0(t) - LQ_n\frac{d\rho_{1n}^0(t)}{dt}. \end{aligned}$$

Denoting

$$G(r) = L\frac{\partial M_*^0(r)}{\partial r}n\tilde{C}_1 r^{n-1} - L\frac{\partial M_*^0}{\partial r}n\tilde{C}_2 r^{-n-1} - 2L\frac{\partial M_*^0}{\partial r} + L\left(\frac{\partial Q_n(R)}{\partial r}\right)^2 A_3\frac{1}{r} + \frac{1}{2}LTr\frac{\partial Q_n}{\partial r}.$$

As a consequence, we can rewrite (4.101) as

$$-\frac{\partial^2 \eta_n^1}{\partial r^2} - \frac{1}{r}\frac{\partial \eta_n^1}{\partial r} + \frac{n^2}{r^2}\eta_n^1 = G(r)\rho_{1n}^0(t) - LQ_n\frac{d\rho_{1n}^0(t)}{dt}, \tag{4.107}$$

and the boundary condition,

$$\eta_n^1(\rho_*^0, t) = P_{1n}^1(\rho_*^0, t) + \frac{DL}{H}M_{1n}^1(\rho_*^0, t). \tag{4.108}$$

From (4.90), we know

$$\frac{\partial \eta_n^1}{\partial r}(R, t) = \frac{\partial P_{1n}^1(R)}{\partial r} + \frac{DL}{H}\frac{\partial M_{1n}^1(R)}{\partial r} = -\frac{DL}{H}M_{1n}^1(R). \tag{4.109}$$

To simplify the calculation, we denote operator $\mathscr{L} = -\partial_{rr} - \frac{1}{r}\partial_r + \frac{n^2}{r^2}$ and denote the solution of (4.107), (4.108), (4.109) as $\eta_n^1 = u_n^{(1)} + u_n^{(2)} + u_n^{(3)}$ where $u_n^{(1)}, u_n^{(2)}, u_n^{(3)}$ satisfy the following equations, respectively. In what follows, we let $\rho_*^0 = 1 - \varepsilon$, and $R = 1$,

$$\begin{cases} \mathscr{L}_n u_n^{(1)} = G(r)\rho_{1n}^0(t), \quad \rho_*^0 < r < R, \\ u_n^{(1)}(\rho_*^0, t) = 0, \\ \frac{\partial u_n^{(1)}}{\partial r}(R) = 0; \end{cases} \tag{4.110}$$

$$\begin{cases} \mathscr{L}_n u_n^{(2)} = -LQ_n\frac{d\rho_{1n}^0(t)}{dt}, \quad \rho_*^0 < r < R, \\ u_n^{(2)}(\rho_*^0, t) = 0, \\ \frac{\partial u_n^{(2)}}{\partial r}(R) = 0; \end{cases} \tag{4.111}$$

$$\begin{cases} \mathscr{L}_n u_n^{(3)} = 0, \quad \rho_*^0 < r < R, \\ u_n^{(3)}(\rho_*^0, t) = P_{1n}^1(\rho_*^0, t) + \frac{DL}{H}M_{1n}^1(\rho_*^0, t), \\ \frac{\partial u_n^{(3)}}{\partial r}(R) = -\frac{DL}{H}M_{1n}^1(R). \end{cases} \tag{4.112}$$

As for (4.110), from Lemma 4.2 of [31], we know

$$u_n^{(1)} = \begin{cases} Ar^n + Br^{-n} + K[G](r)\rho_{1n}^0(t), & n \neq 0, \\ A + K[G](r)\rho_{1n}^0(t), & n = 0. \end{cases}$$

Case 1: $n \geq 2$. We have

$$u_n^{(1)} = Ar^n + Br^{-n} + K[G](r)\rho_{1n}^0(t).$$

Substituting the boundary condition,

$$\begin{cases} A(1-\varepsilon)^n + B(1-\varepsilon)^{-n} + K[G](1-\varepsilon)\rho_{1n}^0(t) = 0, \\ nA - Bn + K[G]'(R)\rho_{1n}^0(t) = 0, \end{cases}$$

we get

$$A = -\frac{1}{1+(1-\varepsilon)^{2n}}[K[G](1-\varepsilon)(1-\varepsilon)^n + \frac{1}{n}K[G]'(1)]\rho_{1n}^0(t),$$

$$B = -\frac{1}{1+(1-\varepsilon)^{2n}}\left[\frac{K[G]'(1)(1-\varepsilon)^{2n}}{n} - K[G](1-\varepsilon)(1-\varepsilon)^n\right]\rho^0_{1n}(t).$$

From [31], we have

$$\begin{aligned}
\frac{\partial u_n^{(1)}}{\partial r} =& [nAr^{n-1} - nB^{-n-1}]\rho^0_{1n}(t) + K[G]'(r)\rho^0_{1n}(t)\\
=& \Bigg(-\frac{nr^{n-1}}{1+(1-\varepsilon)^{2n}}[K[G](1-\varepsilon)(1-\varepsilon)^n + \frac{1}{n}K[G]'(1)]\\
&-\frac{nr^{-n-1}}{1+(1-\varepsilon)^{2n}}\left[\frac{K[G]'(1)(1-\varepsilon)^{2n}}{n} - K[G](1-\varepsilon)(1-\varepsilon)^n\right] + K[G]'(r)\Bigg)\rho^0_{1n}(t)\\
\le& 2(n^3+1)\rho^0_{1n}(t),
\end{aligned}$$

so

$$\left|\frac{\partial u_n^{(1)}}{\partial r}\right| \le 2(n^3+1)\rho^0_{1n}(t).$$

In the same way, in (4.111),

$$\left|\frac{\partial u_n^{(2)}}{\partial r}\right| \le 2(n^3+1)\frac{d\rho^0_{1n}(t)}{dt}.$$

We next calculate $u_n^{(3)}$, from (4.112), we know

$$u_n^{(3)}(r,t) = Ar^n + Br^{-n}.$$

Substituting boundary condition

$$\begin{aligned}
A(\rho^0_*)^n + B(\rho^0_*)^{-n} =& \left[n\tilde{C}_1(\rho^0_*)^{n-1} - n\tilde{C}_2(\rho^0_*)^{-n-1} - \frac{DL}{H}\frac{\partial Q_n(\rho^0_*)}{\partial r}\right]\rho^0_{1n}(t)\rho^1_*\\
&+\frac{n^2-1}{(\rho^0_*)^2}\rho^1_{1n}(t) - \frac{2(n^2-1)\rho^1_*}{(\rho^0_*)^3}\rho^0_{1n}(t) + \frac{DL}{H}M^1_{1n}(\rho^0_*), \qquad (4.113)\\
nAR^{n-1} - nBR^{-n-1} =& -\frac{DL}{H}M^1_{1n}(R). \qquad (4.114)
\end{aligned}$$

We denote the right hand of (4.113) as J.

Furthermore, we calculate M^1_{1n}. From (4.85), (4.86), (4.90), we know

$$M^1_{1n}(r) = D_1 I_n(z_r) + D_2 K_n(z_r).$$

So we get

$$D_1 I_n(z_{\rho^0_*}) + D_2 K_n(z_{\rho^0_*}) = -\frac{\partial M^0_*(\rho^0_*)}{\partial r}\rho^0_{1n}(t) - \frac{\partial^2 M^0_*(\rho^0_*)}{\partial r^2}\rho^1_*\rho^0_{1n}(t) - \frac{\partial M^0_*(\rho^0_*)}{\partial r}\rho^1_{1n}(t) - \frac{\partial M^0_{1n}(\rho^0_*)}{\partial r}\rho^1_*, \qquad (4.115)$$

$$D_1 I_n(z_R) + D_2 K_n(z_R) = -D_1 I_n'(z_R) - D_2 K_n'(z_R), \qquad (4.116)$$

Combining (4.115), (4.116), we get

$$D_1 = -\frac{\frac{\partial M^0_*(\rho^0_*)}{\partial r} + \frac{\partial^2 M^0_*(\rho^0_*)}{\partial r^2}\rho^1_*}{I_n(z_{\rho^0_*}) + KK_n(z_{\rho^0_*})}\rho^0_{1n}(t) - \frac{\frac{\partial M^0_*(\rho^0_*)}{\partial r}}{I_n(z_{\rho^0_*}) + KK_n(z_{\rho^0_*})}\rho^1_{1n}(t) - \frac{\frac{\partial Q_n(\rho^0_*)}{\partial r}\rho^1_*}{I_n(z_{\rho^0_*}) + KK_n(z_{\rho^0_*})}\rho^0_{1n}(t),$$

$D_2 = KD_1.$

We denote $D_1 = H(\rho_*^0, \rho_*^1)\rho_{1n}^0(t) + S\rho_{1n}^1(t)$, where K is as (4.56) and

$$S = \frac{\frac{\partial M_*^0(\rho_*^0)}{\partial r}}{I_n(z_{\rho_*^0}) + KK_n(z_{\rho_*^0})} = \tilde{B_1}.$$

As a result

$$\begin{aligned}
M_{1n}^1(r) &= D_1 I_n(z_r) + D_2 K_n(z_r) \\
&= [H(\rho_*^0, \rho_*^1)\rho_{1n}^0(t) + S\rho_{1n}^1(t)]I_n(z_r) + [KH(\rho_*^0, \rho_*^1)\rho_{1n}^0(t) + KS\rho_{1n}^1(t)]K_n(z_r) \\
&= [H(\rho_*^0, \rho_*^1)I_n(z_r) + KH(\rho_*^0, \rho_*^1)K_n(z_r)]\rho_{1n}^0(t) + [SI_n(z_r) + KSK_n(z_r)]\rho_{1n}^1(t).
\end{aligned}$$

We denote the above formula as $\tilde{H}(\rho_*^0, \rho_*^1, n, K, r)\rho_{1n}^0(t) + \tilde{Q_n}(r)\rho_{1n}^1(t)$. From the formula of $Q_n(r)$, we know $\tilde{Q_n}(r) = Q_n(r)$, therefore

$$M_{1n}^1(r) = \tilde{H}(\rho_*^0, \rho_*^1, n, K, r)\rho_{1n}^0(t) + \tilde{Q_n}(r)\rho_{1n}^1(t)$$

Combining (4.113) and (4.114), we get

$$\begin{aligned}
nA(\rho_*^0)^n R^{-n-1} + nB(\rho_*^0)^{-n}R^{-n-1} &= JnR^{n-1}, \\
nA(\rho_*^0)^{-n} R^{n-1} - nB(\rho_*^0)^{-n}R^{-n-1} &= -\frac{DL}{H}M_{1n}^1(R)(\rho_*^0)^{-n}.
\end{aligned}$$

We further deduce

$$\begin{aligned}
A &= \frac{Jn(\rho_*^0)^n - \frac{DL}{H}M_{1n}^1(R)R^{n+1}}{n((\rho_*^0)^{2n} + R^{2n})}, \\
B &= AR^{2n} + \frac{DL}{H}M_{1n}^1(R)\frac{R^{n+1}}{n},
\end{aligned}$$

hence

$$\frac{\partial u_n^{(3)}}{\partial r}(\rho_*^0) = An(\rho_*^0)^{n-1} - Bn(\rho_*^0)^{-n-1}.$$

Noting that $P_{1n}^1 = \eta_n^1 - \frac{DL}{H}M_{1n}^1$, combining $u_n^{(1)}, u_n^{(2)}, u_n^{(3)}$, thus $\frac{\partial P_{1n}^1(\rho_*^0, t)}{\partial r}$ can be rewritten as

$$\frac{\partial P_{1n}^1(\rho_*^0, t)}{\partial r} = \frac{\partial u_n^{(1)}(\rho_*^0)}{\partial r} + \frac{\partial u_n^{(2)}(\rho_*^0)}{\partial r} + \frac{\partial u_n^{(3)}(\rho_*^0)}{\partial r} - \frac{DL}{H}\frac{\partial M_{1n}^1(\rho_*^0, t)}{\partial r}. \tag{4.117}$$

So far, we have calculated the expressions of all terms in (4.89), $\frac{\partial P_*^0(\rho_*^0)}{\partial r^2}$ in (4.50), $\frac{\partial^3 P_*^0(\rho_*^0)}{\partial r^3}$ in (4.92), $\frac{\partial^2 P_*^1(\rho_*^0)}{\partial r^2}$ in (4.100), $\frac{\partial^2 P_{1n}^0(\rho_*^0, t)}{\partial r^2}$ in (4.93), $\frac{\partial P_{1n}^1(\rho_*^0, t)}{\partial r}$ in (4.117). Substituting the above formula into (4.89), we get

$$\begin{aligned}
\frac{d\rho_{1n}^1(t)}{dt} =& -\frac{\partial^2 P_*^0(\rho_*^0)}{\partial r^2}\rho_{1n}^1(t) - \frac{\partial^3 P_*^0(\rho_*^0)}{\partial r^3}\rho_*^1\rho_{1n}^0(t) - \frac{\partial^2 P_*^1(\rho_*^0)}{\partial r^2}\rho_{1n}^0(t) - \frac{\partial^2 P_{1n}^0(\rho_*^0, t)}{\partial r^2}\rho_*^1 - \frac{\partial P_{1n}^1(\rho_*^0, t)}{\partial r} \\
=& -(T - L)\rho_{1n}^1(t) - \left[\frac{1}{\rho_*^0}LM_*^0(\rho_*^0) + L\left(-\frac{M_*^1(\rho_*^0)}{\rho_*^1}\right) - \frac{T}{\rho_*^0}\right]\rho_*^1\rho_{1n}^0(t)
\end{aligned}$$

$$
\begin{aligned}
&-\left\{\frac{L}{(\rho_*^0)^2}\left\{\int_{\rho_*^0}^{R}\left[-\frac{DL}{H}\left(\frac{\partial M_*^0(r)}{\partial r}\right)^2 r\right]dr + A_3[M_*^0(R)-M_*^0(\rho_*^0)]\right.\right.\\
&\left.\left.+\frac{T(\frac{D}{H})^{\frac{3}{2}}(g(z_R)-g(z_{\rho_*^0}))}{2(A_1 I_0(z_{\rho_*^0})+A_2K_0(z_{\rho_*^0}))}-\frac{\partial M_*^0(\rho_*^0)}{\partial r}\rho_*^1\int_{\rho_*^0}^{R}M_*^0(r)rdr\right\}-Lh(\rho_*^0)\right\}\rho_{1n}^0(t)\\
&-\left[n(n-1)\tilde{C}_1(\rho_*^0)^{n-2}+n(n+1)\tilde{C}_2(\rho_*^0)^{-n-2}-\frac{DL}{H}\frac{\partial^2 Q_n(\rho_*^0)}{\partial r^2}\right]\rho_{1n}^0(t)\rho_*^1\\
&-\frac{\partial u_n^{(1)}(\rho_*^0,t)}{\partial r}-\frac{\partial u_n^{(2)}(\rho_*^0,t)}{\partial r}-\frac{\partial u_n^{(3)}(\rho_*^0,t)}{\partial r}+\frac{DL}{H}\frac{\partial M_{1n}^1(\rho_*^0,t)}{\partial r}\\
=&F(\rho_*^0,\rho_*^1,n)\rho_{1n}^0(t)-(T-L)\rho_{1n}^1(t)-\frac{\partial u_n^{(3)}}{\partial r}(\rho_*^0)+\frac{DL}{H}\frac{\partial M_{1n}^1(\rho_*^0,t)}{\partial r}\\
=&F(\rho_*^0,\rho_*^1,n)\rho_{1n}^0(t)-(T-L)\rho_{1n}^1(t)-An(\rho_*^0)^{n-1}+Bn(\rho_*^0)^{-n-1}+\frac{DL}{H}\frac{\partial M_{1n}^1(\rho_*^0,t)}{\partial r}\\
=&F(\rho_*^0,\rho_*^1,n)\rho_{1n}^0(t)-(T-L)\rho_{1n}^1(t)-An(\rho_*^0)^{n-1}\\
&+\left(AR^{2n}+\frac{DL}{H}M_{1n}^1(R)\frac{R^{n+1}}{n}\right)n(\rho_*^0)^{-n-1}+\frac{DL}{H}\frac{\partial M_{1n}^1(\rho_*^0,t)}{\partial r}\\
=&F(\rho_*^0,\rho_*^1,n)\rho_{1n}^0(t)-(T-L)\rho_{1n}^1(t)-An[(\rho_*^0)^{n-1}-(\rho_*^0)^{-n-1}R^{2n}]\\
&+\frac{DL}{H}M_{1n}^1(R)R^{n+1}(\rho_*^0)^{-n-1}+\frac{DL}{H}\frac{\partial M_{1n}^1(\rho_*^0,t)}{\partial r},
\end{aligned}
$$

and

$$
\begin{aligned}
&An[(\rho_*^0)^{n-1}-(\rho_*^0)^{-n-1}R^{2n}]-\frac{DL}{H}M_{1n}^1(R)R^{n+1}(\rho_*^0)^{-n-1}\\
=&\frac{Jn(\rho_*^0)^n-\frac{DL}{H}M_{1n}^1(R)R^{n+1}}{(\rho_*^0)^{2n}+R^{2n}}[(\rho_*^0)^{n-1}-(\rho_*^0)^{-n-1}R^{2n}]\\
&-\frac{DL}{H}(\tilde{H}(\rho_*^0,\rho_*^1,n,K,R)\rho_{1n}^0(t)+\tilde{Q}_n(R)\rho_{1n}^1(t))R^{n+1}(\rho_*^0)^{-n-1}
\end{aligned}
$$

$$=\frac{\left\{[\tilde{F}(\rho_*^0,\rho_*^1,n)\rho_{1n}^0(t)+\frac{n^2-1}{(\rho_*^0)^2}\rho_*^1(t)+\frac{DL}{H}(\tilde{H}\rho_{1n}^0(t)+\tilde{Q_n}(\rho_*^0)\rho_{1n}^1(t))]n(\rho_*^0)^n\right\}}{(\rho_*^0)^{2n}+R^{2n}}[(\rho_*^0)^{n-1}-(\rho_*^0)^{-n-1}R^{2n}]$$

$$-\frac{\frac{DL}{H}(\tilde{H}\rho_{1n}^0(t)+\tilde{Q_n}(R)\rho_{1n}^1(t))R^{n+1}[(\rho_*^0)^{n-1}-(\rho_*^0)^{-n-1}R^{2n}]}{(\rho_*^0)^{2n}+R^{2n}}$$

$$-\frac{DL}{H}(\tilde{H}\rho_{1n}^0(t)+\tilde{Q_n}(R)\rho_{1n}^1(t))R_{n+1}(\rho_*^0)^{-n-1}.$$

Substituting the above formula into (4.89),

$$\begin{aligned}
&\frac{d\rho_{1n}^1(t)}{dt}\\
=&-\frac{\partial^2P_*^0(\rho_*^0)}{\partial r^2}\rho_{1n}^1(t)-\frac{\partial^3P_*^0(\rho_*^0)}{\partial r^3}\rho_*^1\rho_{1n}^0(t)-\frac{\partial^2P_*^1(\rho_*^0)}{\partial r}\rho_{1n}^0(t)-\frac{\partial^2P_{1n}^0}{\partial r^2}(\rho_*^0,t)\rho_*^1-\frac{\partial P_{1n}^1}{\partial r}(\rho_*^0,t)\\
=&\hat{\tilde{F}}(\rho_*^0,\rho_*^1,n,K)\rho_{1n}^0(t)-(T-L)\rho_{1n}^1(t)+\frac{DL}{H}\tilde{Q_n}(R)\rho_{1n}^1(t)R^{n+1}(\rho_*^0)^{-n-1}+\frac{DL}{H}\frac{\partial M_{1n}^1(\rho_*^0,t)}{\partial r}\\
&-\frac{\left\{\left(\frac{n^2-1}{(\rho_*^0)^2}\rho_{1n}^1(t)+\frac{DL}{H}\tilde{Q_n}(\rho_*^0)\rho_{1n}^1(t)\right)n(\rho_*^0)^n-\frac{DL}{H}\tilde{Q_n}(R)\rho_{1n}^1(t)R^{n+1}\right\}}{(\rho_*^0)^{2n}+R^{2n}}[(\rho_*^0)^{n-1}-(\rho_*^0)^{-n-1}R^{2n}]\\
=&\hat{\tilde{F}}\rho_{1n}^0(t)-\left\{T-L+\frac{\frac{n^2-1}{\rho_*^0}n(\rho_*^0)^n-\frac{DL}{H}\tilde{Q_n}(R)R^{n+1}}{(\rho_*^0)^{2n}+R^{2n}}\frac{(\rho_*^0)^{2n}-R^{2n}}{(\rho_*^0)^{n+1}}-\frac{DL}{H}\tilde{Q_n}(R)R^{n+1}(\rho_*^0)^{-n-1}\right.\\
&\left.+\frac{\frac{DL}{H}\tilde{Q_n}(\rho_*^0)n(\rho_*^0)^n}{(\rho_*^0)^{2n}+R^{2n}}\frac{(\rho_*^0)^{2n}-R^{2n}}{(\rho_*^0)^{n+1}}p\right\}\rho_{1n}^1(t)+\frac{DL}{H}\frac{\partial\tilde{Q_n}(\rho_*^0)}{\partial r}\rho_{1n}^1(t)\\
=&\left\{T-L-\frac{DL}{H}\frac{\partial\tilde{Q_n}(\rho_*^0)}{\partial r}-\frac{2\frac{DL}{H}\tilde{Q_n}(R)R^{n+1}(\rho_*^0)^{n-1}}{(\rho_*^0)^{2n}+R^{2n}}+\frac{n(n^2-1)[(\rho_*^0)^{2n}-R^{2n}]}{(\rho_*^0)^3((\rho_*^0)^{2n}+R^{2n})}\right.\\
&\left.+n\frac{DL}{H}\frac{[(\rho_*^0)^{2n}-R^{2n}]Q_n(\rho_*^0)}{\rho_*^0((\rho_*^0)^{2n}+R^{2n})}\right\}\rho_{1n}^1(t)+\hat{\tilde{F}}(\rho_*^0,\rho_*^1,n,K)\rho_{1n}^0(t),
\end{aligned}$$

and the above formula can be rewritten as

$$\frac{d\rho_{1n}^1(t)}{dt}+\Bigg\{T-L-\frac{DL}{H}\frac{\partial\tilde{Q}_n(\rho_*^0)}{\partial r}-\frac{2\frac{DL}{H}\tilde{Q}_n(R)}{(\rho_*^0)^{2n}+R^{2n}}R^{n+1}(\rho_*^0)^{n-1}$$

$$+\frac{n(n^2-1)[(\rho_*^0)^{2n}-R^{2n}]}{(\rho_*^0)^3((\rho_*^0)^{2n}+R^{2n})}+n\frac{DL}{H}\frac{[(\rho_*^0)^{2n}-R^{2n}]Q_n(\rho_*^0)}{\rho_*^0((\rho_*^0)^{2n}+R^{2n})}\Bigg\}\rho_{1n}^1(t) \tag{4.118}$$

$$=\hat{\hat{F}}(\rho_*^0.\rho_*^1,n,K)\rho_{1n}^0(t)+\left|\frac{\partial u_n^{(1)}}{\partial r}\right|+\left|\frac{\partial u_n^{(2)}}{\partial r}\right|\leq\hat{\hat{F}}^1(\rho_*^0.\rho_*^1,n,K)\rho_{1n}^0(t).$$

In the following, we denote

$$\begin{aligned}V\triangleq&T-L-\frac{DL}{H}\frac{\partial\tilde{Q}_n(\rho_*^0)}{\partial r}-\frac{2\frac{DL}{H}\tilde{Q}_n(R)}{(\rho_*^0)^{2n}+R^{2n}}R^{n+1}(\rho_*^0)^{n-1}+\frac{n(n^2-1)[(\rho_*^0)^{2n}-R^{2n}]}{(\rho_*^0)^3((\rho_*^0)^{2n}+R^{2n})}\\&+n\frac{DL}{H}\frac{[(\rho_*^0)^{2n}-R^{2n}]Q_n(\rho_*^0)}{\rho_*^0((\rho_*^0)^{2n}+R^{2n})},\end{aligned}$$

From Lemma 4.1, we know that $V>0$, and from Lemma 4.7 of [29], we know that, when $n\geq 2, L<L_*$. Applying this lemma again, as for (4.118), we have

$$\left|\rho_{1n}^1(t)\right|\leq Ce^{-\delta n^3 t}.$$

Case 2: $n=0,1$. From Lemma 4.1, we know that $C_2(n,\rho,R)>0$ is decreasing with respect to n, hence

$$C_2(0,\rho,R)>C_2(1,\rho,R)>0.$$

It satisfies [29, Lemma 4.7], thus when $n=0,1$, we have

$$\left|\rho_{1n}^1(t)\right|\leq Ce^{-\delta t}.$$

So far, the proof of Theorem 4.1 is completed.

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Conflict of Interest

This work does not have any conflicts of interest.

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