

STABILITY AND BIFURCATION ANALYSIS OF APPLIED FREE BOUNDARY
PROBLEMS

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Abstract

by

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Free boundary problems (the time dependent problems are also often known as moving boundary problems) deal with systems of partial differential equations (PDEs) where the domain boundary is apriori unknown. Many mathematical models in different disciplines, e.g., biology, ecology, physics, and material science, involve the formulation of free boundary problems. In this thesis, several free boundary problems with real-world applications are studied, which include a tumor growth model with a time delay in cell proliferation, a plaque formation model, and a modified Hele-Shaw problem. Stability and bifurcation analysis are presented to analyze these models. Each chapter is devoted to a separate mathematical model.

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CHAPTER 1

INTRODUCTION

Free boundary problems (the time dependent problems are also often known as moving boundary problems) consist of partial differential equations (PDEs) with unknown functions and unknown domains. Many real-world processes are naturally associated with moving boundaries. As these processes do not have a prescribed domain and the boundaries of these processes would often evolve over time, it is more reasonable and accurate to use free boundary problems rather than PDEs in a fixed domain. For decades, free boundary problems have been applied to a wide variety of problems in

- physics and engineering (e.g., melting or solidification of materials, contact problems in elasticity, fluid flows, see [8, 9, 43, 69, 72, 85, 86]);
- finances (e.g., credit rating migration, optimal exercise value in Black-Scholes models, see [15, 17–20, 71, 79]);
- biology (e.g., tumor growth, wound healing, atherosclerosis, biofilms, see [42, 48–50, 108]);
- and ecology (e.g., introduction of a new species, propagation of diseases, habitat segregation and invasion, see [3, 53, 98, 99, 115]).

While free boundary problems have profound real-world implications, there are many technical challenges. Specifically, these models are often (a) *mixed-type systems* of elliptic, parabolic and hyperbolic equations, where general PDE theories for a particular type of equations cannot be simply applied; (b) *very complex systems*, in which explicit solutions are impossible to be found; and (c) *nonlinear and nonlocal systems*, which would result systems that are not covered by the general PDE theory

and produce additional technical difficulties. Therefore, deeper analysis towards these models calls for new analytical and numerical methods, as well as improvements of existing algorithms and tools.

In this thesis, we would like to study several free boundary problems with real-world applications in biology and physics. Specifically, we will focus on the topics of stability and bifurcation for these models, since these two topics are of practical importance in applications.

In Chapter 2, we develop a new free boundary PDE model to describe the growth of tumor with a small time delay in cell proliferation. The inclusion of the time delay makes the model non-local, which produces technical difficulties for the PDE estimates. For the new proposed model, we not only study the stability of the stationary solution, but also carry out a bifurcation analysis.

Chapter 3 is devoted to study the bifurcation of a complicated plaque formation model. The model is a highly nonlinear and highly coupled free boundary PDE system, which involves high density lipoprotein cholestrols, low density lipoprotein cholestrols, macrophage cells and foam cells. We theoretically establish the existence bifurcation solutions. As plaque in reality is unlikely to be strictly radially symmetric, the result would be useful to explain the asymmetric shapes of plaque.

With the existing theories and tools, theoretical analysis for free boundary problems is often limited to local solution structures. In order to reveal the global solution structures, we seek help from numerical analysis to solve free boundary problems.

In Chapter 4, we take the advantage of machine learning and propose a novel numerical method to solve a free boundary problem (a modified Hele-Shaw problem with surface tension). We theoretically prove the existence of the numerical solution with our new method. In the simulations, we verify the capability of the new approach by computing some non-radially symmetric solutions which are not characterized by any existing theorems.

CHAPTER 2

A TUMOR GROWTH MODEL WITH A TIME DELAY

Over the last few decades, an increasing number of PDE models describing solid tumor growth in forms of free boundary problems have been proposed and studied. All these models provided a better and deeper understanding of the tumor growth. The basic reaction-diffusion tumor growth model was studied in Greenspan [55, 56], Escher *et. al.* [24, 25, 31], Friedman *et. al.* [6, 6, 7, 7, 44, 45]. Furthermore, the basic model can be extended to more sophisticated ones by adding different factors. For example, Byrne and Chaplain [11], Cui [23], Cui and Friedman [26], Wang [101], Wu and Zhou [103, 104], Xu *et. al.* [105–107] analyzed the tumor growth under the effect of inhibitor; Friedman, Hu and Kao [37–39, 47] considered a multiscale tumor model by adding cell cycle; and Friedman *et. al.* [33, 51, 73] added the effect of angiogenesis. See also [2, 16, 35, 46, 78, 88, 92, 95, 96, 102] for other extensions to a variety of different tumor models.

One biological meaningful extension of the basic tumor model is to add the effect of time delays. In real life, time delays can arise everywhere, since every process, whether it is long or short, would consume time. The basic tumor model can be viewed as an approximation of the model with time delay, since time delay τ is rather small compared with the time range $[0, T]$ we consider. However, compared with the basic model, models with time delays are more accurate and consistent with real life.

The idea of incorporating a time delay in the tumor growth model was first introduced by H.M.Byrne [12], and since then, there are some investigations on various

tumor growth models with time delays [27, 34, 105, 107]. Nearly all these studies, however, are restricted by a strong assumption of radially symmetry. Recently, Xu, Zhou, and Bai [107] used a radially symmetric model and established that the stationary tumor is always stable with respect to all radially symmetric perturbations, nevertheless it is unreasonable to assume all the perturbations are radially symmetric in reality. Therefore, in the following section, we shall reformulate a new PDE model to describe the non-radially symmetric tumor growth with a time delay in cell proliferation. The time delay represents the time taken for cells to undergo cell replication (approximately 24 hours).

2.1 The model

In the model, oxygen and glucose are viewed as nutrients, with its concentration σ satisfying the reaction-diffusion equation

$$\lambda\sigma_t = \Delta\sigma - \sigma \quad \text{in the tumor region } \Omega(t), \quad (2.1)$$

where $-\sigma$ is the nutrients consumed by the tumor. Since the diffusion rate of oxygen or glucose (e.g. $\sim 1 \text{ min}^{-1}$) is much faster than the rate of cell proliferation (e.g. $\sim 1 \text{ day}^{-1}$), λ is very small and can sometimes be set to be 0 (quasi-steady state approximation).

By conservation of mass, cell proliferation rate $S = \text{div}\vec{V}$, where \vec{V} denotes the velocity field of cell movements within the tumor. Due to the presence of time delay, we assume the tumor grows at a rate which is related to the nutrient concentration when it starts cell proliferation. For a simple approximation, we assume a linear relationship between the cell proliferation rate and the nutrient concentration (it is

also a first order Taylor expansion for fully nonlinear model):

$$S = \mu[\sigma(\boldsymbol{\xi}(t - \tau; \mathbf{x}, t), t - \tau) - \tilde{\sigma}], \quad (2.2)$$

where $\tilde{\sigma}$ is a threshold concentration, μ is a parameter expressing the “intensity” of tumor expansion, and $\boldsymbol{\xi}(s; \mathbf{x}, t)$ represents the cell location at time s as cells are moving with the velocity field \vec{V} . The function $\boldsymbol{\xi}(s; \mathbf{x}, t)$ satisfies the following backwards ODE:

$$\begin{cases} \frac{d\boldsymbol{\xi}}{ds} = \vec{V}(\boldsymbol{\xi}, s), & t - \tau \leq s \leq t, \\ \boldsymbol{\xi}|_{s=t} = \mathbf{x}. \end{cases} \quad (2.3)$$

In other words, $\boldsymbol{\xi}$ tracks the path of the cell which is currently located at \mathbf{x} . In this problem, (2.3) describes how cells, including both interior cells and cells on the boundary, move due to the presence of time delay.

Furthermore, if the tumor is assumed to be of porous medium type where Darcy’s law (i.e., $\vec{V} = -\nabla p$, where p is the pressure, here we consider extracellular matrix as “porous medium” in which cell moves) can be used, then

$$-\Delta p = \mu[\sigma(\boldsymbol{\xi}(t - \tau; \mathbf{x}, t), t - \tau) - \tilde{\sigma}]. \quad (2.4)$$

Assuming the velocity field is continuous up to the boundary, we obtain the normal velocity of the moving boundary, namely,

$$V_n = -\nabla p \cdot \mathbf{n} = -\frac{\partial p}{\partial n} \quad \text{on } \partial\Omega(t). \quad (2.5)$$

In addition, the boundary conditions for σ and p are assumed to be:

$$\sigma = 1 \quad \text{on } \partial\Omega(t), \quad (2.6)$$

$$p = \kappa \quad \text{on } \partial\Omega(t), \quad (2.7)$$

where κ is the mean curvature. Equation (2.6) represents a constant nutrient supply at the boundary and equation (2.7) represents cell-to-cell adhesiveness.

Finally, it remains to prescribe initial conditions. Instead of defining the initial conditions at time 0, for this time-delay problem, we are required to supply the initial conditions on an interval $[-\tau, 0]$. For simplicity we assume the initial data are time independent on the interval $[-\tau, 0]$ and take

$$\Omega(t) = \Omega_0 \quad -\tau \leq t \leq 0, \quad (2.8)$$

$$\sigma(x, t) = \sigma_0(x) \quad \text{in } \Omega_0, \quad -\tau \leq t \leq 0. \quad (2.9)$$

Now the problem is reduced to mainly finding two unknown functions σ and p , together with the unknown tumor region $\Omega(t)$:

$$\lambda\sigma_t - \Delta\sigma + \sigma = 0, \quad \mathbf{x} \in \Omega(t), \quad t > 0, \quad (2.10)$$

$$-\Delta p = \mu[\sigma(\boldsymbol{\xi}(t - \tau; \mathbf{x}, t), t - \tau) - \tilde{\sigma}], \quad \mathbf{x} \in \Omega(t), \quad t > 0, \quad (2.11)$$

$$\begin{cases} \frac{d\boldsymbol{\xi}}{ds} = -\nabla p(\boldsymbol{\xi}, s), & t - \tau \leq s \leq t, \\ \boldsymbol{\xi} = \mathbf{x}, & s = t, \end{cases} \quad (2.12)$$

$$\sigma = 1, \quad \mathbf{x} \in \partial\Omega(t), \quad t > 0, \quad (2.13)$$

$$p = \kappa, \quad \mathbf{x} \in \partial\Omega(t), \quad t > 0, \quad (2.14)$$

$$V_n = -\frac{\partial p}{\partial n}, \quad \mathbf{x} \in \partial\Omega(t), \quad t > 0, \quad (2.15)$$

$$\Omega(t) = \Omega_0, \quad -\tau \leq t \leq 0, \quad (2.16)$$

$$\sigma(x, t) = \sigma_0(x), \quad x \in \Omega_0, \quad -\tau \leq t \leq 0. \quad (2.17)$$

2.2 Radially symmetry stationary solution

In this section we prove the existence and uniqueness of the radially symmetric stationary solution $(\sigma_*(r), p_*(r), R_*)$ to the system (2.10) — (2.15). After setting all

t -derivative terms to be 0, a stationary solution (σ_*, p_*, R_*) satisfies

$$-\Delta\sigma_*(r) + \sigma_*(r) = 0, \quad r < R_*, \quad (2.18)$$

$$-\Delta p_*(r) = \mu[\sigma_*(\xi_*(-\tau; r, 0)) - \tilde{\sigma}], \quad r < R_*, \quad (2.19)$$

$$\begin{cases} \frac{d\xi_*}{ds}(s; r, 0) = -\frac{\partial p_*}{\partial r}(\xi_*(s; r, 0)), & -\tau \leq s \leq 0, \\ \xi_*(s; r, 0) = r, & s = 0, \end{cases} \quad (2.20)$$

$$\sigma_* = 1, \quad p_* = \frac{1}{R_*}, \quad r = R_*, \quad (2.21)$$

$$\int_0^{R_*} [\sigma_*(\xi_*(-\tau; r, 0)) - \tilde{\sigma}] r dr = 0. \quad (2.22)$$

Lemma 2.1. *For sufficiently small τ , there exists a unique classical solution (σ_*, p_*, R_*) to the problem (2.18)-(2.22).*

Proof. To begin with, we introduce a change of variables

$$\hat{r} = \frac{r}{R_*}, \quad \hat{\sigma}(\hat{r}) = \sigma_*(r), \quad \hat{p}(\hat{r}) = R_* p_*(r), \quad \hat{\xi}(s; \hat{r}, 0) = \frac{\xi_*(s; r, 0)}{R_*}.$$

Solving the ODE (2.20) and substituting the solution in (2.19) and (2.22), we obtain a new system in the fixed domain $\{\hat{r} < 1\}$. After dropping the $\hat{\cdot}$ in the above variables, the new PDE system takes the following form:

$$\begin{cases} \frac{d\xi}{ds}(s; r, 0) = -\frac{1}{R_*^3} \frac{\partial p}{\partial r}(\xi(s; r, 0)), & -\tau \leq s \leq 0, \\ \xi(s; r, 0) = r, & s = 0, \end{cases} \quad (2.23)$$

$$-\Delta_r \sigma + R_*^2 \sigma = 0, \quad \sigma(1) = 1, \quad (2.24)$$

$$-\Delta_r p = \mu R_*^3 \left[\sigma \left(r + \frac{1}{R_*^3} \int_{-\tau}^0 \frac{\partial p}{\partial r}(\xi(s; r, 0)) ds \right) - \tilde{\sigma} \right], \quad p(1) = 1, \quad (2.25)$$

$$\int_0^1 \left[\sigma \left(r + \frac{1}{R_*^3} \int_{-\tau}^0 \frac{\partial p}{\partial r}(\xi(s; r, 0)) ds \right) - \tilde{\sigma} \right] r dr = 0. \quad (2.26)$$

To begin with, equation (2.24) can be solved explicitly as

$$\sigma(r; R_*) = \frac{I_0(R_* r)}{I_0(R_*)}. \quad (2.27)$$

Next, we take R_{\min} and R_{\max} to be determined later. For any $R_{\min} \leq R_* \leq R_{\max}$, it is clear that σ is uniquely determined by (2.27). Substituting (2.27) into (2.25), we shall prove that p is also uniquely determined when R_* is bounded by using the contraction mapping principle.

Note that $\xi(s; r, 0)$ ($-\tau \leq s \leq 0$) might be out of the region $[0, 1]$ by following the ODE (2.23) even if $0 \leq \xi(0; s, 0) = r < 1$ (i.e., started within the unit disk); however $\xi(s; r, 0)$ should be very close to r if τ is small enough. Therefore, it is natural to assume $\xi(s; r, 0)$ locates within $[0, 2]$, so we take

$$\mathcal{P} = \{p \in W^{2,\infty}[0, 2]; \|p\|_{W^{2,\infty}[0,2]} \leq M\}.$$

For each $p \in \mathcal{P}$, we first solve ξ from (2.23), and substitute it into (2.25), from which we obtain a unique \bar{p} ; in other words, \bar{p} is the unique solution to the following system:

$$-\Delta_r \bar{p} = \mu R_*^3 \left[\sigma \left(r + \frac{1}{R_*^3} \int_{-\tau}^0 \frac{\partial p}{\partial r} (\xi(s; r, 0)) ds; R_* \right) - \tilde{\sigma} \right], \quad \bar{p}(1) = 1. \quad (2.28)$$

It follows from integrating (2.28) that

$$\left\| \frac{1}{r} \frac{\partial \bar{p}}{\partial r} \right\|_{L^\infty[0,1]} \leq \frac{\mu}{2} (R_{\max})^3 (\sigma_{\max} + \tilde{\sigma}), \quad (2.29)$$

$$\|\bar{p}\|_{L^\infty[0,1]} \leq 1 + \frac{\mu}{4} (R_{\max})^3 (\sigma_{\max} + \tilde{\sigma}); \quad (2.30)$$

combining with (2.28), we also have

$$\left\| \frac{\partial^2 \bar{p}}{\partial r^2} \right\|_{L^\infty[0,1]} \leq \frac{3\mu}{2} (R_{\max})^3 (\sigma_{\max} + \tilde{\sigma}), \quad (2.31)$$

where $\sigma_{\max} = \max_{0 \leq r \leq 2} \sigma(r; R_*)$. Note that \bar{p} derived from (2.28) is only defined for $r \leq 1$, we shall extend \bar{p} to a bigger region. To do that, we define

$$\tilde{p}(r) = \begin{cases} \bar{p}(r), & r \leq 1, \\ \bar{p}(1) + \bar{p}'(1)(r-1), & 1 < r \leq 2. \end{cases} \quad (2.32)$$

It is easy to check $\|\tilde{p}\| \in W^{2,\infty}[0, 2]$, and $\|\tilde{p}\|_{W^{2,\infty}[0,2]} \leq 2\|\bar{p}\|_{W^{2,\infty}[0,1]}$. Combining with (2.29) — (2.31), we have

$$\|\tilde{p}\|_{W^{2,\infty}[0,2]} \leq 2 \max \left\{ \frac{3\mu}{2} (R_{\max})^3 (\sigma_{\max} + \tilde{\sigma}), 1 + \frac{\mu}{4} (R_{\max})^3 (\sigma_{\max} + \tilde{\sigma}) \right\} \triangleq M_1. \quad (2.33)$$

With \tilde{p} defined by (2.32), we obtain a mapping $\mathcal{L} : p \rightarrow \tilde{p}$. If we choose $M \geq M_1$, then $\tilde{p} \in \mathcal{P}$ based on (2.33), which indicates \mathcal{L} maps \mathcal{P} to itself. In the next step, we shall prove that \mathcal{L} is a contraction.

Let $p_1, p_2 \in \mathcal{P}$, we solve ξ_1, ξ_2 from the following two systems:

$$\begin{cases} \frac{d\xi_1}{ds}(s; r, 0) = -\frac{1}{R_*^3} \frac{\partial p_1}{\partial r}(\xi_1(s; r, 0)), & -\tau \leq s \leq 0, \\ \xi_1(s; r, 0) = r, & s = 0, \end{cases} \quad (2.34)$$

$$\begin{cases} \frac{d\xi_2}{ds}(s; r, 0) = -\frac{1}{R_*^3} \frac{\partial p_2}{\partial r}(\xi_2(s; r, 0)), & -\tau \leq s \leq 0, \\ \xi_2(s; r, 0) = r, & s = 0. \end{cases} \quad (2.35)$$

Integrating (2.34) and (2.35) in s and making a subtraction, we obtain the following estimate

$$\begin{aligned} |\xi_1 - \xi_2| &\leq \tau \frac{1}{R_*^3} \left[\left| \frac{\partial p_1}{\partial r}(\xi_1) - \frac{\partial p_2}{\partial r}(\xi_1) \right| + \left| \frac{\partial p_2}{\partial r}(\xi_1) - \frac{\partial p_2}{\partial r}(\xi_2) \right| \right] \\ &\leq \tau \frac{1}{R_*^3} \left[\|p_1 - p_2\|_{W^{2,\infty}[0,2]} + \|p_2\|_{W^{2,\infty}[0,2]} \max_{\substack{-\tau \leq s \leq 0 \\ 0 \leq r \leq 1}} |\xi_1 - \xi_2| \right] \\ &\leq \tau \frac{1}{R_*^3} \|p_1 - p_2\|_{W^{2,\infty}[0,2]} + \tau \frac{1}{R_*^3} M \max_{\substack{-\tau \leq s \leq 0 \\ 0 \leq r \leq 1}} |\xi_1 - \xi_2| \end{aligned}$$

for all $-\tau \leq s \leq 0$ and $0 \leq r \leq 1$, hence

$$\max_{\substack{-\tau \leq s \leq 0 \\ 0 \leq r \leq 1}} |\xi_1 - \xi_2| \leq \frac{\tau}{R_*^3 - \tau M} \|p_1 - p_2\|_{W^{2,\infty}[0,2]}. \quad (2.36)$$

We then substitute ξ_1, ξ_2 into (2.28) and solve for \bar{p}_1 and \bar{p}_2 , respectively. Using (2.36), we have

$$\begin{aligned} & \left\| \frac{1}{r} \frac{\partial(\bar{p}_1 - \bar{p}_2)}{\partial r} \right\|_{L^\infty[0,1]} \\ & \leq \frac{\mu}{2} R_*^3 \left\| \sigma \left(r + \frac{1}{R_*^3} \int_{-\tau}^0 \frac{\partial p_1}{\partial r}(\xi_1(s)) ds \right) - \sigma \left(r + \frac{1}{R_*^3} \int_{-\tau}^0 \frac{\partial p_2}{\partial r}(\xi_2(s)) ds \right) \right\|_{L^\infty[0,1]} \\ & \leq \frac{\mu}{2} R_*^3 \left[\left\| \frac{\partial \sigma}{\partial r} \right\|_{L^\infty[0,2]} \frac{1}{R_*^3} \int_{-\tau}^0 \left(\frac{\partial p_1}{\partial r}(\xi_1(s)) - \frac{\partial p_2}{\partial r}(\xi_2(s)) \right) ds \right] \\ & \leq \frac{\mu}{2} \left\| \frac{\partial \sigma}{\partial r} \right\|_{L^\infty[0,2]} \tau \left[\|p_1 - p_2\|_{W^{2,\infty}[0,2]} + \|p_2\|_{W^{2,\infty}[0,2]} \max_{\substack{-\tau \leq s \leq 0 \\ 0 \leq r < 1}} |\xi_1 - \xi_2| \right] \\ & \leq M_2 \tau \|p_1 - p_2\|_{W^{2,\infty}[0,2]}, \end{aligned}$$

and similarly,

$$\begin{aligned} & \|\bar{p}_1 - \bar{p}_2\|_{L^\infty[0,1]} \leq M_3 \tau \|p_1 - p_2\|_{W^{2,\infty}[0,2]}, \\ & \left\| \frac{\partial^2(\bar{p}_1 - \bar{p}_2)}{\partial r^2} \right\|_{L^\infty[0,1]} \leq M_4 \tau \|p_1 - p_2\|_{W^{2,\infty}[0,2]}, \end{aligned}$$

where $M_2 = \frac{\mu}{2} \left\| \frac{\partial \sigma}{\partial r} \right\|_{L^\infty[0,2]} \left(1 + \frac{M\tau}{(R_{\min})^3 - M\tau} \right)$, $M_3 = \frac{\mu}{4} \left\| \frac{\partial \sigma}{\partial r} \right\|_{L^\infty[0,2]} \left(1 + \frac{M\tau}{(R_{\min})^3 - M\tau} \right)$ and $M_4 = \frac{3\mu}{2} \left\| \frac{\partial \sigma}{\partial r} \right\|_{L^\infty[0,2]} \left(1 + \frac{M\tau}{(R_{\min})^3 - M\tau} \right)$ are independent of r . It is clear that $M_4 > M_2 > M_3$, thus

$$\|\bar{p}_1 - \bar{p}_2\|_{W^{2,\infty}[0,1]} \leq M_4 \tau \|p_1 - p_2\|_{W^{2,\infty}[0,2]}. \quad (2.37)$$

Next we extend \bar{p}_1 and \bar{p}_2 in the same way as in (2.32), hence

$$(\tilde{p}_1 - \tilde{p}_2)(r) = \begin{cases} (\bar{p}_1 - \bar{p}_2)(r), & r \leq 1, \\ (\bar{p}_1 - \bar{p}_2)(1) + (\bar{p}_1 - \bar{p}_2)'(1)(r - 1), & 1 < r \leq 2. \end{cases} \quad (2.38)$$

Clearly, $\tilde{p}_1 - \tilde{p}_2 \in W^{2,\infty}[0, 2]$, and we have $\|\tilde{p}_1 - \tilde{p}_2\|_{W^{2,\infty}[0,2]} \leq 2\|\bar{p}_1 - \bar{p}_2\|_{W^{2,\infty}[0,1]}$. Combining with (2.37), we claim that

$$\|\mathcal{L}p_1 - \mathcal{L}p_2\|_{W^{2,\infty}[0,2]} = \|\tilde{p}_1 - \tilde{p}_2\|_{W^{2,\infty}[0,2]} \leq 2M_4\tau\|p_1 - p_2\|_{W^{2,\infty}[0,2]}. \quad (2.39)$$

Therefore, we obtain a contraction mapping \mathcal{L} by taking τ small so that $2M_4\tau < 1$.

Now for any particular $R_* \in [R_{\min}, R_{\max}]$, we have shown that σ and p are uniquely determined, it remains to show that there exists a unique solution R_* satisfying (2.26). We substitute (2.27) into (2.26) to find that it is equivalent to show there exists a unique solution to the equation:

$$\int_0^1 \left[\frac{I_0(rR + \frac{1}{R^2} \int_{-\tau}^0 \frac{\partial p}{\partial r}(\xi(s; r, 0)) ds)}{I_0(R)} - \tilde{\sigma} \right] r dr = 0.$$

In order to prove the above statement, we set

$$F(R, \tau) = \int_0^1 \left[\frac{I_0(rR + \frac{1}{R^2} \int_{-\tau}^0 \frac{\partial p}{\partial r}(\xi(s; r, 0)) ds)}{I_0(R)} - \tilde{\sigma} \right] r dr,$$

then $F(R, 0) = \int_0^1 \left[\frac{I_0(rR)}{I_0(R)} - \tilde{\sigma} \right] r dr = P_0(R) - \frac{\tilde{\sigma}}{2}$, where $P_0(R) = \frac{I_1(R)}{RI_0(R)}$. From [30] (pg.61) and [45] (the equations (2.19) (2.21) and (2.26)), it is known that $P_0(R)$ is decreasing in R and $0 < P_0(R) \leq \frac{1}{2}$. Since $0 < \tilde{\sigma} < 1$, there exists a unique solution to the equation $F(R, 0) = 0$, which we denote it by R_S . Recall that $F(R, 0)$ is monotone decreasing in R , then

$$F(\frac{1}{2}R_S, 0) > 0, \quad F(\frac{3}{2}R_S, 0) < 0.$$

After we show this, we take derivative of $F(R, \tau)$ with respect to R and expand the

partial derivative in τ to get

$$\frac{\partial F(R, \tau)}{\partial R} = \frac{\partial F(R, 0)}{\partial R} + \frac{\partial^2 F(R, 0)}{\partial R \partial \tau} \tau + O(\tau^2). \quad (2.40)$$

When τ is small enough, the signs of $\frac{\partial F(R, \tau)}{\partial R}$ and $\frac{\partial F(R, 0)}{\partial R}$ should be the same, thus $F(R, \tau)$ is also monotone decreasing in R . In addition, from the fact that $F(R, \tau)$ is continuous in τ , we have, when τ is small,

$$F\left(\frac{1}{2}R_S, \tau\right) > 0, \quad F\left(\frac{3}{2}R_S, \tau\right) < 0.$$

Hence there exists a unique solution R_* satisfying $F(R_*, \tau) = 0$, i.e., equation (2.26), when τ is small enough; furthermore we have $R_{\min} = \frac{1}{2}R_S < R_* < \frac{3}{2}R_S = R_{\max}$. The proof is complete. \square

Remark 2.1. *Since $\partial p_*/\partial r = 0$ on the boundary for the radially symmetric stationary solution, we have $\xi_*(s; R_*, 0) \equiv R_*$ and $\xi_*(s; r, 0)$ will stay within the unit disk if initially $\xi_*(0; r, 0) = r < R_*$. From (2.19) it is clear that $\frac{\partial p_*}{\partial r}$ is not identically 0 for $0 < r < R_*$, therefore $\xi_*(s; r, 0)$ will not be a constant for $-\tau \leq s \leq 0$.*

For our stationary solution, the free boundary does not move in time. But the velocity field inside the tumor domain is not zero, and movements are necessary to replace dead cells with new daughter cells to reach an equilibrium. Because of the time delay, such replacement requires a time τ for the mitosis to complete and for the daughter cells to move into the right place; and that is incorporated into the equation (2.20). In that sense, the delay-time derivative cannot be set to zero even for our stationary solution and our solution differs from the classical definition of stationary solution where time derivatives are all zero.

2.3 Stability analysis

In this section, we consider the linear stability of the radially symmetric stationary solution (σ_*, p_*, R_*) which we found in Section 2.2. Specifically, we shall determine a critical value μ_* such that (σ_*, p_*, R_*) is linearly stable in the interval $0 < \mu < \mu_*$ and linearly unstable for $\mu > \mu_*$. The stability results are summarized in the following theorem:

Theorem 2.1. *There exists a critical value $\mu_* > 0$ such that for any $\mu < \mu_*$, the radially symmetric stationary solution (σ_*, p_*, R_*) is linearly stable in the sense*

$$|\rho(\theta, t) - (a_1 \cos(\theta) + b_1 \sin(\theta))| \leq Ce^{-\delta t}, \quad t > 0, \quad (2.41)$$

for some constants a_1, b_1 and $\delta > 0$. If $\mu > \mu_*$, this stationary solution is linearly unstable.

Remark 2.2. *The system (2.10) — (2.17) is invariant under coordinate translations, that is the reason why we exclude $a_1 \cos(\theta) + b_1 \sin(\theta)$ in (2.41).*

To prove Theorem 2.1, we begin by making some small non-radially symmetric perturbations on the initial conditions (note that the perturbations are made in a time interval $[-\tau, 0]$ instead of an initial time due to the presence of time delay, and we assume for simplicity that the perturbation is uniform on the interval $[-\tau, 0]$):

$$\partial\Omega(t) : r = R_* + \varepsilon\rho_0(\theta), \quad -\tau \leq t \leq 0, \quad (2.42)$$

$$\sigma(r, \theta, t) = \sigma_*(r) + \varepsilon w_0(r, \theta), \quad -\tau \leq t \leq 0. \quad (2.43)$$

In order to obtain the linearized system of (2.10)–(2.15), we let

$$\begin{aligned} \partial\Omega(t) : r &= R_* + \varepsilon\rho(\theta, t) + O(\varepsilon^2), \\ \sigma(r, \theta, t) &= \sigma_*(r) + \varepsilon w(r, \theta, t) + O(\varepsilon^2), \end{aligned} \quad (2.44)$$

$$p(r, \theta, t) = p_*(r) + \varepsilon q(r, \theta, t) + O(\varepsilon^2).$$

Notice that we are considering a domain which is a small perturbation of a disk, we shall express $\boldsymbol{\xi}(s; r, \theta, t)$ in polar coordinates $(\xi_1(s; r, \theta, t), \xi_2(s; r, \theta, t))$, where ξ_1 represents radius, and ξ_2 represents angle. Thus, the vector $\boldsymbol{\xi}$ is expressed in the form $\boldsymbol{\xi} = \xi_1 \vec{e}_1(\xi_2)$, where $\vec{e}_1(\xi_2) = \cos(\xi_2)\vec{i} + \sin(\xi_2)\vec{j}$ and $\vec{e}_2(\xi_2) = -\sin(\xi_2)\vec{i} + \cos(\xi_2)\vec{j}$ are the two basis vectors in polar coordinates. We then expand ξ_1, ξ_2 in ε as

$$\begin{cases} \xi_1 = \xi_{10} + \varepsilon \xi_{11} + O(\varepsilon^2), \\ \xi_2 = \xi_{20} + \varepsilon \xi_{21} + O(\varepsilon^2). \end{cases} \quad (2.45)$$

Accordingly, $-\nabla$ is also expressed in polar coordinates, i.e., $-\nabla = -\vec{e}_1 \frac{\partial}{\partial r} - \frac{1}{r} \vec{e}_2 \frac{\partial}{\partial \theta}$. Since $\frac{d\vec{e}_1(\xi_2)}{ds} = \vec{e}_2(\xi_2) \frac{d\xi_2}{ds}$, equation (2.12) is equivalent to

$$\begin{aligned} \frac{d\boldsymbol{\xi}}{ds} &= \frac{d(\xi_1 \vec{e}_1(\xi_2))}{ds} = \frac{d\xi_1}{ds} \vec{e}_1(\xi_2) + \xi_1 \frac{d\xi_2}{ds} \vec{e}_2(\xi_2) \\ &= -\nabla p = -\frac{\partial p}{\partial r} \vec{e}_1(\xi_2) - \frac{1}{\xi_1} \frac{\partial p}{\partial \theta} \vec{e}_2(\xi_2), \end{aligned}$$

from which we obtain two sets of ODEs in polar coordinates for $s \in [t - \tau, t]$:

$$\begin{cases} \frac{d\xi_1}{ds} = -\frac{\partial p}{\partial r}(\xi_1, \xi_2, s), \\ \xi_1|_{s=t} = r; \end{cases} \quad \begin{cases} \frac{d\xi_2}{ds} = -\frac{1}{(\xi_1)^2} \frac{\partial p}{\partial \theta}(\xi_1, \xi_2, s), \\ \xi_2|_{s=t} = \theta. \end{cases}$$

Substituting (2.44) and (2.45) into the above ODEs, and dropping higher order terms, we get

$$\begin{cases} \frac{d\xi_{10}}{ds} = -\frac{\partial p_*}{\partial r}(\xi_{10}), & t - \tau \leq s \leq t, \\ \xi_{10}|_{s=t} = r; \end{cases} \quad (2.46)$$

$$\begin{cases} \frac{d\xi_{11}}{ds} = -\frac{\partial^2 p_*}{\partial r^2}(\xi_{10})\xi_{11} - \frac{\partial q}{\partial r}(\xi_{10}, \xi_{20}, s), & t - \tau \leq s \leq t, \\ \xi_{11}|_{s=t} = 0; \end{cases} \quad (2.47)$$

$$\begin{cases} \frac{d\xi_{20}}{ds} = 0, & t - \tau \leq s \leq t, \\ \xi_{20}\big|_{s=t} = \theta; \end{cases} \quad (2.48)$$

$$\begin{cases} \frac{d\xi_{21}}{ds} = -\frac{1}{(\xi_{10})^2} \frac{\partial q}{\partial \theta}(\xi_{10}, \xi_{20}, s), & t - \tau \leq s \leq t \\ \xi_{21}\big|_{s=t} = 0. \end{cases} \quad (2.49)$$

Note that the equation for ξ_{10} is the same as the equation for ξ_* in radially symmetric case (i.e., (2.46) and (2.20) are the same), thus ξ_{10} is independent of θ ; and from (2.48) we can easily derive $\xi_{20} \equiv \theta$.

Substituting (2.44) and (2.46) — (2.49) into (2.10) — (2.15), using also the mean-curvature formula in the 2-dimensional case for the curve $r = \rho$:

$$\kappa = \frac{\rho^2 + 2\rho_\theta^2 - \rho \cdot \rho_{\theta\theta}}{(\rho^2 + (\rho_\theta)^2)^{3/2}},$$

and collecting only the linear terms in ε , we obtain the linearized system in B_{R_*} (B_{R_*} denotes the disk centered at 0 with radius R_*), namely,

$$\Delta w(r, \theta, t) = w(r, \theta, t), \quad w(R_*, \theta, t) = -\frac{\partial \sigma_*}{\partial r}\bigg|_{r=R_*} \rho(\theta, t), \quad (2.50)$$

$$\begin{aligned} \Delta q(r, \theta, t) = & -\mu \frac{\partial \sigma_*}{\partial r}(\xi_{10}(t - \tau; r, t)) \xi_{11}(t - \tau; r, \theta, t) \\ & -\mu w(\xi_{10}(t - \tau; r, t), \theta, t - \tau), \end{aligned} \quad (2.51)$$

$$q(R_*, \theta, t) = -\frac{1}{R_*^2}(\rho(\theta, t) + \rho_{\theta\theta}(\theta, t)), \quad (2.52)$$

$$\frac{d\rho}{dt} = -\frac{\partial^2 p_*}{\partial r^2}\bigg|_{r=R_*} \rho(\theta, t) - \frac{\partial q}{\partial r}\bigg|_{r=R_*}, \quad (2.53)$$

where the equations for ξ_{10} and ξ_{11} are listed in (2.46) and (2.47), respectively. Since ξ_{21} does not appear explicitly in (2.50) — (2.53), it is not needed.

In what follows, we seek solutions of the form

$$w(r, \theta, t) = w_n(r, t) \cos(n\theta),$$

$$q(r, \theta, t) = q_n(r, t) \cos(n\theta),$$

$$\rho(\theta, t) = \rho_n(t) \cos(n\theta),$$

$$\xi_{11}(s; r, \theta, t) = \varphi_n(s; r, t) \cos(n\theta).$$

Noting that in a similar manner, we can also seek solutions of the form

$$w(r, \theta, t) = w_n(r, t) \sin(n\theta),$$

$$q(r, \theta, t) = q_n(r, t) \sin(n\theta),$$

$$\rho(\theta, t) = \rho_n(t) \sin(n\theta),$$

$$\xi_{11}(s; r, \theta, t) = \varphi_n(s; r, t) \sin(n\theta).$$

Using the relation $\Delta = \partial_{rr} + \frac{1}{r}\partial_r + \frac{1}{r^2}\partial_{\theta\theta}$ in (2.50)–(2.53), we obtain the following system in B_{R_*} :

$$-\frac{\partial^2 w_n(r, t)}{\partial r^2} - \frac{1}{r} \frac{\partial w_n(r, t)}{\partial r} + \left(\frac{n^2}{r^2} + 1\right) w_n(r, t) = 0, \quad (2.54)$$

$$w_n(R_*, t) = -\frac{\partial \sigma_*}{\partial r} \Big|_{r=R_*} \rho_n(t), \quad (2.55)$$

$$\begin{aligned} -\frac{\partial^2 q_n(r, t)}{\partial r^2} - \frac{1}{r} \frac{\partial q_n(r, t)}{\partial r} + \frac{n^2}{r^2} q_n(r, t) &= \mu w_n(\xi_{10}(t - \tau; r, t), t - \tau) \\ &+ \mu \frac{\partial \sigma_*}{\partial r}(\xi_{10}(t - \tau; r, t)) \varphi_n(t - \tau; r, t), \end{aligned} \quad (2.56)$$

$$q_n(R_*, t) = \frac{n^2 - 1}{R_*^2} \rho_n(t), \quad (2.57)$$

$$\frac{d\rho_n(t)}{dt} = -\frac{\partial^2 p_*}{\partial r^2} \Big|_{r=R_*} \rho_n(t) - \frac{\partial q_n}{\partial r} \Big|_{r=R_*}, \quad (2.58)$$

where the steady state solution (σ_*, p_*, R_*) satisfies (2.18) — (2.22), ξ_{10} satisfies (2.46)

and φ_n satisfies the following equation:

$$\begin{cases} \frac{\partial \varphi_n(s; r, t)}{\partial s} = -\frac{\partial^2 p_*}{\partial r^2}(\xi_{10})\varphi_n(s; r, t) - \frac{\partial q_n(\xi_{10}, s)}{\partial r}, & t - \tau \leq s \leq t, \\ \varphi_n|_{s=t} = 0. \end{cases} \quad (2.59)$$

While it is impossible to solve the system (2.54) — (2.59) explicitly, we would like to study the impact of τ on this system. Recall that the time delay τ is actually very small, hence we look for the expansions in τ for all variables. Let us denote

$$R_* = R_*^0 + \tau R_*^1 + O(\tau^2),$$

$$\sigma_* = \sigma_*^0 + \tau \sigma_*^1 + O(\tau^2),$$

$$p_* = p_*^0 + \tau p_*^1 + O(\tau^2),$$

$$w_n = w_n^0 + \tau w_n^1 + O(\tau^2),$$

$$q_n = q_n^0 + \tau q_n^1 + O(\tau^2),$$

$$\rho_n = \rho_n^0 + \tau \rho_n^1 + O(\tau^2),$$

and we need to derive the equations for these variables. To begin with, let us expand system (2.18) — (2.22) in τ . It follows from (2.18) and (2.21) that

$$\sigma_*(r) = \frac{I_0(r)}{I_0(R_*)} = \frac{I_0(r)}{I_0(R_*^0)} + \tau \frac{I_0(r)(-I_1(R_*^0))R_*^1}{I_0^2(R_*^0)} + O(\tau^2),$$

and therefore,

$$\sigma_*^0(r) = \frac{I_0(r)}{I_0(R_*^0)}, \quad (2.60)$$

$$\sigma_*^1(r) = -\frac{I_0(r)I_1(R_*^0)}{I_0^2(R_*^0)}R_*^1. \quad (2.61)$$

Next, we shall find the formula of $\frac{\partial^2 p_*}{\partial r^2}$ in (2.58). Integrating equation (2.20) over the

interval $(-\tau, 0)$, we obtain

$$r - \xi_*(-\tau; r, 0) = \int_{-\tau}^0 -\frac{\partial p_*}{\partial r}(\xi_*(s; r, 0))ds,$$

i.e.,

$$\xi_*(-\tau; r, 0) = r + \int_{-\tau}^0 \frac{\partial p_*}{\partial r}(\xi_*(s; r, 0))ds = r + \tau \frac{\partial p_*^0(r)}{\partial r} + O(\tau^2).$$

We then substitute the above expression for $\xi_*(-\tau; r, 0)$ into (2.19), since

$$\begin{aligned} \sigma_*(\xi_*(-\tau; r, 0)) &= \sigma_*\left(r + \tau \frac{\partial p_*^0(r)}{\partial r} + O(\tau^2)\right) \\ &= \sigma_*^0\left(r + \tau \frac{\partial p_*^0(r)}{\partial r}\right) + \tau \sigma_*^1\left(r + \tau \frac{\partial p_*^0(r)}{\partial r}\right) + O(\tau^2) \\ &= \sigma_*^0(r) + \tau \left(\frac{\partial \sigma_*^0}{\partial r}(r) \frac{\partial p_*^0}{\partial r}(r) + \sigma_*^1(r)\right) + O(\tau^2), \end{aligned} \quad (2.62)$$

we derive the equations for p_*^0 and p_*^1 , respectively,

$$-\frac{\partial^2 p_*^0}{\partial r^2} - \frac{1}{r} \frac{\partial p_*^0}{\partial r} = \mu[\sigma_*^0 - \tilde{\sigma}], \quad (2.63)$$

$$-\frac{\partial^2 p_*^1}{\partial r^2} - \frac{1}{r} \frac{\partial p_*^1}{\partial r} = \mu \frac{\partial \sigma_*^0}{\partial r} \frac{\partial p_*^0}{\partial r} + \mu \sigma_*^1. \quad (2.64)$$

The boundary condition $p_*(R_*) = \frac{1}{R_*}$ is expanded as follows:

$$p_*^0(R_*^0) + \tau \frac{\partial p_*^0}{\partial r}(R_*^0) R_*^1 + \tau p_*^1(R_*^0) + O(\tau^2) = \frac{1}{R_*^0} - \tau \frac{R_*^1}{(R_*^0)^2} + O(\tau^2).$$

Thus, we have

$$p_*^0(R_*^0) = \frac{1}{R_*^0}, \quad (2.65)$$

$$p_*^1(R_*^0) = -\frac{R_*^1}{(R_*^0)^2} - \frac{\partial p_*^0}{\partial r}(R_*^0) R_*^1. \quad (2.66)$$

Next we expand the integral equation (2.22) using (2.62):

$$\begin{aligned}
0 &= \int_0^{R_*} [\sigma_*(\xi_*(-\tau; r, 0)) - \tilde{\sigma}] r dr \\
&= \int_0^{R_*} [\sigma_*^0(r) - \tilde{\sigma}] r dr + \tau \int_0^{R_*^0} \left[\frac{\partial \sigma_*^0}{\partial r}(r) \frac{\partial p_*^0}{\partial r}(r) + \sigma_*^1(r) \right] r dr + O(\tau^2).
\end{aligned} \tag{2.67}$$

By (2.60), the first part of (2.67) is integrated explicitly as

$$\begin{aligned}
\int_0^{R_*} [\sigma_*^0(r) - \tilde{\sigma}] r dr &= \int_0^{R_*} \left[\frac{I_0(r)}{I_0(R_*^0)} - \tilde{\sigma} \right] r dr = \frac{R_* I_1(R_*)}{I_0(R_*^0)} - \frac{\tilde{\sigma}}{2} (R_*)^2 \\
&= \frac{R_*^0 I_1(R_*^0)}{I_0(R_*^0)} - \frac{\tilde{\sigma}}{2} (R_*^0)^2 + \tau \left[\frac{R_*^1 I_1(R_*^0)}{I_0(R_*^0)} + \frac{R_*^0 (I_0(R_*^0) + I_2(R_*^0))}{2I_0(R_*^0)} R_*^1 - \tilde{\sigma} R_*^0 R_*^1 \right] + O(\tau^2).
\end{aligned} \tag{2.68}$$

Combining (2.67) with (2.68), we derive

$$\begin{aligned}
R_*^0 \left(\frac{I_1(R_*^0)}{I_0(R_*^0)} - \frac{\tilde{\sigma}}{2} R_*^0 \right) &+ \tau \left[\frac{R_*^1 I_1(R_*^0)}{I_0(R_*^0)} + \frac{R_*^0 (I_0(R_*^0) + I_2(R_*^0))}{2I_0(R_*^0)} R_*^1 \right. \\
&\quad \left. - \tilde{\sigma} R_*^0 R_*^1 + \int_0^{R_*^0} \left(\frac{\partial \sigma_*^0}{\partial r}(r) \frac{\partial p_*^0}{\partial r}(r) + \sigma_*^1(r) \right) r dr \right] = O(\tau^2),
\end{aligned}$$

which leads to a set of two equations,

$$\frac{I_1(R_*^0)}{I_0(R_*^0)} - \frac{\tilde{\sigma}}{2} R_*^0 = 0, \tag{2.69}$$

$$\begin{aligned}
\frac{R_*^1 I_1(R_*^0)}{I_0(R_*^0)} &+ \frac{R_*^0 (I_0(R_*^0) + I_2(R_*^0))}{2I_0(R_*^0)} R_*^1 - \tilde{\sigma} R_*^0 R_*^1 \\
&+ \int_0^{R_*^0} \left(\frac{\partial \sigma_*^0}{\partial r}(r) \frac{\partial p_*^0}{\partial r}(r) + \sigma_*^1(r) \right) r dr = 0.
\end{aligned} \tag{2.70}$$

These two equations determine R_*^0 and R_*^1 , respectively.

After considering system (2.18) — (2.22), we then deduce the expansion of system (2.54) — (2.59). First of all, w_n^0 and w_n^1 satisfy the same equation (2.54). Expanding (2.55) in τ we find

$$w_n^0(R_*^0 + \tau R_*^1, t) + \tau w_n^1(R_*^0, t) = - \left(\frac{\partial \sigma_*^0}{\partial r}(R_*^0 + \tau R_*^1) + \tau \frac{\partial \sigma_*^1}{\partial r}(R_*^0) \right) [\rho_n^0(t) + \tau \rho_n^1(t)] + O(\tau^2),$$

which gives the boundary conditions for w_n^0 and w_n^1 :

$$w_n^0(R_*^0, t) = -\frac{\partial \sigma_*^0}{\partial r}(R_*^0) \rho_n^0(t), \quad (2.71)$$

$$\begin{aligned} w_n^1(R_*^0, t) = & -\frac{\partial w_n^0}{\partial r}(R_*^0, t) R_*^1 - \frac{\partial \sigma_*^0}{\partial r}(R_*^0) \rho_n^1(t) \\ & - \frac{\partial^2 \sigma_*^0}{\partial r^2}(R_*^0) R_*^1 \rho_n^0(t) - \frac{\partial \sigma_*^1}{\partial r}(R_*^0) \rho_n^0(t). \end{aligned} \quad (2.72)$$

The next step is to expand (2.56) and (2.59) in τ . Noting that

$$\begin{aligned} \varphi_n(t - \tau; r, t) &= \varphi_n(t; r, t) + \frac{\partial \varphi_n}{\partial s}(t; r, t)(-\tau) + O(\tau^2) \\ &= 0 + \left(-\frac{\partial^2 p_*}{\partial r^2}(\xi_{10}) \varphi_n(t; r, t) - \frac{\partial q_n}{\partial r}(r, t) \right)(-\tau) + O(\tau^2) \\ &= 0 + \left(0 - \frac{\partial q_n^0}{\partial r}(r, t) \right)(-\tau) + O(\tau^2) \\ &= \tau \frac{\partial q_n^0}{\partial r}(r, t) + O(\tau^2), \end{aligned} \quad (2.73)$$

and using (2.46),

$$\begin{aligned} \frac{\partial \sigma_*}{\partial r}(\xi_{10}(t - \tau; r, t)) \varphi_n(t - \tau; r, t) &= \left(\frac{\partial \sigma_*^0}{\partial r}(r) + O(\tau) \right) \left(\tau \frac{\partial q_n^0}{\partial r}(r, t) + O(\tau^2) \right) \\ &= \tau \frac{\partial \sigma_*^0}{\partial r}(r) \frac{\partial q_n^0}{\partial r}(r, t) + O(\tau^2), \end{aligned} \quad (2.74)$$

we deduce,

$$\begin{aligned} w_n(\xi_{10}(t - \tau; r, t), t - \tau) &= w_n^0(\xi_{10}(t - \tau; r, t), t - \tau) + \tau w_n^1(r, t) + O(\tau^2) \\ &= w_n^0\left(r + \int_{t-\tau}^t \frac{\partial p_*}{\partial r}(\xi_{10}(s; r, t)) ds, t - \tau\right) + \tau w_n^1(r, t) + O(\tau^2) \\ &= w_n^0(r, t) + \tau \left[\frac{\partial w_n^0}{\partial r}(r, t) \frac{\partial p_*^0}{\partial r}(r) - \frac{\partial w_n^0}{\partial t}(r, t) + w_n^1(r, t) \right] + O(\tau^2). \end{aligned} \quad (2.75)$$

Substituting (2.73) — (2.75) into (2.56), we derive equations for q_n^0 and q_n^1 , respec-

tively,

$$-\frac{\partial^2 q_n^0}{\partial r^2} - \frac{1}{r} \frac{\partial q_n^0}{\partial r} + \frac{n^2}{r^2} q_n^0 = \mu w_n^0, \quad (2.76)$$

$$-\frac{\partial^2 q_n^1}{\partial r^2} - \frac{1}{r} \frac{\partial q_n^1}{\partial r} + \frac{n^2}{r^2} q_n^1 = \mu \frac{\partial \sigma_*^0}{\partial r} \frac{\partial q_n^0}{\partial r} + \mu \frac{\partial w_n^0}{\partial r} \frac{\partial p_*^0}{\partial r} - \mu \frac{\partial w_n^0}{\partial t} + \mu w_n^1. \quad (2.77)$$

To get the boundary conditions for q_n^0 and q_n^1 , we write (2.57) as

$$q_n^0(R_*^0 + \tau R_*^1, t) + \tau q_n^1(R_*^0, t) = \frac{n^2 - 1}{(R_*^0 + \tau R_*^1)^2} [\rho_n^0(t) + \tau \rho_n^1(t)] + O(\tau^2),$$

and hence

$$q_n^0(R_*^0, t) = \frac{n^2 - 1}{(R_*^0)^2} \rho_n^0(t), \quad (2.78)$$

$$q_n^1(R_*^0, t) = -\frac{\partial q_n^0}{\partial r}(R_*^0, t) R_*^1 + \frac{n^2 - 1}{(R_*^0)^2} \rho_n^1(t) - \frac{2(n^2 - 1) R_*^1}{(R_*^0)^3} \rho_n^0(t). \quad (2.79)$$

Finally from (2.58) we have

$$\begin{aligned} \frac{d}{dt} [\rho_n^0(t) + \tau \rho_n^1(t)] = & - \left(\frac{\partial^2 p_*^0}{\partial r^2}(R_*^0 + \tau R_*^1) + \tau \frac{\partial^2 p_*^1}{\partial r^2}(R_*^0) \right) [\rho_n^0(t) + \tau \rho_n^1(t)] \\ & - \frac{\partial(q_n^0 + \tau q_n^1)}{\partial r}(R_*^0 + \tau R_*^1) + O(\tau^2), \end{aligned}$$

which implies

$$\frac{d\rho_n^0(t)}{dt} = -\frac{\partial^2 p_*^0}{\partial r^2}(R_*^0) \rho_n^0(t) - \frac{\partial q_n^0}{\partial r}(R_*^0, t), \quad (2.80)$$

$$\begin{aligned} \frac{d\rho_n^1(t)}{dt} = & -\frac{\partial^2 p_*^0}{\partial r^2}(R_*^0) \rho_n^1(t) - \frac{\partial^3 p_*^0}{\partial r^3}(R_*^0) R_*^1 \rho_n^0(t) \\ & - \frac{\partial^2 p_*^1}{\partial r^2}(R_*^0) \rho_n^0(t) - \frac{\partial^2 q_n^0}{\partial r^2}(R_*^0, t) R_*^1 - \frac{\partial q_n^1}{\partial r}(R_*^0, t). \end{aligned} \quad (2.81)$$

We now group all the zeroth-order terms and the first-order terms in τ , respectively, leading to two separate systems.

2.3.1 The system of all zeroth-order terms

Collecting the zeroth-order terms from (2.60), (2.63), (2.65), (2.69), (2.71), (2.76), (2.78), and (2.80), we obtain the following system in $B_{R_*^0}$,

$$-\frac{\partial^2 \sigma_*^0}{\partial r^2} - \frac{1}{r} \frac{\partial \sigma_*^0}{\partial r} = -\sigma_*^0, \quad \sigma_*^0(R_*^0) = 1, \quad \text{i.e.,} \quad \sigma_*^0(r) = \frac{I_0(r)}{I_0(R_*^0)}, \quad (2.82)$$

$$\frac{I_1(R_*^0)}{I_0(R_*^0)} - \frac{\tilde{\sigma}}{2} R_*^0 = 0, \quad \text{i.e.,} \quad \frac{\tilde{\sigma}}{2} = \frac{I_1(R_*^0)}{R_*^0 I_0(R_*^0)}, \quad (2.83)$$

$$-\frac{\partial^2 p_*^0}{\partial r^2} - \frac{1}{r} \frac{\partial p_*^0}{\partial r} = \mu[\sigma_*^0 - \tilde{\sigma}], \quad p_*^0(R_*^0) = \frac{1}{R_*^0}, \quad (2.84)$$

$$-\frac{\partial^2 w_n^0}{\partial r^2} - \frac{1}{r} \frac{\partial w_n^0}{\partial r} + \left(\frac{n^2}{r^2} + 1\right) w_n^0 = 0, \quad w_n^0(R_*^0, t) = -\frac{\partial \sigma_*^0}{\partial r}(R_*^0) \rho_n^0(t), \quad (2.85)$$

$$-\frac{\partial^2 q_n^0}{\partial r^2} - \frac{1}{r} \frac{\partial q_n^0}{\partial r} + \frac{n^2}{r^2} q_n^0 = \mu w_n^0, \quad q_n^0(R_*^0, t) = \frac{n^2 - 1}{(R_*^0)^2} \rho_n^0(t), \quad (2.86)$$

$$\frac{d\rho_n^0(t)}{dt} = -\frac{\partial^2 p_*^0}{\partial r^2}(R_*^0) \rho_n^0(t) - \frac{\partial q_n^0}{\partial r}(R_*^0, t). \quad (2.87)$$

We first solve $p_*^0(r)$ and $w_n^0(r, t)$ from (2.84) and (2.85) as

$$p_*^0(r) = \frac{1}{4} \mu \tilde{\sigma} r^2 - \mu \frac{I_0(r)}{I_0(R_*^0)} + \frac{1}{R_*^0} + \mu - \frac{1}{4} \mu \tilde{\sigma} (R_*^0)^2, \quad (2.88)$$

$$w_n^0(r, t) = -\frac{I_1(R_*^0) I_n(r)}{I_0(R_*^0) I_n(R_*^0)} \rho_n^0(t), \quad (2.89)$$

from which we compute the following terms needed in the subsequent computation,

$$\frac{\partial w_n^0}{\partial r}(r, t) = -\frac{I_1(R_*^0)}{I_0(R_*^0) I_n(R_*^0)} \left(I_{n+1}(r) + \frac{n}{r} I_n(r) \right) \rho_n^0(t), \quad (2.90)$$

$$\frac{\partial^2 p_*^0}{\partial r^2}(R_*^0) = \frac{1}{2} \mu \tilde{\sigma} - \mu \left(1 - \frac{I_1(R_*^0)}{R_*^0 I_0(R_*^0)} \right) = \mu \left[\frac{2I_1(R_*^0)}{R_*^0 I_0(R_*^0)} - 1 \right], \quad (2.91)$$

$$\frac{\partial^3 p_*^0}{\partial r^3}(R_*^0) = \mu \left[\frac{1}{R_*^0} - \frac{2I_1(R_*^0)}{(R_*^0)^2 I_0(R_*^0)} - \frac{I_1(R_*^0)}{I_0(R_*^0)} \right]. \quad (2.92)$$

Note that in deriving (2.91) we also made use of (2.83). Next we would like to find q_n^0 . To do that, we first let $\eta_n^0 = q_n^0 + \mu w_n^0$. Combining (2.85) and (2.86), we find that

η_n^0 satisfies

$$-\frac{\partial^2 \eta_n^0}{\partial r^2} - \frac{1}{r} \frac{\partial \eta_n^0}{\partial r} + \frac{n^2}{r^2} \eta_n^0 = 0, \quad \text{in } B_{R_*^0},$$

and its solution is given in the form $\eta_n^0(r, t) = C_1(t)r^n$, thus,

$$q_n^0(r, t) = \eta_n^0(r, t) - \mu w_n^0(r, t) = C_1(t)r^n - \mu w_n^0(r, t), \quad (2.93)$$

where $C_1(t)$ is determined by the boundary condition (2.86). Using also (2.89), we get

$$C_1(t) = \frac{1}{(R_*^0)^n} \left[\frac{n^2 - 1}{(R_*^0)^2} - \mu \frac{I_1(R_*^0)}{I_0(R_*^0)} \right] \rho_n^0(t). \quad (2.94)$$

To calculate $\frac{\partial q_n^0}{\partial t}(R_*^0, t)$ in (2.87), we use (2.89), (2.93), (2.94), and the properties of Bessel functions in Appendix A to obtain

$$\begin{aligned} \frac{\partial q_n^0}{\partial r}(R_*^0, t) &= C_1(t)n(R_*^0)^{n-1} - \mu \frac{\partial w_n^0}{\partial r} \Big|_{r=R_*^0} \\ &= \left[\frac{n(n^2 - 1)}{(R_*^0)^3} + \mu \frac{I_1(R_*^0)I_{n+1}(R_*^0)}{I_0(R_*^0)I_n(R_*^0)} \right] \rho_n^0(t). \end{aligned} \quad (2.95)$$

Taking another derivative with respect to r , we have, for $n \geq 2$,

$$\begin{aligned} \frac{\partial^2 q_n^0}{\partial r^2}(R_*^0, t) &= \left[\frac{n(n-1)}{(R_*^0)^2} \left(\frac{n^2 - 1}{(R_*^0)^2} - \frac{\mu I_1(R_*^0)}{I_0(R_*^0)} \right) \right. \\ &\quad \left. - \frac{\mu I_1(R_*^0)I_{n+1}(R_*^0)}{R_*^0 I_0(R_*^0)I_n(R_*^0)} + \frac{\mu((R_*^0)^2 + n^2 - n)I_1(R_*^0)}{(R_*^0)^2 I_0(R_*^0)} \right] \rho_n^0(t), \end{aligned} \quad (2.96)$$

which will be needed in the subsequent calculations. After we obtain $\frac{\partial^2 p_*^0}{\partial r^2}(R_*^0)$ from (2.91) and $\frac{\partial q_n^0}{\partial r}(R_*^0, t)$ from (2.95), we now substitute these two results into (2.87) to obtain

$$\frac{d\rho_n^0(t)}{dt} = \left[\mu \left(1 - \frac{2I_1(R_*^0)}{R_*^0 I_0(R_*^0)} - \frac{I_1(R_*^0)I_{n+1}(R_*^0)}{I_0(R_*^0)I_n(R_*^0)} \right) - \frac{n(n^2 - 1)}{(R_*^0)^3} \right] \rho_n^0(t),$$

which integrates to

$$\rho_n^0(t) = \rho_n^0(0) \exp \left\{ \left[\mu \left(1 - \frac{2I_1(R_*^0)}{R_*^0 I_0(R_*^0)} - \frac{I_1(R_*^0) I_{n+1}(R_*^0)}{I_0(R_*^0) I_n(R_*^0)} \right) - \frac{n(n^2 - 1)}{(R_*^0)^3} \right] t \right\}. \quad (2.97)$$

We shall discuss the long-time behavior of $\rho_n^0(t)$ based on (2.97). As will be seen, the analysis is different for $n = 0$, $n = 1$, and $n \geq 2$.

Lemma 2.2. *For $n = 0$ and any $\mu > 0$, there exists $\delta > 0$ such that $|\rho_0^0(t)| \leq |\rho_0^0(0)|e^{-\delta t}$, for all $t > 0$.*

Proof. When $n = 0$, $\frac{n(n^2-1)}{(R_*^0)^3} = 0$, (2.97) becomes

$$\rho_0^0(t) = \rho_0^0(0) \exp \left\{ \left[1 - \frac{2I_1(R_*^0)}{R_*^0 I_0(R_*^0)} - \frac{I_1^2(R_*^0)}{I_0^2(R_*^0)} \right] \mu t \right\}.$$

It suffices to show

$$1 - \frac{2I_1(x)}{xI_0(x)} - \frac{I_1^2(x)}{I_0^2(x)} < 0, \quad \text{for } x > 0. \quad (2.98)$$

This inequality is equivalent to (3.22) in [74], which has been established already. \square

Remark 2.3. $n = 0$ represents radially-symmetric perturbations. Indeed, in this case, if we ignore $O(\varepsilon^2)$ and $O(\tau^2)$ terms, we have

$$r = R_* + \varepsilon \rho_0(t) \cos(0\theta) = R_*^0 + \varepsilon \rho_0^0(t) + \tau(R_*^1 + \varepsilon \rho_0^1(t)).$$

When τ is small, we do not expect the first-order terms in τ to have a major contribution, hence Lemma 2.2 indicates that the stationary solution is always stable with respect to radially-symmetric perturbations. It is just another indication that the stability discussed in [107] is valid for all μ .

Lemma 2.3. *For $n = 1$ and any $\mu > 0$, we have $\rho_1^0(t) = \rho_1^0(0)$, for all $t > 0$.*

Proof. When $n = 1$, $\frac{n(n^2-1)}{(R_*^0)^3} = 0$, by (2.97), we have

$$\rho_1^0(t) = \rho_1^0(0) \exp \left\{ \left[1 - \frac{2I_1(R_*^0)}{R_*^0 I_0(R_*^0)} - \frac{I_2(R_*^0)}{I_0(R_*^0)} \right] \mu t \right\} = \rho_1^0(0),$$

since $I_0(x) - I_2(x) = \frac{2}{x} I_1(x)$ by (A.7). □

Lemma 2.4. For $n \geq 2$,

$$1 - \frac{2I_1(x)}{xI_0(x)} - \frac{I_1(x)I_{n+1}(x)}{I_0(x)I_n(x)} > 0, \quad x > 0. \quad (2.99)$$

The proof of this lemma can be found in [74] (Lemma 3.3). For $n \geq 2$, we define μ_n^0 to be the solution to

$$\mu_n^0 \left(1 - \frac{2I_1(R_*^0)}{R_*^0 I_0(R_*^0)} - \frac{I_1(R_*^0)I_{n+1}(R_*^0)}{I_0(R_*^0)I_n(R_*^0)} \right) - \frac{n(n^2-1)}{(R_*^0)^3} = 0,$$

that is,

$$\mu_n^0 = \left[\frac{n(n^2-1)}{(R_*^0)^3} \right] / \left[1 - \frac{2I_1(R_*^0)}{R_*^0 I_0(R_*^0)} - \frac{I_1(R_*^0)I_{n+1}(R_*^0)}{I_0(R_*^0)I_n(R_*^0)} \right]. \quad (2.100)$$

Lemma 2.4 implies that $\mu_n^0 > 0$. We then have the following lemma.

Lemma 2.5. For $n \geq 2$, $\mu_n^0 < \mu_{n+1}^0$.

Proof. By (2.100), we only need to establish the inequality

$$\frac{\frac{n(n^2-1)}{x^3}}{1 - \frac{2I_1(x)}{xI_0(x)} - \frac{I_1(x)I_{n+1}(x)}{I_0(x)I_n(x)}} < \frac{\frac{(n+1)[(n+1)^2-1]}{x^3}}{1 - \frac{2I_1(x)}{xI_0(x)} - \frac{I_1(x)I_{n+2}(x)}{I_0(x)I_{n+1}(x)}}, \quad x > 0.$$

Using Lemma 2.4, it suffices to show

$$(n+2)x \frac{I_{n+1}(x)}{I_n(x)} - (n-1)x \frac{I_{n+2}(x)}{I_{n+1}(x)} - 3x \frac{I_0(x)}{I_1(x)} + 6 < 0, \quad x > 0. \quad (2.101)$$

The above inequality has been established in [74]. The proof is complete. □

Since Lemmas 2.2 and 2.3 are valid for all μ , we define $\mu_0^0 = \mu_1^0 = \infty$. And set

$$\mu_* = \min\{\mu_0^0, \mu_1^0, \mu_2^0, \mu_3^0, \dots\}. \quad (2.102)$$

Then by Lemma 2.5,

$$\mu_* = \mu_2^0. \quad (2.103)$$

Combining Lemmas 2.4, 2.5 and equation (2.103), it is easy to derive the following result.

Lemma 2.6. *For $n \geq 2$ and $\mu < \mu_*$, there exists $\delta > 0$ such that*

$$|\rho_n^0(t)| \leq |\rho_n^0(0)|e^{-\delta n^3 t}, \text{ for all } t > 0, \quad (2.104)$$

where δ is independent of n .

Proof. Since $\mu < \mu_*$, there exists $\delta_1 > 0$ independent of n such that

$$\mu \left(1 - \frac{2I_1(R_*^0)}{R_*^0 I_0(R_*^0)} - \frac{I_1(R_*^0)I_{n+1}(R_*^0)}{I_0(R_*^0)I_n(R_*^0)} \right) - \frac{n(n^2 - 1)}{(R_*^0)^3} < -\delta_1 n^3$$

is valid for n sufficiently large, i.e., $n > n_0$. On the other hand, for each $n \in [2, n_0]$, there exists a corresponding $\delta_n > 0$ such that

$$\mu \left(1 - \frac{2I_1(R_*^0)}{R_*^0 I_0(R_*^0)} - \frac{I_1(R_*^0)I_{n+1}(R_*^0)}{I_0(R_*^0)I_n(R_*^0)} \right) - \frac{n(n^2 - 1)}{(R_*^0)^3} < -\delta_n n^3.$$

Choosing $0 < \delta < \min\{\delta_1, \delta_2, \dots, \delta_{n_0}\}$, we thus have

$$\mu \left(1 - \frac{2I_1(R_*^0)}{R_*^0 I_0(R_*^0)} - \frac{I_1(R_*^0)I_{n+1}(R_*^0)}{I_0(R_*^0)I_n(R_*^0)} \right) - \frac{n(n^2 - 1)}{(R_*^0)^3} < -\delta n^3$$

holds for all $n \geq 2$. Therefore, it follows from (2.97) that

$$\begin{aligned} |\rho_n^0(t)| &= |\rho_n^0(0)| \exp \left\{ \left[\mu \left(1 - \frac{2I_1(R_*^0)}{R_*^0 I_0(R_*^0)} - \frac{I_1(R_*^0) I_{n+1}(R_*^0)}{I_0(R_*^0) I_n(R_*^0)} \right) - \frac{n(n^2 - 1)}{(R_*^0)^3} \right] t \right\} \\ &\leq |\rho_n^0(0)| e^{-\delta n^3 t}, \quad \text{for all } t > 0, \end{aligned}$$

which completes the proof. \square

Remark 2.4. Lemma 2.6 indicates that when the time delay τ is small enough, and tumor proliferation intensity μ is smaller than a critical value (i.e., $\mu < \mu_*$), then the stationary solution (σ_*, p_*, R_*) is linearly stable even under non-radially symmetric perturbations. However, in contrast to the result in [107], we showed that the system is unstable with respect to perturbations when $\mu > \mu_*$. As indicated earlier, the instability comes from $n = 2$ mode, which does not contradict the result in [107].

2.3.2 The system of all first-order terms

In the following, we are going to tackle the system involving all the first-order terms in τ . We now collect first-order equations and their respective boundary conditions from (2.61), (2.64), (2.66), (2.70), (2.72), (2.77), (2.79), and (2.81):

$$-\frac{\partial^2 \sigma_*^1}{\partial r^2} - \frac{1}{r} \frac{\partial \sigma_*^1}{\partial r} = -\sigma_*^1, \quad \sigma_*^1(R_*^0) = -\frac{I_1(R_*^0)}{I_0(R_*^0)} R_*^1 \Rightarrow \sigma_*^1(r) = -\frac{I_0(r) I_1(R_*^0)}{I_0^2(R_*^0)} R_*^1, \quad (2.105)$$

$$\frac{2R_*^1 I_1(R_*^0) + R_*^1 R_*^0 (I_0(R_*^0) + I_2(R_*^0))}{2I_0(R_*^0)} - \tilde{\sigma} R_*^0 R_*^1 + \int_0^{R_*^0} \left(\frac{\partial \sigma_*^0}{\partial r}(r) \frac{\partial p_*^0}{\partial r}(r) + \sigma_*^1(r) \right) r dr = 0, \quad (2.106)$$

$$-\frac{\partial^2 p_*^1}{\partial r^2} - \frac{1}{r} \frac{\partial p_*^1}{\partial r} = \mu \frac{\partial \sigma_*^0}{\partial r} \frac{\partial p_*^0}{\partial r} + \mu \sigma_*^1, \quad p_*^1(R_*^0) = -\frac{R_*^1}{(R_*^0)^2} - \frac{\partial p_*^0}{\partial r}(R_*^0) R_*^1, \quad (2.107)$$

$$\begin{cases} -\frac{\partial^2 w_n^1}{\partial r^2} - \frac{1}{r} \frac{\partial w_n^1}{\partial r} + \left(\frac{n^2}{r^2} + 1 \right) w_n^1 = 0, \\ w_n^1(R_*^0, t) = -\frac{\partial w_n^0}{\partial r}(R_*^0, t) R_*^1 - \frac{\partial \sigma_*^0}{\partial r}(R_*^0) \rho_n^1(t) - \frac{\partial^2 \sigma_*^0}{\partial r^2}(R_*^0) R_*^1 \rho_n^0(t) - \frac{\partial \sigma_*^1}{\partial r}(R_*^0) \rho_n^0(t), \end{cases} \quad (2.108)$$

$$\begin{cases} -\frac{\partial^2 q_n^1}{\partial r^2} - \frac{1}{r} \frac{\partial q_n^1}{\partial r} + \frac{n^2}{r^2} q_n^1 = \mu \frac{\partial \sigma_*^0}{\partial r} \frac{\partial q_n^0}{\partial r} + \mu \frac{\partial w_n^0}{\partial r} \frac{\partial p_*^0}{\partial r} - \mu \frac{\partial w_n^0}{\partial t} + \mu w_n^1, \\ q_n^1(R_*^0, t) = -\frac{\partial q_n^0}{\partial r}(R_*^0, t) R_*^1 + \frac{n^2 - 1}{(R_*^0)^2} \rho_n^1(t) - \frac{2(n^2 - 1) R_*^1}{(R_*^0)^3} \rho_n^0(t), \end{cases} \quad (2.109)$$

$$\begin{aligned} \frac{d\rho_n^1(t)}{dt} = & -\frac{\partial^2 p_*^0}{\partial r^2}(R_*^0)\rho_n^1(t) - \frac{\partial^3 p_*^0}{\partial r^3}(R_*^0)R_*^1\rho_n^0(t) - \frac{\partial^2 p_*^1}{\partial r^2}(R_*^0)\rho_n^0(t) - \frac{\partial^2 q_n^0}{\partial r^2}(R_*^0, t)R_*^1 \\ & - \frac{\partial q_n^1}{\partial r}(R_*^0, t). \end{aligned} \quad (2.110)$$

In the equation (2.110), p_*^0 and q_n^0 are already computed in the last section, we only need to compute $\frac{\partial^2 p_*^1}{\partial r^2}(R_*^0)$ and $\frac{\partial q_n^1}{\partial r}(R_*^0, t)$. Integrating (2.107) over $(0, r)$ with rdr , we obtain

$$\frac{\partial p_*^1}{\partial r}(r) = -\frac{\mu}{r} \int_0^r \left(\frac{\partial \sigma_*^0}{\partial r}(y) \frac{\partial p_*^0}{\partial r}(y) + \sigma_*^1(y) \right) y dy.$$

We then substitute the expressions of σ_*^0 from (2.82), p_*^0 from (2.88), and σ_*^1 from (2.105) into the above equality to derive

$$\frac{\partial p_*^1}{\partial r}(r) = -\frac{\mu}{r} \int_0^r \left[\frac{\mu I_1(y)}{I_0(R_*^0)} \left(\frac{1}{2} \tilde{\sigma} y - \frac{I_1(y)}{I_0(R_*^0)} \right) - \frac{I_0(y) I_1(R_*^0)}{I_0^2(R_*^0)} R_*^1 \right] y dy. \quad (2.111)$$

Since, by (A.4) and (A.5),

$$\frac{d}{dr} \left(r^2 I_0(r) - 2r I_1(r) \right) = r^2 I_1(r),$$

$$\frac{d}{dr} \left(\frac{r^2 (I_1^2(r) - I_0^2(r))}{2} + r I_0(r) I_1(r) \right) = r I_1^2(r),$$

$$\frac{d}{dr} \left(r I_1(r) \right) = r I_0(r),$$

the integral in (2.111) evaluates to

$$\frac{\mu^2 \tilde{\sigma}}{2I_0(R_*^0)} [2I_1(r) - r I_0(r)] + \frac{\mu^2}{I_0^2(R_*^0)} \left(\frac{r(I_1^2(r) - I_0^2(r))}{2} + I_0(r) I_1(r) \right) + \frac{\mu I_1(R_*^0)}{I_0^2(R_*^0)} R_*^1 I_1(r).$$

Using (A.4), (A.5), and (A.7), taking another derivative and evaluating at R_*^0 , recall-

ing also the equality $\tilde{\sigma} = \frac{I_1(R_*^0)}{R_*^0 I_0(R_*^0)}$ from (2.83), we derive

$$\begin{aligned} \frac{\partial^2 p_*^1}{\partial r^2}(R_*^0) &= \frac{\mu^2 I_1(R_*^0)}{R_*^0 I_0^2(R_*^0)} \left[-R_*^0 I_1(R_*^0) + I_2(R_*^0) \right] + \frac{\mu^2}{2I_0^2(R_*^0)} \left[I_0^2(R_*^0) + I_1^2(R_*^0) \right. \\ &\quad \left. - \frac{2I_0(R_*^0)I_1(R_*^0)}{R_*^0} + \right] + \frac{\mu R_*^1 I_1(R_*^0)}{I_0^2(R_*^0)} \left[I_0(R_*^0) - \frac{I_1(R_*^0)}{R_*^0} \right], \end{aligned} \quad (2.112)$$

which completes the computation of $\frac{\partial^2 p_*^1}{\partial r^2}(R_*^0)$. Next we proceed a long and tedious journey to compute $\frac{\partial q_n^1}{\partial r}(R_*^0, t)$. From (2.108), $w_n^1(r, t)$ can be solved in the form

$$w_n^1(r, t) = C_3(t) I_n(r). \quad (2.113)$$

Combining with the boundary condition in (2.108), using also (A.4), (A.5), (2.82), (2.90), and (2.105), we derive

$$C_3(t) I_n(R_*^0) = \left[\frac{I_1(R_*^0) I_{n+1}(R_*^0)}{I_0(R_*^0) I_n(R_*^0)} + \frac{(n+1) I_1(R_*^0)}{R_*^0 I_0(R_*^0)} - 1 + \frac{I_1^2(R_*^0)}{I_0^2(R_*^0)} \right] R_*^1 \rho_n^0(t) - \frac{I_1(R_*^0)}{I_0(R_*^0)} \rho_n^1(t),$$

which indicates that $C_3(t)$ is uniquely determined. We then have

$$\begin{aligned} w_n^1(r, t) = C_3(t) I_n(r) &= -\frac{I_1(R_*^0) I_n(r)}{I_0(R_*^0) I_n(R_*^0)} \rho_n^1(t) + \\ &\quad \left[\frac{I_1(R_*^0) I_{n+1}(R_*^0)}{I_0(R_*^0) I_n(R_*^0)} + \frac{(n+1) I_1(R_*^0)}{R_*^0 I_0(R_*^0)} - 1 + \frac{I_1^2(R_*^0)}{I_0^2(R_*^0)} \right] \frac{I_n(r)}{I_n(R_*^0)} R_*^1 \rho_n^0(t). \end{aligned} \quad (2.114)$$

Similar as in the computation of q_n^0 and w_n^0 , we let $\eta_n^1 = q_n^1 + \mu w_n^1$. Combining (2.108) with (2.109), we find that η_n^1 satisfies

$$-\frac{\partial^2 \eta_n^1}{\partial r^2} - \frac{1}{r} \frac{\partial \eta_n^1}{\partial r} + \frac{n^2}{r^2} \eta_n^1 = \mu \frac{\partial \sigma_*^0}{\partial r} \frac{\partial q_n^0}{\partial r} + \mu \frac{\partial w_n^0}{\partial r} \frac{\partial p_*^0}{\partial r} - \mu \frac{\partial w_n^0}{\partial t}, \quad \text{in } B_{R_*^0}, \quad (2.115)$$

with the boundary condition

$$\eta_n^1(R_*^0, t) = q_n^1(R_*^0, t) + \mu w_n^1(R_*^0, t). \quad (2.116)$$

For simplicity, let us denote the differential operator by $L_n := -\partial_{rr} - \frac{1}{r}\partial_r + \frac{n^2}{r^2}$ and rewrite η_n^1 as $\eta_n^1 = u_n^{(1)} + u_n^{(2)} + u_n^{(3)} + u_n^{(4)}$, where, by (2.115) and (2.116), $u_n^{(1)}, u_n^{(2)}, u_n^{(3)}$, and $u_n^{(4)}$ satisfy the following equations,

$$\begin{cases} L_n u_n^{(1)} = \mu \frac{\partial \sigma_*^0}{\partial r} \frac{\partial q_n^0}{\partial r} & \text{in } B_{R_*^0}, \\ u_n^{(1)}(R_*^0, t) = 0; \end{cases} \quad \begin{cases} L_n u_n^{(2)} = \mu \frac{\partial w_n^0}{\partial r} \frac{\partial p_*^0}{\partial r} & \text{in } B_{R_*^0}, \\ u_n^{(2)}(R_*^0, t) = 0; \end{cases}$$

$$\begin{cases} L_n u_n^{(3)} = -\mu \frac{\partial w_n^0}{\partial t} & \text{in } B_{R_*^0}, \\ u_n^{(3)}(R_*^0, t) = 0; \end{cases} \quad \begin{cases} L_n u_n^{(4)} = 0 & \text{in } B_{R_*^0}, \\ u_n^{(4)}(R_*^0, t) = q_n^1(R_*^0, t) + \mu w_n^1(R_*^0, t). \end{cases}$$

We start by analyzing $u_n^{(1)}$. Substituting (2.82) and (2.93) into the equation for $u_n^{(1)}$, recalling also (A.5), (2.90), and (2.94), we rewrite the equation as:

$$\begin{aligned} L_n u_n^{(1)} &= \mu \frac{\partial \sigma_*^0}{\partial r} \frac{\partial q_n^0}{\partial r} \\ &= \mu \frac{I_1(r)}{I_0(R_*^0)} \left[C_1(t) n r^{n-1} + \frac{I_1(R_*^0)}{I_0(R_*^0) I_n(R_*^0)} \left(I_{n+1}(r) + \frac{n}{r} I_n(r) \right) \rho_n^0(t) \right] \\ &= \mu \frac{I_1(r)}{I_0(R_*^0)} \left[\frac{n r^{n-1}}{(R_*^0)^n} \left(\frac{n^2 - 1}{(R_*^0)^2} - \mu \frac{I_1(R_*^0)}{I_0(R_*^0)} \right) + \mu \frac{I_1(R_*^0) I_{n+1}(r)}{I_0(R_*^0) I_n(R_*^0)} \right. \\ &\quad \left. + \mu \frac{n I_1(R_*^0) I_n(r)}{r I_0(R_*^0) I_n(R_*^0)} \right] \rho_n^0(t). \end{aligned} \tag{2.117}$$

Using the definition of Bessel function $I_n(r)$ in (A.2), we have $\lim_{r \rightarrow 0} \frac{I_1(r)}{r} = \frac{1}{2}$ and $\lim_{r \rightarrow 0} \frac{I_n(r)}{r} = 0$ for $n \geq 2$, thus the right-hand side of (2.117) is less than $Q(n) \rho_n^0(t)$ when $0 \leq r < R_*^0$. Here $Q(n)$ is a polynomial function of n .

Since $\rho_n^0(t)$ has different behaviors under $n \geq 2$, $n = 0$, and $n = 1$, we divide the following discussion into three cases: (i) $n \geq 2$; (ii) $n = 0$; and (iii) $n = 1$.

Case 1: $n \geq 2$ We introduce the following lemma to estimate $u_n^{(1)}$.

Lemma 2.7. *Consider the elliptic problem*

$$L_n w = -\frac{\partial^2 w}{\partial r^2} - \frac{1}{r} \frac{\partial w}{\partial r} + \frac{n^2}{r^2} w = b(r, t) \quad \text{in } B_R, \quad (2.118)$$

$$w|_{r=R} = 0, \quad (2.119)$$

where $n \geq 2$. If $b(\cdot, t) \in L^2(B_R)$, then this problem admits a unique solution w in $H^2(B_R)$ with estimates

$$\|w(\cdot, t)\|_{H^2(B_R)} \leq C \left[\int_0^R |b(r, t)|^2 r dr \right]^{1/2}, \quad (2.120)$$

$$\left| \frac{\partial w(R, t)}{\partial r} \right| \leq C \left[\int_0^R |b(r, t)|^2 r dr \right]^{1/2}, \quad (2.121)$$

where the constant C in (2.120) and (2.121) is independent of n .

Proof. Let us consider the approximate equation to (2.118) in $\varepsilon < r < R$ with zero boundary values on $x = R$ and $x = \varepsilon$, where $\varepsilon > 0$ is arbitrarily small. We denote by w_ε the corresponding classical solution. Multiplying (2.118) by $\frac{w_\varepsilon}{r^2}$ and integrating over $B_R \setminus B_\varepsilon$, we obtain:

$$\begin{aligned} \int_\varepsilon^R \left| \frac{\partial w_\varepsilon}{\partial r} \right|^2 \frac{1}{r} dr + n^2 \int_\varepsilon^R |w_\varepsilon|^2 \frac{1}{r^3} dr &= \int_\varepsilon^R b(r, t) \frac{w_\varepsilon}{r} dr + 2 \int_\varepsilon^R \frac{\partial w_\varepsilon}{\partial r} \frac{w_\varepsilon}{r^2} dr \\ &\leq \frac{1}{2n^2} \int_\varepsilon^R |b(r, t)|^2 r dr + \frac{n^2}{2} \int_\varepsilon^R |w_\varepsilon|^2 \frac{1}{r^3} dr \\ &\quad + \frac{2}{3} \int_\varepsilon^R \left| \frac{\partial w_\varepsilon}{\partial r} \right|^2 \frac{1}{r} dr + \frac{3}{2} \int_\varepsilon^R |w_\varepsilon|^2 \frac{1}{r^3} dr, \end{aligned}$$

from which it follows that

$$\frac{1}{3} \int_\varepsilon^R \left| \frac{1}{r} \frac{\partial w_\varepsilon}{\partial r} \right|^2 r dr + \left(\frac{n^2}{2} - \frac{3}{2} \right) \int_\varepsilon^R \left| \frac{w_\varepsilon}{r^2} \right|^2 r dr \leq \frac{1}{2n^2} \int_\varepsilon^R |b(r, t)|^2 r dr. \quad (2.122)$$

The equation (2.118), together with the fact that $b(\cdot, t) \in L^2(B_R)$, implies $\frac{\partial^2 w_\varepsilon}{\partial r^2} \in$

$L^2(B_R \setminus B_\varepsilon)$. Therefore $w_\varepsilon \in H^2(B_R \setminus B_\varepsilon)$, and

$$\|w_\varepsilon(\cdot, t)\|_{H^2(B_R \setminus B_\varepsilon)} \leq C \left[\int_0^R |b(r, t)|^2 r dr \right]^{1/2}, \quad (2.123)$$

where C is independent of n . Letting $\varepsilon \rightarrow 0$, we obtain a solution w to (2.118) and (2.119) with estimate (2.120). The uniqueness of the solution in $H^2(B_R)$ follows by taking $b = 0$ and using (2.120).

Next, since $H^2(B_R \setminus B_{R/2}) \hookrightarrow C^{1+1/2}(B_R \setminus B_{R/2})$, we have

$$\|w(\cdot, t)\|_{C^{1+1/2}(B_R \setminus B_{R/2})} \leq C \left[\int_0^R |b(r, t)|^2 r dr \right]^{1/2},$$

which immediately implies (2.121). \square

Applying Lemma 2.7 on (2.117), we obtain when $n \geq 2$,

$$\|u_n^{(1)}\|_{H^2(B_R)} \leq Q(n)|\rho_n^0(t)|, \quad \left| \frac{\partial u_n^{(1)}(R_*, t)}{\partial r} \right| \leq Q(n)|\rho_n^0(t)|.$$

By Lemma 2.6, we know that when $n \geq 2$ and $\mu < \mu_*$, there exists a constant $\delta > 0$ such that $|\rho_n^0(t)| \leq |\rho_n^0(0)|e^{-\delta n^3 t}$, for all $t > 0$. Therefore, we have

$$\|u_n^{(1)}\|_{H^2(B_R)} \leq Q(n)|\rho_n^0(t)| \leq Ce^{-\delta n^3 t}, \quad \left| \frac{\partial u_n^{(1)}(R_*, t)}{\partial r} \right| \leq Q(n)|\rho_n^0(t)| \leq Ce^{-\delta n^3 t}.$$

In a similar manner, we can derive the same estimates for $u_n^{(2)}$ and $u_n^{(3)}$, namely,

$$\begin{aligned} \|u_n^{(2)}\|_{H^2(B_R)} &\leq Ce^{-\delta n^3 t}, & \left| \frac{\partial u_n^{(2)}(R_*, t)}{\partial r} \right| &\leq Ce^{-\delta n^3 t}; \\ \|u_n^{(3)}\|_{H^2(B_R)} &\leq Ce^{-\delta n^3 t}, & \left| \frac{\partial u_n^{(3)}(R_*, t)}{\partial r} \right| &\leq Ce^{-\delta n^3 t}. \end{aligned}$$

With these estimates at hand, the stability for the case $\mu < \mu_*$ will be determined by $u_n^{(4)}$. Recall that the equation for $u_n^{(4)}$ is $L_n u_n^{(4)} = 0$, and the solution is clearly

given in the form $u_n^{(4)}(r, t) = C_4(t)r^n$, where $C_4(t)$ is determined by the boundary condition. Combining the boundary condition from (2.109) and (2.114), we have

$$\begin{aligned} C_4(t)(R_*^0)^n &= q_n^1(R_*^0) + \mu w_n^1(R_*^0, t) = \left[\frac{n^2 - 1}{(R_*^0)^2} - \mu \frac{I_1(R_*^0)}{I_0(R_*^0)} \right] \rho_n^1(t) + H(R_*^0, R_*^1) \rho_n^0(t), \\ \Rightarrow C_4(t) &= \frac{1}{(R_*^0)^n} \left[\frac{n^2 - 1}{(R_*^0)^2} - \mu \frac{I_1(R_*^0)}{I_0(R_*^0)} \right] \rho_n^1(t) + \tilde{H}(R_*^0, R_*^1) \rho_n^0(t), \end{aligned}$$

where H and \tilde{H} are functions of R_*^0 and R_*^1 . Now let us add $u_n^{(1)}$, $u_n^{(2)}$, $u_n^{(3)}$, and $u_n^{(4)}$, we derive

$$q_n^1(r, t) = \eta_n^1 - \mu w_n^1 = u_n^{(1)} + u_n^{(2)} + u_n^{(3)} + u_n^{(4)} - \mu w_n^1.$$

Note that we only need to evaluate $\frac{\partial q_n^1}{\partial r}(R_*^0, t)$, and

$$\frac{\partial q_n^1(R_*^0, t)}{\partial r} = \frac{\partial u_n^{(1)}(R_*^0, t)}{\partial r} + \frac{\partial u_n^{(2)}(R_*^0, t)}{\partial r} + \frac{\partial u_n^{(3)}(R_*^0, t)}{\partial r} + \frac{\partial u_n^{(4)}(R_*^0, t)}{\partial r} - \mu \frac{\partial w_n^1(R_*^0, t)}{\partial r}. \quad (2.124)$$

So far, we have calculated all the expressions needed in (2.110). To get the equation for $\rho_n^1(t)$, we substitute $\frac{\partial^2 p_*^0}{\partial r^2}$ from (2.91), $\frac{\partial^3 p_*^0}{\partial r^3}$ from (2.92), $\frac{\partial^2 p_*^1}{\partial r^2}$ from (2.112), $\frac{\partial^2 q_n^0}{\partial r^2}$ from (2.96), and $\frac{\partial q_n^1}{\partial r}$ from (2.124) into (2.110), and get for $n \geq 2$,

$$\begin{aligned} \frac{d\rho_n^1(t)}{dt} &= -\frac{\partial^2 p_*^0}{\partial r^2}(R_*^0) \rho_n^1(t) - \frac{\partial^3 p_*^0}{\partial r^3}(R_*^0) R_*^1 \rho_n^0(t) - \frac{\partial^2 p_*^1}{\partial r^2}(R_*^0) \rho_n^0(t) - \frac{\partial^2 q_n^0}{\partial r^2}(R_*^0, t) R_*^1 \\ &\quad - \frac{\partial q_n^1}{\partial r}(R_*^0, t) \\ &= \left[\mu - \mu \frac{2I_1(R_*^0)}{R_*^0 I_0(R_*^0)} - \frac{n(n^2 - 1)}{(R_*^0)^3} - \mu \frac{I_1(R_*^0) I_{n+1}(R_*^0)}{I_1(R_*^0) I_n(R_*^0)} \right] \rho_n^1(t) - \frac{\partial u_n^{(1)}(R_*^0, t)}{\partial r} \\ &\quad - \frac{\partial u_n^{(2)}(R_*^0, t)}{\partial r} - \frac{\partial u_n^{(3)}(R_*^0, t)}{\partial r} + C(n, R_*^0, R_*^1) \rho_n^0(t), \end{aligned}$$

thus,

$$\begin{aligned} &\left| \frac{d\rho_n^1(t)}{dt} + \left(\mu \frac{2I_1(R_*^0)}{R_*^0 I_0(R_*^0)} + \frac{n(n^2 - 1)}{(R_*^0)^3} + \mu \frac{I_1(R_*^0) I_{n+1}(R_*^0)}{I_1(R_*^0) I_n(R_*^0)} - \mu \right) \rho_n^1(t) \right| \\ &\leq |C(n, R_*^0, R_*^1) \rho_n^0(t)| + \left| \frac{\partial u_n^{(1)}(R_*^0, t)}{\partial r} \right| + \left| \frac{\partial u_n^{(2)}(R_*^0, t)}{\partial r} \right| + \left| \frac{\partial u_n^{(3)}(R_*^0, t)}{\partial r} \right| \end{aligned}$$

$$\leq C e^{-\delta n^3 t}. \quad (2.125)$$

Lemma 2.8. *Suppose $f(t)$ satisfies*

$$\left| \frac{df(t)}{dt} + d_1 f \right| \leq C e^{-d_2 t}, \quad \forall t > 0 \quad (2.126)$$

with $d_1, d_2 > 0$ and the initial value $|f(0)|$ bounded, then we have

$$|f(t)| \leq C e^{-dt}, \quad (2.127)$$

where $d = \min\{d_1, d_2\}$.

Proof. The condition (2.126) is equivalent to

$$-C e^{-d_2 s} \leq \frac{df(s)}{ds} + d_1 f \leq C e^{-d_2 s},$$

and thus

$$-C e^{(d_1 - d_2)s} \leq \frac{d(e^{d_1 s} f(s))}{ds} \leq C e^{(d_1 - d_2)s}.$$

Integrating s from 0 to t , we derive for any $t > 0$,

$$-C \int_0^t e^{(d_1 - d_2)s} ds \leq e^{d_1 t} f(t) - f(0) \leq C \int_0^t e^{(d_1 - d_2)s} ds,$$

$$\left[f(0) + \frac{C}{d_1 - d_2} \right] e^{-d_1 t} - \frac{C}{d_1 - d_2} e^{-d_2 t} \leq f(t) \leq \left[f(0) - \frac{C}{d_1 - d_2} \right] e^{-d_1 t} + \frac{C}{d_1 - d_2} e^{-d_2 t}.$$

If $d_1 \geq d_2 > 0$, $e^{-d_1 t} \leq e^{-d_2 t}$, then the above equation implies $|f(t)| \leq C e^{-d_2 t}$; if $d_1 < d_2$, the above equation implies $|f(t)| \leq C e^{-d_1 t}$. The proof is complete. \square

From Lemma 2.6, when $\mu < \mu_*$, we have

$$\mu \frac{2I_1(R_*^0)}{R_*^0 I_0(R_*^0)} + \frac{n(n^2 - 1)}{(R_*^0)^3} + \mu \frac{I_1(R_*^0) I_{n+1}(R_*^0)}{I_1(R_*^0) I_n(R_*^0)} - \mu \geq \delta n^3 > 0.$$

Thus applying Lemma 2.8 on (2.125) gives $|\rho_n^1(t)| \leq Ce^{-\delta n^3 t}$, i.e., $|\rho_n^1(t)|$ is exponentially decreasing.

Case 2: $n = 0$ In this case, the estimates (4.71) and (4.72) follow from the standard L^2 and Schauder theory for elliptic equations. By Lemma 4.1, there exists $\delta > 0$ such that $|\rho_0^0(t)| \leq Ce^{-\delta t}$. Following similar procedures as in case 1, we can derive

$$\left| \frac{d\rho_0^1(t)}{dt} + \mu \left(-1 + \frac{2I_1(R_*^0)}{R_*^0 I_0(R_*^0)} + \frac{I_1^2(R_*^0)}{I_0^2(R_*^0)} \right) \rho_0^1(t) \right| \leq Ce^{-\delta t}. \quad (2.128)$$

We again apply Lemma 2.2 to derive,

$$\mu \left(-1 + \frac{2I_1(R_*^0)}{R_*^0 I_0(R_*^0)} + \frac{I_1^2(R_*^0)}{I_0^2(R_*^0)} \right) > \delta > 0.$$

Based on Lemma 2.8, estimate (2.128) implies $|\rho_0^1(t)| \leq Ce^{-\delta t}$; in other words, $|\rho_0^1(t)|$ is also exponentially decreasing.

Case 3: $n = 1$ Actually, $n = 1$ mode dose not affect the stability, which is an indication of the following theorem. The proof is very lengthy and needs a lot of messy computations (see [111]). For readers' convenience, we omit the proof.

Theorem 2.2. *For $n = 1$ and any $\mu > 0$, we have $\rho_1^1(t) = \rho_1^1(0)$, for all $t > 0$.*

Remark 2.5. *We just established, for $n = 1$, after ignoring $O(\varepsilon^2)$ and $O(\tau^2)$ terms,*

$$\begin{aligned} r &= R_* + \varepsilon \rho_1(t) \cos \theta = R_* + \varepsilon (\rho_1^0(t) + \tau \rho_1^1(t)) \cos \theta \\ &= R_* + \varepsilon (\rho_1^0(0) + \tau \rho_1^1(0)) \cos \theta \triangleq R_* + \varepsilon C_1 \cos(\theta), \end{aligned}$$

where $C_1 = \rho_1^0(0) + \tau \rho_1^1(0)$. In this case, the boundary of the perturbed solution can

be written as (after dropping $O(\varepsilon^2)$ terms):

$$(x - \varepsilon \frac{C_1}{R_*})^2 + y^2 = 1,$$

which is just an ε -translation of the origin of the initial state. Therefore, $n = 1$ mode would not affect the stability.

2.3.3 Proof of Theorem 2.1

Proof. Combining Lemma 2.6 with the Case 1 in Section 2.3.2, we know that for $n \geq 2$ and $\mu < \mu_*$ (where μ_* is defined in (2.103)), both $|\rho_n^0(t)|$ and $|\rho_n^1(t)|$ are exponentially decaying, which indicates that the radially symmetric stationary solution is linearly stable in this case. However, if $\mu > \mu_*$, $|\rho_2^0(t)|$ tends to infinity as time evolves; as the behavior of the perturbed solution is dominated by the zeroth-order terms when τ is small, the stationary solution is unstable in this case. The proof is thus complete. \square

2.4 Bifurcation analysis

As the radially symmetric steady state solution was established in Section 2.2, a very interesting and natural question is whether there are non-radially symmetric solutions to the system (2.10) — (2.17) and further what are the values of the controlling parameters where bifurcation happens. To answer this question, we study the corresponding stationary problem of (2.10) — (2.17):

$$-\Delta\sigma + \sigma = 0 \quad \text{in } \Omega, \quad (2.129)$$

$$-\Delta p = \mu[\sigma(\boldsymbol{\xi}(-\tau; \mathbf{x})) - \tilde{\sigma}] \quad \text{in } \Omega, \quad (2.130)$$

$$\begin{cases} \frac{d\boldsymbol{\xi}}{ds}(s; \mathbf{x}) = -\nabla p(\boldsymbol{\xi}, s) & -\tau \leq s \leq 0, \\ \boldsymbol{\xi}(s; \mathbf{x}) = \mathbf{x} & s = 0, \end{cases} \quad (2.131)$$

$$\sigma = 1, \quad p = \kappa \quad \text{on } \partial\Omega, \quad (2.132)$$

$$\mathbf{V}_n = -\frac{\partial p}{\partial \mathbf{n}} = 0 \quad \text{on } \partial\Omega. \quad (2.133)$$

The main result is as follows:

Theorem 2.3. *For each even $n \geq 2$, there exists $\tilde{T} > 0$, such that when $\tau \in (0, \tilde{T})$, there exists μ_n^τ which is close to μ_n^0 , and $(0, \mu_n^\tau)$ is a bifurcation point of the symmetry-breaking stationary solution of the system (2.129) — (2.133). The bifurcation point μ_n^0 corresponds to the case with no time-delay (i.e., $\tau = 0$), and is defined in (2.158). Furthermore, the free boundary of this bifurcation solution is of the form*

$$r = R_* + \varepsilon \cos(n\theta) + o(\varepsilon).$$

Remark 2.6. *It has been proved in the last section that the symmetric solution is stable when $\mu < \mu_*$ and unstable when $\mu > \mu_*$, and the instability stems from a change of stability for $n = 2$ mode, therefore $\mu = \mu_2^\tau$ is the most significant bifurcation point biologically.*

To prove this bifurcation result, we start with considering a family of domains with perturbed boundaries in polar coordinates

$$\partial\Omega_\varepsilon : r = R_* + \tilde{R}(\theta) = R_* + \varepsilon S(\theta), \quad (2.134)$$

and let (σ, p) be the solution of the system

$$-\Delta\sigma + \sigma = 0 \quad \text{in } \Omega_\varepsilon, \quad (2.135)$$

$$-\Delta p = \mu[\sigma(\boldsymbol{\xi}(-\tau; \mathbf{x})) - \tilde{\sigma}] \quad \text{in } \Omega_\varepsilon, \quad (2.136)$$

$$\begin{cases} \frac{d\boldsymbol{\xi}}{ds}(s; \mathbf{x}) = -\nabla p(\boldsymbol{\xi}(s; \mathbf{x})) & -\tau \leq s \leq 0, \\ \boldsymbol{\xi}(s; \mathbf{x}) = \mathbf{x} & s = 0, \end{cases} \quad (2.137)$$

$$\sigma = 1, \quad p = \kappa \quad \text{on } \partial\Omega_\varepsilon. \quad (2.138)$$

Without the restriction on the free boundary, there is no guarantee that the solution ξ started with $\xi(0; \mathbf{x}) = \mathbf{x} \in \overline{\Omega}_\varepsilon$ will stay inside $\overline{\Omega}_\varepsilon$, therefore we need to extend the right-hand sides of (2.136) and (2.137) so that $\sigma(\xi(-\tau; \mathbf{x}))$ and $\nabla p(\xi(s; \mathbf{x}))$ are well-defined. From (2.137), $\xi(s; \mathbf{x})$ ($-\tau \leq s \leq 0$) should be very close to the initial value \mathbf{x} if τ is small enough, hence it is natural to assume $\xi(s; \mathbf{x})$ locates within B_{R_*+1} .

For notational convenience, we shall use the same letter to denote the same function in polar coordinate system or rectangular coordinate system. For example, we write $\sigma(r, \theta) = \sigma(\mathbf{x})$, with the understanding that $\mathbf{x} = r(\cos \theta, \sin \theta)$. The notation should be clear from the context. Throughout this paper, when an extension is needed for the right-hand side function m in Ω_ε , we use the inversion formula

$$m(r, \theta) = \begin{cases} m(r, \theta) & r \leq R_* + \varepsilon S(\theta), \\ 2m(R_* + \varepsilon S(\theta), \theta) - m\left(\frac{(R_* + \varepsilon S(\theta))^2}{r}, \theta\right) & r > R_* + \varepsilon S(\theta). \end{cases} \quad (2.139)$$

Functions extended this way will keep the first order derivatives continuous across the original boundary, *while its derivatives up to second order depend only on the same order of derivatives of the original function.*

For every (σ, p) , we define an extension of σ as

$$g(\mathbf{x}; \sigma) = \begin{cases} \sigma - \tilde{\sigma} & \text{in } \overline{\Omega}_\varepsilon, \\ 2\sigma(R_* + \varepsilon S(\theta), \theta) - \sigma\left(\frac{(R_* + \varepsilon S(\theta))^2}{r}, \theta\right) - \tilde{\sigma} & \text{in } B_{R_*+1} \setminus \overline{\Omega}_\varepsilon. \end{cases} \quad (2.140)$$

In this way, if $\sigma \in C^2(\overline{\Omega}_\varepsilon)$ and $S \in C^2(\Sigma)$, then $g \in W^{2,\infty}(B_{R_*+1})$. Equation (2.136) is thus replaced by

$$-\Delta p = \mu g(\xi(-\tau; \mathbf{x}); \sigma) \quad \text{in } \Omega_\varepsilon. \quad (2.141)$$

Denote $\mathbf{f}(\mathbf{x}; p) = \mathbf{f}(\mathbf{x}) = -\nabla p$, then $\mathbf{f} \in C^{1+\alpha}(\overline{\Omega}_\varepsilon)$ if $p \in C^{2+\alpha}(\overline{\Omega}_\varepsilon)$. Similarly, we define an extension of \mathbf{f} as

$$\hat{\mathbf{f}}(\mathbf{x}; p) = \begin{cases} \mathbf{f}(r, \theta) & \text{in } \Omega_\varepsilon, \\ 2\mathbf{f}(R_* + \varepsilon S(\theta), \theta) - \mathbf{f}\left(\frac{(R_* + \varepsilon S(\theta))^2}{r}, \theta\right) & \text{in } B_{R_*+1} \setminus \Omega_\varepsilon. \end{cases} \quad (2.142)$$

We can easily verify that $\hat{\mathbf{f}}$ is C^1 in B_{R_*+1} , and for $\mathbf{x}^{(1)}, \mathbf{x}^{(2)} \in B_{R_*+1}$,

$$\begin{aligned} |\hat{\mathbf{f}}(\mathbf{x}^{(1)}; p) - \hat{\mathbf{f}}(\mathbf{x}^{(2)}; p)| &\leq \|\hat{\mathbf{f}}\|_{C^1(\overline{B}_{R_*+1})} |\mathbf{x}^{(1)} - \mathbf{x}^{(2)}| \\ &\leq C \|\mathbf{f}\|_{C^1(\overline{\Omega}_\varepsilon)} |\mathbf{x}^{(1)} - \mathbf{x}^{(2)}|, \end{aligned} \quad (2.143)$$

where C is a constant. Using the above extensions, we replace (2.137) by

$$\frac{d\xi}{ds}(s; \mathbf{x}) = \hat{\mathbf{f}}(\xi(s; \mathbf{x}); p), \quad \xi(0; \mathbf{x}) = \mathbf{x}. \quad (2.144)$$

It has been proved in [113] that the extended system (2.135) (2.138) (2.141) (2.144) (for brevity, it is represented as System (E)) admits a unique solution satisfying $\sigma \in C^{4+\alpha}$ and $p \in C^{2+\alpha}$, which is stated in the following theorem. *We emphasize that the uniqueness depends on the extension indicated above.*

Lemma 2.9. *Assume S belongs to $C^{4+\alpha}(\Sigma)$ (Σ denotes the unit disk), $0 < \varepsilon < 1$, $\|S\|_{C^{4+\alpha}(\Sigma)} \leq 1$, and τ is small enough, then there exists a unique solution (σ, p) to System (E) with σ belongs to $C^{4+\alpha}(\overline{\Omega}_\varepsilon)$, and p belongs to $C^{2+\alpha}(\overline{\Omega}_\varepsilon)$.*

Since we are considering a domain which is a small perturbation of a disk, let us rewrite equation (2.137) (or equivalently, (2.144)). Similar as in Section 2.2, we express $\xi(s; \mathbf{x})$ in the form $\xi = \xi_1 \mathbf{e}_r(\xi_2)$, where in polar coordinates, ξ_1 represents radius, ξ_2 represents angle; $\mathbf{e}_r(\xi_2) = \cos(\xi_2) \mathbf{i} + \sin(\xi_2) \mathbf{j}$ and $\mathbf{e}_\theta(\xi_2) = -\sin(\xi_2) \mathbf{i} + \cos(\xi_2) \mathbf{j}$ are the two basis vectors. Since $\frac{d\mathbf{e}_r(\xi_2)}{ds} = -\sin(\xi_2) \frac{d\xi_2}{ds} \mathbf{i} + \cos(\xi_2) \frac{d\xi_2}{ds} \mathbf{j} =$

$\mathbf{e}_\theta(\xi_2) \frac{d\xi_2}{ds}$, equation (2.144) is equivalent to

$$\frac{d\boldsymbol{\xi}}{ds} = \frac{d(\xi_1 \mathbf{e}_r(\boldsymbol{\xi}))}{ds} = \frac{d\xi_1}{ds} \mathbf{e}_r(\boldsymbol{\xi}) + \xi_1 \frac{d\xi_2}{ds} \mathbf{e}_\theta(\boldsymbol{\xi}) = \hat{\mathbf{f}}(\boldsymbol{\xi}).$$

We thus obtain two sets of ODEs in polar coordinates:

$$\begin{cases} \frac{d\xi_1}{ds}(s; r, \theta) = \hat{\mathbf{f}}(\boldsymbol{\xi}) \cdot \mathbf{e}_r(\boldsymbol{\xi}) & -\tau \leq s \leq 0, \\ \xi_1(s; r, \theta) = r & s = 0; \end{cases} \quad (2.145)$$

$$\begin{cases} \frac{d\xi_2}{ds}(s; r, \theta) = \frac{1}{\xi_1} \hat{\mathbf{f}}(\boldsymbol{\xi}) \cdot \mathbf{e}_\theta(\boldsymbol{\xi}) & -\tau \leq s \leq 0, \\ \xi_2(s; r, \theta) = \theta & s = 0. \end{cases} \quad (2.146)$$

Accordingly, ∇ is also expressed in polar coordinates, i.e., $\nabla = \mathbf{e}_r \frac{\partial}{\partial r} + \frac{1}{r} \mathbf{e}_\theta \frac{\partial}{\partial \theta}$. Combining with (2.142), we derive the expressions of $\hat{\mathbf{f}}(\boldsymbol{\xi}) \cdot \mathbf{e}_r(\boldsymbol{\xi})$ and $\frac{1}{\xi_1} \hat{\mathbf{f}}(\boldsymbol{\xi}) \cdot \mathbf{e}_\theta(\boldsymbol{\xi})$ in (2.145) and (2.146), respectively,

$$\mathbf{f}(\boldsymbol{\xi}) \cdot \mathbf{e}_r(\boldsymbol{\xi}) = \begin{cases} -\frac{\partial p}{\partial r}(\xi_1, \xi_2) & \xi_1 \leq R_* + \varepsilon S(\xi_2), \\ -2\frac{\partial p}{\partial r}(R_* + \varepsilon S(\xi_2), \xi_2) + \frac{\partial p}{\partial r}\left(\frac{(R_* + \varepsilon S(\xi_2))^2}{\xi_1}, \xi_2\right) & \xi_1 > R_* + \varepsilon S(\xi_2); \end{cases}$$

$$\frac{1}{\xi_1} \mathbf{f}(\boldsymbol{\xi}) \cdot \mathbf{e}_\theta(\boldsymbol{\xi}) = \begin{cases} -\frac{1}{\xi_1^2} \frac{\partial p}{\partial \theta}(\xi_1, \xi_2) & \xi_1 \leq R_* + \varepsilon S(\xi_2), \\ \frac{-2}{(R_* + \varepsilon S(\xi_2))\xi_1} \frac{\partial p}{\partial \theta}(R_* + \varepsilon S(\xi_2), \xi_2) \\ + \frac{1}{(R_* + \varepsilon S(\xi_2))^2} \frac{\partial p}{\partial \theta}\left(\frac{(R_* + \varepsilon S(\xi_2))^2}{\xi_1}, \xi_2\right) & \xi_1 > R_* + \varepsilon S(\xi_2). \end{cases}$$

From Lemma 2.9, we know that p is uniquely determined with the extensions (2.140) and (2.142). We then define a function F as

$$F(\tilde{R}, \mu) = \frac{\partial p}{\partial \mathbf{n}} \Big|_{\partial \Omega_\varepsilon}. \quad (2.147)$$

It is clear that (σ, p) is a symmetry-breaking solution if and only if $F(\tilde{R}, \mu) = 0$.

Next, we introduce the following Banach spaces:

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

$$X_2^{l+\alpha} = \text{closure of the linear space spanned by } \{\cos(j\theta), j = 0, 2, 4, \dots\} \text{ in } X^{l+\alpha},$$

where Σ is the unit disk. It was shown in [113] that $F(\cdot, \mu)$ maps $X^{l+4+\alpha}$ into $X^{l+\alpha}$. Notice that $\cos(j(\pi - \theta)) = \cos(j\theta)$ holds if and only if j is even. Thus $X_2^{l+\alpha}$ is the subspace of $X^{l+\alpha}$ consisting of function u that satisfies $u(\theta) = u(\pi - \theta)$. The following lemma ensures that $F(\cdot, \mu)$ maps $X_2^{l+4+\alpha}$ into the space $X_2^{l+\alpha}$.

Lemma 2.10. *If $S \in X_2^{4+\alpha}$, the solution (σ, p) to the System (E) satisfies*

$$\sigma(r, \theta) = \sigma(r, \pi - \theta), \quad p(r, \theta) = p(r, \pi - \theta). \quad (2.148)$$

Proof. Since System (E), together with (2.145) and (2.146), are true for any r and θ , we replace θ with $\pi - \theta$, and obtain

$$\begin{aligned} -\Delta\sigma(r, \pi - \theta) + \sigma(r, \pi - \theta) &= 0 && \text{in } \Theta_\varepsilon, \\ -\Delta p(r, \pi - \theta) &= \mu g(\boldsymbol{\xi}(-\tau; r, \pi - \theta)) && \text{in } \Theta_\varepsilon, \\ \left\{ \begin{array}{l} \frac{d\xi_1}{ds}(s; r, \pi - \theta) = \mathbf{f}(\boldsymbol{\xi}(s; r, \pi - \theta)) \cdot \mathbf{e}_r(\boldsymbol{\xi}(s; r, \pi - \theta)) \\ \xi_1(s; r, \pi - \theta) = r \end{array} \right. && \begin{array}{l} -\tau \leq s \leq 0, \\ s = 0, \end{array} \\ \left\{ \begin{array}{l} \frac{d\xi_2}{ds}(s; r, \pi - \theta) = \frac{1}{\xi_1(s; r, \pi - \theta)} \mathbf{f}(\boldsymbol{\xi}(s; r, \pi - \theta)) \cdot \mathbf{e}_\theta(\boldsymbol{\xi}(s; r, \pi - \theta)) \\ \xi_2(s; r, \pi - \theta) = \pi - \theta \end{array} \right. && \begin{array}{l} -\tau \leq s \leq 0, \\ s = 0, \end{array} \\ \sigma(r, \pi - \theta) = 1, \quad p(r, \pi - \theta) = \kappa && \text{on } \partial\Theta_\varepsilon, \end{aligned}$$

where $\Theta_\varepsilon = \{0 \leq r < R_* + \varepsilon S(\pi - \theta)\}$. For simplicity of notation, we denote the above system by System (E1). Since $S \in X_2^{4+\alpha}$, we have $S(\theta) = S(\pi - \theta)$, and thus $\Theta_\varepsilon \equiv \Omega_\varepsilon$.

Letting $\eta = \pi - \theta$, we denote $\bar{\sigma}(r, \eta) = \sigma(r, \pi - \theta)$, $\bar{p}(r, \eta) = p(r, \pi - \theta)$, $\bar{\xi}_1(s; r, \eta) = \xi_1(s; r, \pi - \theta)$, and $\bar{\xi}_2 = \pi - \xi_2(s; r, \pi - \theta)$. Notice that

$$\frac{\partial \bar{p}}{\partial r} = \frac{\partial p}{\partial r}, \quad \frac{\partial \bar{p}}{\partial \eta} = -\frac{\partial p}{\partial \theta},$$

and a similar manner works for $\bar{\sigma}$. Based on the System (E1), and the expressions of $\mathbf{f} \cdot \mathbf{e}_r$ and $\frac{1}{\xi_1} \mathbf{f} \cdot \mathbf{e}_\theta$, we can easily derive the equations for $\bar{\sigma}$, \bar{p} , $\bar{\xi}_1$, and $\bar{\xi}_2$, which are exactly the same as those in the System (E), together with (2.145) and (2.146). From Lemma 2.9, we know that the System (E) admits a unique solution, in other words, we have $\bar{\sigma}(r, \eta) = \sigma(r, \pi - \theta) = \sigma(r, \theta)$ and $\bar{p}(r, \eta) = p(r, \pi - \theta) = p(r, \theta)$. \square

With F mapping from $X_2^{l+4+\alpha}$ into $X_2^{l+\alpha}$, we need to compute the Fréchet derivatives of F in order to use the Crandall-Rabinowitz theorem (Theorem B.1 in Appendix A). To do this, we shall analyze expansions of $(\sigma, p, \xi_1, \xi_2)$ in ε , namely, for any $\mu > 0$, we formally write

$$\sigma = \sigma_* + \varepsilon w + O(\varepsilon^2), \quad (2.149)$$

$$p = p_* + \varepsilon q + O(\varepsilon^2), \quad (2.150)$$

$$\xi_1 = \xi_* + \varepsilon \xi_{11} + O(\varepsilon^2), \quad (2.151)$$

$$\xi_2 = \theta + O(\varepsilon). \quad (2.152)$$

It should be pointed out that both p_* and σ_* are independent of θ , hence we only need the $O(1)$ term in (2.152).

It has been established in [113] that the expansions (2.149) — (2.152) are mathematically valid when $r > K$ for some small positive constant K ; the proof is very lengthy, hence it will not be discussed here; for the detailed proof, see Lemmas 3.4 — 3.8 in [113].

Substituting (2.149) — (2.152) into the System (E), and collecting only the linear

terms in ε , we obtain the system for w , q , and ξ_{11} :

$$\begin{cases} -\Delta w + w = 0 & \text{in } B_{R_*}, \\ w(r, \theta) = -\frac{\partial \sigma_*(R_*)}{\partial r} S(\theta) = -\frac{I_1(R_*)}{I_0(R_*)} S(\theta) & \text{on } \partial B_{R_*}; \end{cases} \quad (2.153)$$

$$\begin{cases} -\Delta q(r, \theta) = \mu \frac{\partial \sigma_*(\xi_*(-\tau; r))}{\partial r} \xi_{11}(-\tau; r, \theta) + \mu w(\xi_*(-\tau; r), \theta) & \text{in } B_{R_*}, \\ q(r, \theta) = -\frac{1}{R_*^2} (S(\theta) + S_{\theta\theta}(\theta)) & \text{on } \partial B_{R_*}; \end{cases} \quad (2.154)$$

$$\begin{cases} \frac{d\xi_{11}(s; r, \theta)}{ds} = -\frac{\partial^2 p_*(\xi_*(s; r))}{\partial r^2} \xi_{11}(s; r, \theta) - \frac{\partial q(\xi_*(s; r), \theta)}{\partial r} & -\tau \leq s \leq 0, \\ \xi_{11}(s; r, \theta) = 0 & s = 0. \end{cases} \quad (2.155)$$

Clearly, it follows from (2.153) that w can be explicitly solved as

$$w(r, \theta) = -\frac{I_1(R_*) I_n(r)}{I_0(R_*) I_n(R_*)} S(\theta). \quad (2.156)$$

On the other hand, based on (2.149) — (2.152), the Fréchet derivative of F can be calculated as follows:

Lemma 2.11. *The Fréchet derivative of $F(\tilde{R}, \mu)$ in \tilde{R} at the point $(0, \mu)$ is given by*

$$[F_{\tilde{R}}(0, \mu)]S(\theta) = \frac{\partial^2 p_*(R_*)}{\partial r^2} S(\theta) + \frac{\partial q(R_*, \theta)}{\partial r}. \quad (2.157)$$

In the following, we will use (2.157) to prove our bifurcation theorem. The main challenge lies in calculating $p_*(r)$ and $q(r, \theta)$ in (2.157). Due to the presence of time delay τ , it is impossible to get the explicit formulas for $p_*(r)$ and $q(r, \theta)$, and the absent of explicit forms makes it difficult to verify the Crandall-Rabinowitz theorem. However, the problem can be completely solved when $\tau = 0$, which provides a foundation for the analysis when $\tau > 0$. In the following discussion, we plan to begin with the case when $\tau = 0$ — we shall verify the four assumptions of the Crandall-Rabinowitz theorem and derive a series of bifurcation points μ_n^0 based on the theorem. Then we proceed to the case when $\tau > 0$. Although we could not calculate the Fréchet

derivative expression explicitly, we may infer that the bifurcation points in this case are close to μ_n^0 when τ is very small.

To begin with, we let the perturbation $S(\theta) = \cos(n\theta)$ for $n = 0, 2, 4, \dots$, since the set $\{\cos(n\theta), n = 0, 2, 4, \dots\}$ is clearly a basis of the Banach space $X_2^{l+\alpha}$.

Case 1: $\tau = 0$ This is equivalent to the case when we ignore the small time delay in cell proliferation. In the rest of this chapter, we use a superscript 0 for all the variables to differentiate them with the corresponding variables in the case when $\tau > 0$.

When $\tau = 0$, (2.19) becomes $-\Delta p_*^0 = \mu[\sigma_*^0 - \tilde{\sigma}]$ (i.e., equation (2.84)). From (2.91), we have the formula of $\frac{\partial^2 p_*^0}{\partial r^2}(R_*^0)$:

$$\frac{\partial^2 p_*^0}{\partial r^2}(R_*^0) = \mu \left[\frac{2I_1(R_*^0)}{R_*^0 I_0(R_*^0)} - 1 \right].$$

Next, we can calculate q^0 in a similar manner as in (2.93) — (2.95); based on (2.95) and the fact $S(\theta) = \cos(n\theta)$, we obtain

$$\frac{\partial q^0(R_*^0, \theta)}{\partial r} = \left[\frac{n(n^2 - 1)}{(R_*^0)^2} + \mu \frac{I_1(R_*^0)I_{n+1}(R_*^0)}{I_0(R_*^0)I_n(R_*^0)} \right] \cos(n\theta)$$

Substituting these two equations into (2.157), we derive

$$[F_{\tilde{R}}(0, \mu)] \cos(n\theta) = \left[\mu \frac{2I_1(R_*^0)}{R_*^0 I_0(R_*^0)} - \mu + \frac{n(n^2 - 1)}{(R_*^0)^3} + \mu \frac{I_1(R_*^0)I_{n+1}(R_*^0)}{I_0(R_*^0)I_n(R_*^0)} \right] \cos(n\theta).$$

From the properties of Bessel functions in Appendix A, we know that when $n = 1$, the terms in the bracket [...] cancel out, hence $[F_{\tilde{R}}(0, \mu)] \cos(\theta) \equiv 0$ for $\forall \mu > 0$. In addition, it is clear that when $n \neq 1$, $[F_{\tilde{R}}(0, \mu)] \cos(n\theta) = 0$ if and only if

$$\mu \frac{2I_1(R_*^0)}{R_*^0 I_0(R_*^0)} - \mu + \frac{n(n^2 - 1)}{(R_*^0)^3} + \mu \frac{I_1(R_*^0)I_{n+1}(R_*^0)}{I_0(R_*^0)I_n(R_*^0)} = 0.$$

For $n \neq 1$, we denote the solution to the above equation by $\mu_n^0(R_*)^0$, namely,

$$\mu_n^0(R_*)^0 = \left[\frac{n(n^2 - 1)}{(R_*^0)^3} \right] / \left[1 - \frac{2I_1(R_*^0)}{R_*^0 I_0(R_*^0)} - \frac{I_1(R_*^0)I_{n+1}(R_*^0)}{I_0(R_*^0)I_n(R_*^0)} \right]. \quad (2.158)$$

For $\mu_n^0(R_*)^0$, we have the following lemmas from [111] (Lemma 4.1, Lemma 4.3 and Lemma 4.4).

Lemma 2.12. *For the denominator in (2.158), the following inequalities are true:*

$$1 - \frac{2I_1(x)}{xI_0(x)} - \frac{I_1^2(x)}{I_0^2(x)} < 0, \quad \text{for } x > 0; \quad (2.159)$$

$$1 - \frac{2I_1(x)}{xI_0(x)} - \frac{I_1(x)I_{n+1}(x)}{I_0(x)I_n(x)} > 0, \quad \text{for } n \geq 2 \text{ and } x > 0. \quad (2.160)$$

Lemma 2.13. *For $n \geq 2$, $\mu_n^0(R_*)^0$ is monotonically increasing, i.e.,*

$$0 < \mu_2^0(R_*)^0 < \mu_3^0(R_*)^0 < \mu_4^0(R_*)^0 < \cdots. \quad (2.161)$$

With the monotonicity of μ_n^0 , we are able to verify the four assumptions of the Crandall-Rabinowitz theorem when $\tau = 0$. To begin with, the first assumption is naturally satisfied. For the second assumption, we have computed,

$$[F_{\tilde{R}}(0, \mu)] \cos(n\theta) = \left[\mu \frac{2I_1(R_*^0)}{R_*^0 I_0(R_*^0)} - \mu + \frac{n(n^2 - 1)}{(R_*^0)^3} + \mu \frac{I_1(R_*^0)I_{n+1}(R_*^0)}{I_0(R_*^0)I_n(R_*^0)} \right] \cos(n\theta);$$

it follows from (2.158) that for $n \neq 1$, the kernel of the operator $[F_{\tilde{R}}(0, \mu)]$ is

$$\text{Ker } [F_{\tilde{R}}(0, \mu_n^0)] = \bigoplus_{\{j: \mu_j^0 = \mu_n^0\}} \text{span}\{\cos(j\theta)\}.$$

Together with the monotonicity in Lemma 2.13, we immediately know that μ_n^0 are all

distinct for even n . Therefore, for the mapping $F(\cdot, \mu_n^0) : X_2^{l+4+\alpha} \rightarrow X_2^{4+\alpha}$, we have

$$\text{Ker}[F_{\tilde{R}}(0, \mu_n^0)] = \text{span}\{\cos(n\theta)\} \quad \text{for even } n \geq 2,$$

which indicates

$$\dim(\text{Ker}[F_{\tilde{R}}(0, \mu_n^0)]) = 1, \quad \text{for even } n \geq 2.$$

On the other hand, if k and n are both even with $n \geq 2$ and $k \neq n$, then $\mu_n^0 \frac{2I_1(R_*^0)}{R_*^0 I_0(R_*^0)} - \mu_n^0 + \frac{k(k^2-1)}{(R_*^0)^3} + \mu_n^0 \frac{I_1(R_*^0)I_{k+1}(R_*^0)}{I_0(R_*^0)I_k(R_*^0)} \neq 0$, and

$$[F_{\tilde{R}}(0, \mu_n^0)] \cos(k\theta) = \left[\mu_n^0 \frac{2I_1(R_*^0)}{R_*^0 I_0(R_*^0)} - \mu_n^0 + \frac{k(k^2-1)}{(R_*^0)^3} + \mu_n^0 \frac{I_1(R_*^0)I_{k+1}(R_*^0)}{I_0(R_*^0)I_k(R_*^0)} \right] \cos(k\theta).$$

This implies that $Y_1 = \text{Im}[F_{\tilde{R}}(0, \mu_n^0)] = \text{span}\{1, \cos(2\theta), \cos(4\theta), \dots, \cos((n-2)\theta), \cos((n+2)\theta), \dots\}$. Since $Y_1 \oplus \text{span}\{\cos(n\theta)\} = Y$, we conclude $\text{codim } Y_1 = 1$.

Finally, it is clear that

$$[F_{\mu\tilde{R}}(0, \mu_n^0)] \cos(n\theta) = \left[\frac{2I_1(R_*^0)}{R_*^0 I_0(R_*^0)} - 1 + \frac{I_1(R_*^0)I_{n+1}(R_*^0)}{I_0(R_*^0)I_n(R_*^0)} \right] \cos(n\theta) \notin Y_1.$$

According to the above analysis, the four assumptions are satisfied, we thus apply the Crandall-Rabinowitz theorem to conclude:

Theorem 2.4. *When $\tau = 0$, the points $(0, \mu_n^0)$ (n even and ≥ 2) defined by (2.158) are bifurcation points for the system (2.129) — (2.133), and the corresponding free boundaries are of the form*

$$r = R_*^0 + \varepsilon \cos(n\theta) + o(\varepsilon).$$

Case 2: $\tau > 0$ In this case, as mentioned, we cannot calculate $q(r, \theta)$ explicitly. However, the solution (q, ξ_{11}) is unique; if we can find a solution (q, ξ_{11}) of the following form

$$q(r, \theta) = q_n(r) \cos(n\theta), \quad \xi_{11}(s; r, \theta) = \zeta_n(s; r) \cos(n\theta) \quad (2.162)$$

then it is the unique solution of (2.154) and (2.155). Substituting (2.162) into (2.154) and (2.155), we need to find q_n and ζ_n satisfying

$$\begin{cases} -q_n''(r) - \frac{1}{r}q_n'(r) + \frac{n^2}{r^2}q_n(r) = \mu \frac{I_1(\xi_*(-\tau; r))}{I_0(R_*)} \zeta_n(-\tau; r) - \mu \frac{I_1(R_*)I_n(\xi_*(-\tau; r))}{I_0(R_*)I_n(R_*)} & \text{in } B_{R_*}, \\ q_n(R_*) = \frac{n^2-1}{R_*^2} & \text{on } \partial B_{R_*}; \end{cases} \quad (2.163)$$

$$\begin{cases} \frac{d\zeta_n(s; r)}{ds} = -\frac{\partial^2 p_*(\xi_*(s; r))}{\partial r^2} \zeta_n(s; r) - q_n'(\xi_*(s; r)) & -\tau \leq s \leq 0, \\ \zeta_n(s; r) = 0 & s = 0. \end{cases} \quad (2.164)$$

We can solve (2.164) as

$$\zeta_n(-\tau; r) = \int_{-\tau}^0 q_n'(\xi_*(s; r)) \left(\exp \int_{-\tau}^s \frac{\partial^2 p_*(\xi_*(c; r))}{\partial r^2} dc \right) ds.$$

Substituting it into (2.163) we get one linear inhomogeneous integro-differential equation in B_{R_*} :

$$\begin{cases} -q_n''(r) - \frac{1}{r}q_n'(r) + \frac{n^2}{r^2}q_n(r) = \mu \frac{I_1(\xi_*(-\tau; r))}{I_0(R_*)} \int_{-\tau}^0 q_n'(\xi_*(s; r)) \left(\exp \int_{-\tau}^s \frac{\partial^2 p_*(\xi_*(c; r))}{\partial r^2} dc \right) ds \\ \quad - \mu \frac{I_1(R_*)I_n(\xi_*(-\tau; r))}{I_0(R_*)I_n(R_*)}, \\ q_n(R_*) = \frac{n^2-1}{R_*^2}. \end{cases} \quad (2.165)$$

Lemma 2.14. *There exists a small $T_1 > 0$, independent of n , such that (2.165) admits a solution $q_n \in C^2(B_{R_*})$ for $0 < \tau < T_1$. Furthermore, the following estimates*

hold:

$$\left| q'_n(R_*) - \frac{n(n^2 - 1)}{R_*^2} - \mu \frac{I_1(R_*)I_{n+1}(R_*)}{I_0(R_*)I_n(R_*)} \right| \leq C\tau(n^3 + 1) \quad \forall n \geq 0, \quad (2.166)$$

where the constant C is independent of τ and n ; we emphasis that both the constants T_1 and C depend on μ .

Proof. The existence and uniqueness of such a solution $q_n \in C^2(B_{R_*})$ can be justified through the contraction mapping principal. To further obtain (2.166), we denote $\Psi_n(r) = q_n(r) - \frac{r^n}{R_*^n} \left(\frac{n^2 - 1}{R_*^2} - \mu \frac{I_1(R_*)}{I_0(R_*)} \right) - \mu \frac{I_1(R_*)I_n(r)}{I_0(R_*)I_n(R_*)}$. By simple calculations, Ψ_n satisfies

$$-\Psi_n''(r) - \frac{1}{r}\Psi_n'(r) + \frac{n^2}{r^2}\Psi_n(r) = \mu[f_4(\Psi_n', r) + f_5(r)] \quad \text{in } B_{R_*}, \quad \text{and} \quad \Psi_n(R_*) = 0. \quad (2.167)$$

where

$$\begin{aligned} f_4 &= \frac{I_1(\xi_*(-\tau; r))}{I_0(R_*)} \int_{-\tau}^0 \Psi_n'(\xi_*(s; r)) \left(\exp \int_{-\tau}^s \frac{\partial^2 p_*(\xi_*(c; r))}{\partial r^2} dc \right) ds, \\ f_5 &= \frac{I_1(\xi_*(-\tau; r))}{I_0(R_*)} \int_{-\tau}^0 \left[\frac{n(\xi_*(s; r))^{n-1}}{R_*^n} \left(\frac{n^2 - 1}{R_*^2} - \mu \frac{I_1(R_*)}{I_0(R_*)} \right) + \mu \frac{I_1(R_*)I_n'(\xi_*(s; r))}{I_0(R_*)I_n(R_*)} \right] \\ &\quad \left(\exp \int_{-\tau}^s \frac{\partial^2 p_*(\xi_*(c; r))}{\partial r^2} dc \right) ds + \frac{I_1(R_*)}{I_0(R_*)I_n(R_*)} [I_n(r) - I_n(\xi_*(-\tau; r))]. \end{aligned}$$

Instead of analyzing (2.167) directly, let us consider the following system:

$$\begin{cases} -\Psi_n''(r) - \frac{1}{r}\Psi_n'(r) + \frac{n^2}{r^2}\Psi_n(r) = \mu[\delta f_4(\Psi_n', r) + f_5(r)], & \text{in } B_{R_*}, \\ -\Psi_n(R_*) = 0 & \text{on } \partial B_{R_*}; \end{cases} \quad (2.168)$$

it is not difficult to establish the existence and uniqueness of a solution Ψ_n to the above system for all $0 \leq \delta \leq 1$. To further obtain its estimate, we proceed to study (2.168) in two steps.

Step 1: For $n \geq 2$, if $\delta = 0$, (2.168) becomes

$$-\Psi_n''(r) - \frac{1}{r}\Psi_n'(r) + \frac{n^2}{r^2}\Psi_n(r) = \mu f_5(r),$$

integrating the above equation in B_r gives (recall that the space dimension is 2)

$$-r\Psi_n'(r) + n^2 \int_0^r \frac{1}{\xi}\Psi_n(\xi)d\xi = \mu \int_0^r \xi f_5(\xi)d\xi,$$

and hence

$$|\Psi_n'(r)| \leq \frac{n^2}{r} \int_0^r \frac{1}{\xi}|\Psi_n(\xi)|d\xi + \frac{\mu}{r} \int_0^r \xi |f_5(\xi)|d\xi. \quad (2.169)$$

In estimating $|f_5|$, we use the properties of Bessel functions (A.3) (A.11) and the fact that $\xi_*(s; r) \leq R_*$ in Remark 2.1, hence

$$\begin{aligned} \frac{I_n'(\xi_*(s; r))}{I_n(R_*)} &= \frac{I_{n+1}(\xi_*(s; r))}{I_n(R_*)} + \frac{nI_n(\xi_*(s; r))}{\xi_*(s; r)I_n(R_*)} \\ &\leq \frac{I_{n+1}(R_*)}{I_n(R_*)} + n \frac{I_n(R_*)}{R_* I_n(R_*)} \leq \frac{R_*}{2n} + \frac{n}{R_*} \leq Cn. \end{aligned}$$

As a result, $|f_5| \leq Cn^3\tau$, where constant C is independent of n ; but C depends on μ . Furthermore, since the maximum principal for the operator $L = -\frac{d^2}{dr^2} - \frac{1}{r}\frac{d}{dr} + \frac{n^2}{r^2}$ has been established in Appendix C (Lemma C.1), we choose $\bar{\Psi} = Mn\tau r$, with constant M large enough so that $\bar{\Psi}$ is a supersolution. By the maximum principal, we have $|\Psi_n(r)| \leq Mn\tau r$, $\forall 0 \leq r \leq R_*$. Substituting the above estimates into (2.169), we then obtain

$$|\Psi_n'(r)| \leq \frac{n^2}{r} \int_0^r Mn\tau d\xi + \frac{\mu}{r} \int_0^r Cn^3\tau \xi d\xi \leq \left(M + \frac{C}{2}\mu R_*\right)n^3\tau \leq Cn^3\tau,$$

and the above estimate holds for all $0 < r \leq R_*$; that is to say, $\|\Psi_n'\|_{L^\infty(B_{R_*})} \leq Cn^3\tau$.

Again, we emphasis that the constant C depends on μ .

Step 2: For $n \geq 2$, if $0 < \delta \leq 1$, we also need to estimate f_4 . To do so, we first

assume

$$\|\Psi'_n\|_{L^\infty(B_{R_*})} \leq n^3,$$

substituting it into the expression of f_4 , and using the fact that $\xi_*(s; r) \leq R_*$, we derive

$$|f_4| \leq \mu \frac{I_1(R_*)}{I_0(R_*)} \int_{-\tau}^0 \|\Psi'_n\|_{L^\infty(B_{R_*})} e^{\|p_*\|_{W^{2,\infty}(B_{R_*})}(s+\tau)} ds \leq Cn^3\tau,$$

where C is independent of τ and n . Together with the estimates for $|f_5|$, it follows $|\mu[\delta f_4 + f_5]| \leq Cn^3\tau$ for each $0 < \delta \leq 1$. Similar as in step 1, $\bar{\Psi} = Mn\tau r$ can be a supersolution when M is large enough, hence $|\Psi_n(r)| \leq Mn\tau r$ still holds for all $0 \leq r \leq R_*$. Integrating (2.168) in B_r leads to

$$\Psi'_n(r) = \frac{n^2}{r} \int_0^r \frac{1}{\xi} \Psi_n(\xi) d\xi - \frac{\mu\delta}{r} \int_0^r \xi f_4(\Psi'_n, \xi) d\xi - \frac{\mu}{r} \int_0^r \xi f_5(\xi) d\xi,$$

and hence

$$\begin{aligned} |\Psi'_n(r)| &\leq \frac{n^2}{r} \int_0^r \frac{1}{\xi} |\Psi_n(\xi)| d\xi + \frac{\mu\delta}{r} \int_0^r \xi |f_4(\Psi'_n, \xi)| d\xi + \frac{\mu}{r} \int_0^r \xi |f_5(\xi)| d\xi \\ &\leq \left(M + \frac{C}{2}\mu\delta R_* + \frac{C}{2}\mu R_*\right) n^3\tau \leq Cn^3\tau, \end{aligned}$$

which is equivalent to $\|\Psi'_n\|_{L^\infty(B_{R_*})} \leq Cn^3\tau$; similar as in Step 1, the constant C depends on μ .

Applying Lemma C.2 in Appendix, it follows that $\|\Psi'_n\|_{L^\infty(B_{R_*})} \leq C(\mu)n^3\tau$ is also valid for $\delta = 1$, if $0 < \tau < T_1$, where T_1 is small enough so that $C(\mu)T_1 < 1$. Therefore, we immediately get (2.166) when $0 < \tau < T_1$.

Although we only proved Lemma 2.14 for $n \geq 2$, it is easy to verify (2.166) still holds for $n = 0$ and $n = 1$. To do so, the idea is basically the same as above, except that a suitable supersolution in this case is $\bar{\Psi} = M\tau(R_*^2 - r^2)$. \square

Now, we are ready to prove the main bifurcation result, Theorem 2.3.

Proof of Theorem 2.3. Substituting (2.162) into (2.157), we rewrite the Fréchet derivative of $F(\tilde{R}, \mu)$ as:

$$[F_{\tilde{R}}(0, \mu)] \cos(n\theta) = \left(\frac{\partial^2 p_*(R_*)}{\partial r^2} + \frac{\partial q_n(R_*)}{\partial r} \right) \cos(n\theta).$$

Since $\frac{\partial^2 p_*(R_*)}{\partial r^2} = \frac{\partial^2 p_*^0(R_*^0)}{\partial r^2} + O(\tau) = \mu \frac{2I_1(R_*^0)}{R_*^0 I_0(R_*^0)} - \mu + O(\tau) = \mu \frac{2I_1(R_*)}{R_* I_0(R_*)} - \mu + O(\tau)$, where the last equality holds due to the fact that $\lim_{\tau \rightarrow 0} R_* = R_*^0$. Together with Lemma 2.14, we can find a function $J(n, \mu)$ bounded in n , such that

$$\begin{aligned} [F_{\tilde{R}}(0, \mu)] \cos(n\theta) = & \left(\mu \frac{2I_1(R_*)}{R_* I_0(R_*)} - \mu + \frac{n(n^2 - 1)}{R_*^3} + \mu \frac{I_1(R_*) I_{n+1}(R_*)}{I_0(R_*) I_n(R_*)} \right. \\ & \left. + J(n, \mu) n^3 \tau \right) \cos(n\theta) \end{aligned} \quad (2.170)$$

is valid when $0 < \tau < T_1$, where T_1 is defined in Lemma 2.14.

For an even $n \geq 2$, fixed, we find that $[F_{\tilde{R}}(0, \mu)] \cos(n\theta) = 0$ if and only if

$$M_n(\mu, \tau) \triangleq \mu \frac{2I_1(R_*)}{R_* I_0(R_*)} - \mu + \frac{n(n^2 - 1)}{R_*^3} + \mu \frac{I_1(R_*) I_{n+1}(R_*)}{I_0(R_*) I_n(R_*)} + J(n, \mu) n^3 \tau = 0. \quad (2.171)$$

We shall claim that there is a unique solution $\mu = \mu_n^\tau$ satisfying the above equation. To prove this statement, we recall that $M_n(\mu_n^0, 0) = 0$. Next we take partial derivative with respect to μ on both sides of (2.171) and evaluate the value at $(\mu, 0)$, it follows

$$\begin{aligned} \frac{\partial}{\partial \mu} M_n(\mu, 0) &= \left[\frac{2I_1(R_*)}{R_* I_0(R_*)} - 1 + \frac{I_1(R_*) I_{n+1}(R_*)}{I_0(R_*) I_n(R_*)} + \frac{\partial}{\partial \mu} J(n, \mu) n^3 \tau \right] \Big|_{\tau=0} \\ &= \frac{2I_1(R_*)}{R_* I_0(R_*)} - 1 + \frac{I_1(R_*) I_{n+1}(R_*)}{I_0(R_*) I_n(R_*)}. \end{aligned} \quad (2.172)$$

It is clear that $\frac{\partial}{\partial \mu} M_n(\mu, 0) \neq 0$ from Lemma 2.12. By the implicit function theorem, there exists a unique solution, which is close to μ_n^0 , satisfying (2.171); we denote the unique solution by μ_n^τ . In what follows, we shall justify that $(\tilde{R}, \mu) = (0, \mu_n^\tau)$ is a bifurcation point for the problem (2.129) — (2.133).

What we need to do is to verify the four assumptions of the Crandall-Rabinowitz theorem at $(\tilde{R}, \mu) = (0, \mu_n^\tau)$. To begin with, it is clear that the assumption (1) is naturally satisfied. For the assumptions (2) and (3), it suffices to show that for every even m , $m \neq n$,

$$\mu_m^\tau \neq \mu_n^\tau, \quad (2.173)$$

or equivalently,

$$G(m) \triangleq \mu_n^\tau \frac{2I_1(R_*)}{R_* I_0(R_*)} - \mu_n^\tau + \frac{m(m^2 - 1)}{R_*^3} + \mu_n^\tau \frac{I_1(R_*) I_{m+1}(R_*)}{I_0(R_*) I_m(R_*)} + J(m, \mu_n^\tau) m^3 \tau \neq 0. \quad (2.174)$$

① As is seen, the leading term for $G(m)$ is m^3 , so we first prove (2.174) is true for large m . By Lemma 2.14, $J(m, \mu_n^\tau)$ is bounded in m , i.e., there exists a constant $C(\mu_n^\tau)$ which is independent of m , such that $|J(m, \mu_n^\tau)| \leq C(\mu_n^\tau)$ for all m . We choose $T_2 = \frac{1}{2C(\mu_n^\tau)} \frac{1}{R_*^3}$. If $0 < \tau < T_2$, then $\frac{1}{R_*^3} + J(m, \mu_n^\tau) \tau > \frac{1}{2R_*^3}$, and (2.174) leads to

$$G(m) > \mu_n^\tau \frac{2I_1(R_*)}{R_* I_0(R_*)} - \mu_n^\tau + \mu_n^\tau \frac{I_1(R_*) I_{m+1}(R_*)}{I_0(R_*) I_m(R_*)} + \frac{m^3}{2R_*^3} - \frac{m}{R_*^3}. \quad (2.175)$$

Hence, there exists an even integer M_0 , such that, for $m \geq M_0$,

$$G(m) > \mu_n^\tau \frac{2I_1(R_*)}{R_* I_0(R_*)} - \mu_n^\tau + \mu_n^\tau \frac{I_1(R_*) I_{m+1}(R_*)}{I_0(R_*) I_m(R_*)} + \frac{m^3}{2R_*^3} - \frac{m}{R_*^3} > 0.$$

Obviously, $G(m) \neq 0$, and hence (2.174) is true in this case.

② Next we prove that (2.174) (or equivalently, (2.173)) is true for $m = 2, 4, \dots, n - 2, n + 2, \dots, M_0 - 2$ when τ is small. To do that, we make use of the monotonicity of μ_n^0 and the fact that μ_n^τ should be close to μ_n^0 .

Recall that, for each l , we have $\lim_{\tau \rightarrow 0} \mu_l^\tau(R_*) = \mu_l^0(R_*)$; we emphasize here that the limit is not uniform in l . In $\varepsilon - \delta$ languages, it tells that, for each even $l \geq 2$, and given $\tilde{\varepsilon}_l = \frac{1}{3} \min\{\mu_l^0 - \mu_{l-1}^0, \mu_{l+1}^0 - \mu_l^0\}$, there exists \tilde{T}_l such that $|\mu_l^\tau - \mu_l^0| < \tilde{\varepsilon}_l$ holds

if $0 < \tau < \tilde{T}_l$. Take

$$\tilde{\varepsilon} = \min\{\tilde{\varepsilon}_2, \tilde{\varepsilon}_4, \dots, \tilde{\varepsilon}_{n-2}, \tilde{\varepsilon}_n, \tilde{\varepsilon}_{n+2}, \dots, \tilde{\varepsilon}_{M_0-2}\},$$

$$T_3 = \min\{\tilde{T}_2, \tilde{T}_4, \dots, \tilde{T}_{n-2}, \tilde{T}_n, \tilde{T}_{n+2}, \dots, \tilde{T}_{M_0-2}\},$$

then if $0 < \tau < T_3$, $|\mu_l^\tau - \mu_l^0| < \tilde{\varepsilon}$ holds for all $l = 2, 4, \dots, M_0 - 2$. Therefore, it is easy to derive, for $m = 2, 4, \dots, n - 2, n + 2, \dots, M_0 - 2$, $|\mu_n^\tau - \mu_m^\tau| > \frac{1}{3}\tilde{\varepsilon} > 0$, which immediately implies (2.173).

③ Finally let us prove (2.174) is also true for $m = 0$. Obviously, due to (2.159) in Lemma 2.12,

$$G(0) = \mu_n^\tau \frac{2I_1(R_*)}{R_* I_0(R_*)} - \mu_n^\tau + \mu_n^\tau \frac{I_1^2(R_*)}{I_0^2(R_*)} = \mu_n^\tau \left[\frac{2I_1(R_*)}{R_* I_0(R_*)} - 1 + \frac{I_1^2(R_*)}{I_0^2(R_*)} \right] \neq 0, \quad (2.176)$$

Based on ① ② and ③, the assumptions (2) and (3) are satisfied when τ is small enough. It remains to prove the assumption (4) in the Crandall-Rabinowitz theorem. From (2.170), it follows

$$[F_{\mu\tilde{R}}(0, \mu_n^\tau)] \cos(n\theta) = \left(\frac{2I_1(R_*)}{R_* I_0(R_*)} - 1 + \frac{I_1(R_*)I_{n+1}(R_*)}{I_0(R_*)I_n(R_*)} + \frac{\partial J(n, \mu_n^\tau)}{\partial \mu} n^3 \tau \right) \cos(n\theta).$$

Since $\frac{2I_1(R_*)}{R_* I_0(R_*)} - 1 + \frac{I_1(R_*)I_{n+1}(R_*)}{I_0(R_*)I_n(R_*)} > 0$ by (2.160), we can find a positive T_4 such that $\left(\frac{2I_1(R_*)}{R_* I_0(R_*)} - 1 + \frac{I_1(R_*)I_{n+1}(R_*)}{I_0(R_*)I_n(R_*)} + \frac{\partial J(n, \mu_n^\tau)}{\partial \mu} n^3 \tau \right) > 0$ when $0 < \tau < T_4$. Hence the assumption (4) is also verified.

Choosing $\tilde{T} = \min\{T_1, T_2, T_3, T_4\}$, we have all the assumptions of the Crandall-Rabinowitz theorem are satisfied when $0 < \tau < \tilde{T}$; so we conclude that the point $(0, \mu_n^\tau)$ is a bifurcation point. \square

2.5 Biological implications

From the stability analysis in Section 2.3, we know that the stationary solution is stable when the tumor aggressiveness parameter $\mu < \mu_*$, and becomes unstable when $\mu > \mu_*$. We interpret this stability result to mean that the tumor will remain benign as long as μ is small; in other words, tumor with a greater aggressiveness parameter would trigger instability, which is often viewed as a malignant tumor.

On the other hand, bifurcation solutions with free boundaries $r = R_* + \varepsilon \cos(n\theta) + O(\varepsilon^2)$ are often regarded as tumor protrusions, or “fingers”. They are associated with the invasion of tumors into their surrounding stroma. The bifurcation results in Section 2.4 indicates that the smallest value of μ which generates protrusions is μ_2^T . Combining with the stability results, we know that as the tumor aggressiveness parameter μ increases, the tumor will lose its spherical shapes, develop fingers, and become invasive.

CHAPTER 3

A PLAQUE FORMATION MODEL

Atherosclerosis, known as an inflammatory disease, is a major cause of disability and premature death in the United States and worldwide. It occurs when fat, cholesterol, and other substances build up in and on the artery walls. These deposits are called plaques, which harden and narrow the arteries over time. Plaques can rupture, triggering a blood clot which restricts blood flow. During this process, a heart attack, stroke, or sudden cardiac death may occur. Every year about 735,000 Americans have a heart attack, and about 610,000 people die of heart diseases in the United States — that is 1 in every 4 deaths [97].

There are several mathematical models that describe the growth of plaque in the arteries (see [13, 21, 41, 42, 59, 82, 84]). All of these models recognize the critical role of the “bad” cholesterol, low density lipoprotein (LDL), and the “good” cholesterol, high density lipoprotein (HDL), in determining whether a plaque will grow or shrink. Recently, a free boundary PDE model was proposed in [59], in which a risk-map was generated for any pair values of (LDL, HDL), showing the important influence of LDL and HDL on plaque formation. Later, on the foundation of the model, Hao and Friedman added the impact of reverse cholesterol transport (RCT) in [41]. In addition, the existence of a small radially symmetric stationary plaque and its stability condition were theoretically established for a simplified free boundary model in [42]. Nevertheless, there is no theoretical work to analyze the bifurcation of plaque model. As the plaque in reality is unlikely to be radially symmetric, it is necessary to investigate the non-radially symmetric solutions. Hence in this chapter

we shall carry out the bifurcation analysis for a plaque formation model proposed in [42] (also see [40, Chapters 7 and 8]).

3.1 The model

The process of plaque formation is as follows: when a lesion develops in the inner surface of the arterial wall, it enables LDL and HDL to move into the intima and become oxidized by free radicals. Oxidized LDL triggers endothelial cells to secrete chemoattractant proteins that attract macrophages (M) from the blood. macrophages can engulf oxidized LDL, they then become foam cells (F), and the accumulation of foam cells results in the formation of a plaque. The effect of oxidized LDL on plaque growth can be reduced by the good cholesterol, HDL: HDL can remove harmful bad cholesterol out from the foam cells and revert foam cells back into macrophages; moreover, HDL also competes with LDL on free radicals, decreasing the amount of radicals that are available to oxidize LDL. In the model, we let

$$\begin{aligned} L &= \text{concentration of LDL,} & H &= \text{concentration of HDL,} \\ M &= \text{density of macrophages,} & F &= \text{density of foam cells.} \end{aligned}$$

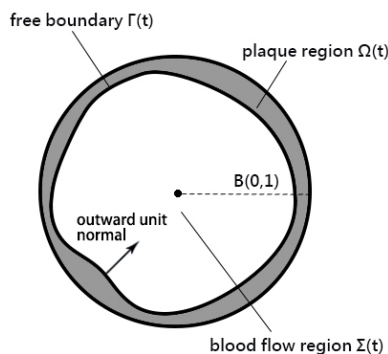


Figure 3.1. The cross section of an artery.

Assuming the artery is a very long circular cylinder with radius 1 (after normalization), we consider a circular cross section of the artery. As can be seen in Fig. 3.1, the cross section is divided into two regions: blood flow region $\Sigma(t)$ and plaque region $\Omega(t)$, with a moving boundary $\Gamma(t)$ separating these two regions (since the plaque can either grow or shrink). The variables L, H, M, F satisfy the following equations in the plaque region $\{\Omega(t), t > 0\}$ (cf., [40, Chapters 7 and 8] and [42]):

$$\frac{\partial L}{\partial t} - \Delta L = -k_1 \frac{ML}{K_1 + L} - \rho_1 L, \quad (3.1)$$

$$\frac{\partial H}{\partial t} - \Delta H = -k_2 \frac{HF}{K_2 + F} - \rho_2 H, \quad (3.2)$$

$$\frac{\partial M}{\partial t} - D\Delta M + \nabla \cdot (M\vec{v}) = -k_1 \frac{ML}{K_1 + L} + k_2 \frac{HF}{K_2 + F} + \lambda \frac{ML}{\gamma + H} - \rho_3 M, \quad (3.3)$$

$$\frac{\partial F}{\partial t} - D\Delta F + \nabla \cdot (F\vec{v}) = k_1 \frac{ML}{K_1 + L} - k_2 \frac{HF}{K_2 + F} - \rho_4 F, \quad (3.4)$$

where ρ_1, ρ_2, ρ_3 and ρ_4 denote the natural death rate of L, H, M , and F , respectively. In equations (3.1) — (3.4), the aforementioned transitions between macrophages (M) and foam cells (F) are included: $k_1 \frac{ML}{K_1 + L}$ 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 (3.3), 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 λML ; on the other hand, since HDL is antagonistic to LDL, this rate is then reduced by H .

We assume that the density of cells in the plaque is approximately a constant, and take

$$M + F \equiv M_0 \quad \text{in } \Omega(t). \quad (3.5)$$

Since there are cells migrating into and out of the plaque, the total number of cells keeps changing and, under the assumption (3.5), cells are continuously “pushing” each other. This gives rise to an internal pressure among the cells which is associated

with the velocity \vec{v} in (3.3) and (3.4). We further assume that the plaque texture is of a porous medium type, and invoke Darcy's law

$$\vec{v} = -\nabla p \quad (\text{the proportional constant is normalized to 1}), \quad (3.6)$$

where p is the internal pressure *relative to the outside pressure* (and therefore can admit positive or negative sign). Combining (3.3) — (3.6), we derive

$$-\Delta p = \frac{1}{M_0} \left[\lambda \frac{(M_0 - F)L}{\gamma + H} - \rho_3(M_0 - F) - \rho_4 F \right]. \quad (3.7)$$

Due to the assumption (3.5), we can decrease the number of equations by 1, and replace M by $M_0 - F$ in (3.1) — (3.4), hence we shall have 4 PDEs, for L , H , F and p , respectively. In particular, combining with (3.7), we write the equation for F as:

$$\frac{\partial F}{\partial t} - D\Delta F - \nabla F \cdot \nabla p = k_1 \frac{(M_0 - F)L}{K_1 + L} - k_2 \frac{HF}{K_2 + F} - \lambda \frac{F(M_0 - F)L}{M_0(\gamma + H)} + (\rho_3 - \rho_4) \frac{(M_0 - F)F}{M_0}. \quad (3.8)$$

We now turn to the boundary conditions. We assume no flux condition on the blood vessel wall ($r = 1$) for all variables (no exchange through the blood vessel):

$$\frac{\partial L}{\partial r} = \frac{\partial H}{\partial r} = \frac{\partial F}{\partial r} = \frac{\partial p}{\partial r} = 0 \quad \text{at } r = 1; \quad (3.9)$$

while on the free boundary $\Gamma(t)$, we take

$$\frac{\partial L}{\partial \mathbf{n}} + \beta_1(L - L_0) = 0, \quad \frac{\partial H}{\partial \mathbf{n}} + \beta_1(H - H_0) = 0 \quad \text{on } \Gamma(t), \quad (3.10)$$

$$\frac{\partial F}{\partial \mathbf{n}} + \beta_2 F = 0 \quad \text{on } \Gamma(t), \quad (3.11)$$

$$p = \kappa \quad \text{on } \Gamma(t), \quad (3.12)$$

where \mathbf{n} is the outward unit normal for $\Gamma(t)$ which points inward towards the blood region (as shown in Fig. 3.1), and κ is the corresponding mean curvature in the

direction of \mathbf{n} (i.e., $\kappa = -\frac{1}{R(t)}$ if $\Gamma(t) = \{r = R(t)\}$). The cell-to-cell adhesiveness constant in front of κ is normalized to 1. The flux boundary condition (3.10) is based on the fact that the concentrations of L and H in the blood are L_0 and H_0 , respectively; and the meaning of (3.11) is similar: there are, of course, no foam cells in the blood.

Furthermore, we assume that the velocity is continuous up to the boundary, so that the free boundary $\Gamma(t)$ moves in the outward normal direction \mathbf{n} with velocity \vec{v} ; based on (3.6), the normal velocity of the free boundary is defined by

$$V_n = -\frac{\partial p}{\partial \mathbf{n}} \quad \text{on } \Gamma(t). \quad (3.13)$$

In [42], Friedman et al. analyzed the system (3.1) — (3.13) in the radially symmetric case and established the existence of a unique radially symmetric steady state solution in a ring-region $1 - \varepsilon < r < 1$ with ε being small. It is, however, unreasonable to assume plaque is of strictly radially symmetric shape, hence we'd like to investigate the symmetric-breaking bifurcation for the system. To do that, we study the corresponding stationary problem of (3.1) — (3.13):

$$\begin{aligned} -\Delta L &= -k_1 \frac{(M_0 - F)L}{K_1 + L} - \rho_1 L && \text{in } \Omega, \\ -\Delta H &= -k_2 \frac{HF}{K_2 + F} - \rho_2 H && \text{in } \Omega, \\ -D\Delta F - \nabla F \cdot \nabla p &= k_1 \frac{(M_0 - F)L}{K_1 + L} - k_2 \frac{HF}{K_2 + F} - \lambda \frac{F(M_0 - F)L}{M_0(\gamma + H)} + (\rho_3 - \rho_4) \frac{(M_0 - F)F}{M_0} && \text{in } \Omega, \\ -\Delta p &= \frac{1}{M_0} \left[\lambda \frac{(M_0 - F)L}{\gamma + H} - \rho_3(M_0 - F) - \rho_4 F \right] && \text{in } \Omega, \\ \frac{\partial L}{\partial r} &= \frac{\partial H}{\partial r} = \frac{\partial F}{\partial r} = \frac{\partial p}{\partial r} = 0 && r = 1, \\ \frac{\partial L}{\partial \mathbf{n}} + \beta_1(L - L_0) &= 0, \quad \frac{\partial H}{\partial \mathbf{n}} + \beta_1(H - H_0) = 0 && \text{on } \Gamma, \\ \frac{\partial F}{\partial \mathbf{n}} + \beta_2 F &= 0 && \text{on } \Gamma, \\ p &= \kappa && \text{on } \Gamma, \\ V_n = -\frac{\partial p}{\partial \mathbf{n}} &= 0 && \text{on } \Gamma. \end{aligned}$$

For notational convenience, we denote the above system by System (P).

We shall show that, for System (P), there exists a series of bifurcation points at which a non-radially symmetric solution branch bifurcates from the radially symmetric solution branch. The main challenges of this work lie in: (a) the system is highly nonlinear and all the variables are coupled together. Even in the radially symmetric steady state case, there is no explicit solution; (b) the absent of explicit solution makes it difficult to verify the bifurcation theorem; and (c) the region of the radially symmetric stationary solution depends on a small variable $\varepsilon > 0$, which requires more careful work in deriving PDE estimates. In order to meet these challenges and present the bifurcation results, we will establish a lot of delicate estimates in the following sections.

3.2 Main results

The main results are stated in the following theorems: For convenience we shall use $\mu = \frac{1}{\varepsilon}[\lambda L_0 - \rho_3(\gamma + H_0)]$ as our bifurcation parameter. We will keep all parameters fixed except L_0 and ρ_4 , and vary μ by changing L_0 .

Theorem 3.1. *For each integer $n \geq 2$, we can find a small $E > 0$ and for each $0 < \varepsilon < E$, there exists a unique $\mu_n = (\gamma + H_0)n^2(1 - n^2) + O(n^5\varepsilon)$ such that if $\mu_n > \mu_c$ (μ_c is defined in (3.24)), then $\mu = \mu_n$ is a bifurcation point of the symmetry-breaking stationary solution of the System (P). Moreover, the free boundary of this bifurcation solution is of the form*

$$r = 1 - \varepsilon + \tau \cos(n\theta) + o(\tau), \quad \text{where} \quad |\tau| \ll \varepsilon.$$

Remark 3.1. *Unlike tumor protrusions which are usually unstable and may cause metastases, the protrusions of plaques are towards the blood region with limited **spatial freedom**. As n gets bigger, μ_n becomes negative with larger absolute value.*

By the definition of μ_n , this means that the concentration of the **good cholesterol (HDL)** must be substantially larger than the concentration of the **bad cholesterol (LDL)** for the bifurcation to occur. The more protrusions, the larger H_0 over L_0 will be required to balance the protrusion forces. Based on the stability results from [42], it is likely to have some stable bifurcation branches.

We want to emphasize that the solutions on the $n = 1$ bifurcation branch are also non-radially symmetric in this problem. Notice that there are two boundaries in System (P) and the outer boundary $r = 1$ is fixed. Therefore, 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 not radially symmetric, as shown in the Figure 3.2, and we theoretically establish this bifurcation branch in the following theorem.

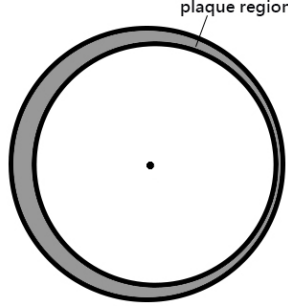


Figure 3.2. A symmetry-breaking solution in the $n = 1$ bifurcation branch

Theorem 3.2. Assume that $\mu_c < 0$ and $\beta_1 \neq \beta_2$. For $\mu_1 = O(\varepsilon)$ defined as the solution to the following equation

$$\frac{\partial^2 p_*(1 - \varepsilon)}{\partial r^2} + \frac{\partial p_1^1(1 - \varepsilon)}{\partial r} = 0,$$

we can find a small $E > 0$, such that for $0 < \varepsilon < E$, $\mu = \mu_1$ is a bifurcation point

of the symmetry-breaking stationary solution of the System (P). Moreover, the free boundary of this bifurcation solution is of the form

$$r = 1 - \varepsilon + \tau \cos(\theta) + o(\tau), \quad \text{where } |\tau| \ll \varepsilon. \quad (3.14)$$

Remark 3.2. From mathematical point of view, $\mu = \mu_1 = O(\varepsilon)$ is the first bifurcation point, which often coincides with the change of stability for the system. In fact, it has been proved in [42] 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, $\mu = \mu_1 = O(\varepsilon)$ is also **the most significant bifurcation point biologically**, as the arterial plaque is often accumulated more on one side of the artery in reality (see Figures in [57, 76, 87]).

3.3 Radially symmetric stationary solution

We consider a radially symmetric stationary solution in a small ring-region $\Omega_* = \{1 - \varepsilon < r < 1\}$, and denote the solution by (L_*, H_*, F_*, p_*) . Based on equations in System (P), (L_*, H_*, F_*, p_*) satisfies

$$-\Delta L_* = -k_1 \frac{(M_0 - F_*)L_*}{K_1 + L_*} - \rho_1 L_* \quad \text{in } \Omega_*, \quad (3.15)$$

$$-\Delta H_* = -k_2 \frac{H_* F_*}{K_2 + F_*} - \rho_2 H_* \quad \text{in } \Omega_*, \quad (3.16)$$

$$\begin{aligned} -D\Delta F_* - \frac{\partial F_*}{\partial r} \frac{\partial p_*}{\partial r} &= k_1 \frac{(M_0 - F_*)L_*}{K_1 + L_*} - k_2 \frac{H_* F_*}{K_2 + F_*} \\ &\quad - \lambda \frac{F_* (M_0 - F_*)L_*}{M_0(\gamma + H_*)} + (\rho_3 - \rho_4) \frac{(M_0 - F_*)F_*}{M_0} \end{aligned} \quad \text{in } \Omega_*, \quad (3.17)$$

$$-\Delta p_* = \frac{1}{M_0} \left[\lambda \frac{(M_0 - F_*)L_*}{\gamma + H_*} - \rho_3(M_0 - F_*) - \rho_4 F_* \right] \quad \text{in } \Omega_*, \quad (3.18)$$

$$\frac{\partial L_*}{\partial r} = \frac{\partial H_*}{\partial r} = \frac{\partial F_*}{\partial r} = \frac{\partial p_*}{\partial r} = 0 \quad r = 1, \quad (3.19)$$

$$-\frac{\partial L_*}{\partial r} + \beta_1(L_* - L_0) = 0, \quad -\frac{\partial H_*}{\partial r} + \beta_1(H_* - H_0) = 0 \quad r = 1 - \varepsilon, \quad (3.20)$$

$$-\frac{\partial F_*}{\partial r} + \beta_2 F_* = 0 \quad r = 1 - \varepsilon, \quad (3.21)$$

$$p_* = -\frac{1}{1 - \varepsilon} \quad r = 1 - \varepsilon, \quad (3.22)$$

$$\frac{\partial p_*}{\partial r} = 0 \quad r = 1 - \varepsilon. \quad (3.23)$$

Viewing $\frac{\partial p_*}{\partial r}$ as $-v$, and following *Theorem 3.1* in [42], for every $H_0 = O(1)$ and ε small, we can find a unique L_0 and a constant K_* , such that there is a unique classical solution to the above system with $|\lambda L_0 - \rho_3(H_0 + \gamma)| < K_*\varepsilon$. The existence theorem for radially symmetric solution of this form, however, *is not good enough* for the bifurcation theorem.

There are many parameters in our system. We need to choose one as the bifurcation parameter. We let $\mu = \frac{1}{\varepsilon}[\lambda L_0 - \rho_3(\gamma + H_0)]$ to be our bifurcation parameter. We can vary μ by, say, keeping $\lambda, \gamma, \rho_3, H_0$ and ε fixed while changing L_0 only. For simplicity, we shall assume all the parameters are fixed and of order $O(1)$ except L_0 and ρ_4 . With these settings, varying L_0 corresponds to varying μ . In the following, *we shall thus use μ and ρ_4 as our parameters.*

Here is our existence theorem for the radially symmetric solutions. We define

$$\mu_c = \frac{\rho_3}{\beta_1} \left\{ (\gamma + H_0) \left(\frac{\lambda k_1 M_0}{\lambda K_1 + \rho_3(\gamma + H_0)} + \rho_1 \right) - \rho_2 H_0 \right\}. \quad (3.24)$$

Theorem 3.3. *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 ρ_4 such that the system (3.15) — (3.23) admits a unique solution (L_*, H_*, F_*, p_*) .*

Proof. The proof is similar to that in [42] but much more involved. Following *Lemma 3.1* of [42], for all parameters of order $O(1)$, the system (3.15) — (3.22) admits a unique solution for small ε . In order for this solution to be the solution of our problem, we need to verify (3.23). We shall do so by keeping all parameters fixed except ρ_4 .

Note that (3.23) is equivalent to

$$\Phi(\rho_4, \varepsilon, \mu) = 0, \quad \text{where } \Phi(\rho_4, \varepsilon, \mu) \triangleq \int_{1-\varepsilon}^1 \left[\lambda \frac{(M_0 - F_*)L_*}{\gamma + H_*} - \rho_3(M_0 - F_*) - \rho_4 F_* \right] r dr. \quad (3.25)$$

As in [42, (3.29)–(3.32)] (the formulas in [42, (3.23)–(3.25), (3.26)–(3.28), (3.29)] are all missing minus signs; as a result, the corrected [42, (3.29)] should read (C is a constant):

$$L_*(r) = L_0 - \left(\frac{k_1 M_0 L_0}{K_1 + L_0} + \rho_1 L_0 \right) \left(\xi(r) + \frac{\varepsilon}{\beta_1} \right) + C\varepsilon^2 + O(\varepsilon^3), \quad ([42, (3.29)])$$

and [42, (3.30), (3.31)] should be corrected in a similar manner; this correction does not change the proof in [42]), we can establish the following:

$$\begin{aligned} L_*(r) &= L_0 - \frac{\varepsilon}{\beta_1} \left(\frac{k_1 M_0 L_0}{K_1 + L_0} + \rho_1 L_0 \right) + O(\varepsilon^2) \\ &= \frac{\rho_3(\gamma + H_0)}{\lambda} + \varepsilon \left[\frac{\mu}{\lambda} - \frac{\rho_3(\gamma + H_0)}{\beta_1} \left(\frac{k_1 M_0}{\lambda K_1 + \rho_3(\gamma + H_0)} + \frac{\rho_1}{\lambda} \right) \right] + O(\varepsilon^2) \\ &\triangleq \frac{\rho_3(\gamma + H_0)}{\lambda} + \varepsilon L_*^1 + O(\varepsilon^2), \end{aligned} \quad (3.26)$$

$$H_*(r) = H_0 - \varepsilon \frac{\rho_2 H_0}{\beta_1} + O(\varepsilon^2) \triangleq H_0 + \varepsilon H_*^1 + O(\varepsilon^2), \quad (3.27)$$

$$\begin{aligned} F_*(r) &= \frac{\varepsilon}{\beta_2} \frac{k_1 M_0 L_0}{D(K_1 + L_0)} + O(\varepsilon^2) \\ &= \varepsilon \frac{\rho_3(\gamma + H_0)}{\beta_2 D} \frac{k_1 M_0}{\lambda K_1 + \rho_3(\gamma + H_0)} + O(\varepsilon^2) \triangleq \varepsilon F_*^1 + O(\varepsilon^2). \end{aligned} \quad (3.28)$$

Substituting these expressions into the formula (3.25) for Φ , we find that the $O(1)$ terms in the bracket $[\dots]$ cancel out, and

$$\Phi(\rho_4, \varepsilon, \mu) = \int_{1-\varepsilon}^1 \left\{ \varepsilon \left[\frac{M_0(\lambda L_*^1 - \rho_3 H_*^1)}{\gamma + H_0} - \rho_4 F_*^1 \right] + O(\varepsilon^2) \right\} r dr. \quad (3.29)$$

A direct computation shows that

$$\frac{M_0(\lambda L_*^1 - \rho_3 H_*^1)}{\gamma + H_0} = \frac{M_0}{\gamma + H_0} (\mu - \mu_c). \quad (3.30)$$

It follows that, for small ε , $\Phi(0, \varepsilon, \mu) > 0$ and $\Phi(\rho_4, \varepsilon, \mu) < 0$ for large ρ_4 , hence there must be a value of ρ_4 on which $\Phi(\rho_4, \varepsilon, \mu) = 0$.

To finish the proof, it suffices to show $\frac{\partial}{\partial \rho_4} \Phi(\rho_4, \varepsilon) < 0$; the proof is similar to that of [42, Theorem 3.1] in the second part, but is actually a little easier. \square

Remark 3.3. *By ODE theories, the solution (L_*, H_*, F_*, p_*) can be extended to the bigger region $\Omega_{2\varepsilon} = \{1 - 2\varepsilon < r < 1\}$ while maintaining C^∞ regularity. For notational convenience, we still use (L_*, H_*, F_*, p_*) to denote the extended solution.*

Remark 3.4. *The case $\mu_c < 0$ is certainly true within reasonable parameter range.*

Following the above proof, we also derive

Lemma 3.1. *Let $\mu > \mu_c$. Then*

$$\rho_4 = \frac{1}{F_*^1} \frac{M_0}{\gamma + H_0} (\mu - \mu_c) + O(\varepsilon) = \frac{\beta_2 D[\lambda K_1 + \rho_3(\gamma + H_0)]}{\rho_3 k_1 (\gamma + H_0)^2} (\mu - \mu_c) + O(\varepsilon), \quad (3.31)$$

$$\frac{\partial \rho_4}{\partial \mu} = \frac{1}{F_*^1} \frac{M_0}{\gamma + H_0} + O(\varepsilon) = \frac{\beta_2 D[\lambda K_1 + \rho_3(\gamma + H_0)]}{\rho_3 k_1 (\gamma + H_0)^2} + O(\varepsilon). \quad (3.32)$$

Proof. From the proof of Theorem 2.1, we know that ρ_4 is chosen such that $\Phi(\rho_4, \varepsilon, \mu) = 0$. By (2.14) and (2.15), we have

$$\frac{M_0}{\gamma + H_0} (\mu - \mu_c) - \rho_4 F_*^1 = O(\varepsilon), \quad (3.33)$$

which leads to equation (2.16), and (2.17) is a direct consequence of (2.16) by taking derivative with respect to μ . \square

Remark 3.5. *In contrast to [73, 101, 113], where $\tilde{\sigma}$ is independent of μ , here the explicit dependence of ρ_4 with respect to μ is given in the above lemma.*

The following estimates are useful later on:

Lemma 3.2. *The following estimate holds for first derivatives,*

$$|L'_*(r)| + |H'_*(r)| + |F'_*(r)| + |p'_*(r)| \leq C\varepsilon, \quad 1 - \varepsilon \leq r \leq 1. \quad (3.34)$$

Proof. From (3.26)–(3.28) we derive that $|\Delta L_*| \leq C$, $|\Delta H_*| \leq C$, $|\Delta p_*| \leq C$. Using the boundary condition $L'_*(1) = 0$, we find that

$$|rL'_*(r)| = \left| \int_r^1 (\xi L'_*(\xi))' d\xi \right| \leq C\varepsilon, \quad 1 - \varepsilon \leq r \leq 1.$$

The estimates for $H'_*(r)$ and for $p'_*(r)$ are similar. Finally, for $F'_*(r)$, using the above estimates we find

$$|(rF'_*(r))'| \leq C + \frac{C\varepsilon}{D} \max_{1-\varepsilon \leq r \leq 1} |rF'_*(r)|.$$

We then integrate over $(r, 1)$ and use $F'_*(1) = 0$ to derive

$$|rF'_*(r)| \leq C\varepsilon + \frac{C\varepsilon^2}{D} \max_{1-\varepsilon \leq r \leq 1} |rF'_*(r)|,$$

which implies $|rF'_*(r)| \leq C\varepsilon$. □

3.4 Preparations for the bifurcation theorem

In order to tackle the existence of symmetry-breaking stationary solutions to System (P), we would like to apply the Crandall-Rabinowitz theorem (Appendix B). The preparations are similar as in Chapter 2, hence we omit some detailed proofs here.

We consider a family of perturbed domains $\Omega_\tau = \{1 - \varepsilon + \tilde{R} < r < 1\}$ and denote the corresponding inner boundary to be Γ_τ , where $\tilde{R} = \tau S(\theta)$, $|\tau| \ll \varepsilon$ and $|S| \leq 1$. Let (L, H, F, p) be the solution of the system:

$$-\Delta L = -k_1 \frac{(M_0 - F)L}{K_1 + L} - \rho_1 L \quad \text{in } \Omega_\tau, \quad (3.35)$$

$$-\Delta H = -k_2 \frac{HF}{K_2 + F} - \rho_2 H \quad \text{in } \Omega_\tau, \quad (3.36)$$

$$\begin{aligned} -D\Delta F - \nabla F \cdot \nabla p &= k_1 \frac{(M_0 - F)L}{K_1 + L} - k_2 \frac{HF}{K_2 + F} \\ &\quad - \lambda \frac{F(M_0 - F)L}{M_0(\gamma + H)} + (\rho_3 - \rho_4) \frac{(M_0 - F)F}{M_0} \end{aligned} \quad \text{in } \Omega_\tau, \quad (3.37)$$

$$-\Delta p = \frac{1}{M_0} \left[\lambda \frac{(M_0 - F)L}{\gamma + H} - \rho_3(M_0 - F) - \rho_4 F \right] \quad \text{in } \Omega_\tau, \quad (3.38)$$

$$\frac{\partial L}{\partial r} = \frac{\partial H}{\partial r} = \frac{\partial F}{\partial r} = \frac{\partial p}{\partial r} = 0, \quad r = 1, \quad (3.39)$$

$$\frac{\partial L}{\partial \mathbf{n}} + \beta_1(L - L_0) = 0 \quad \frac{\partial H}{\partial \mathbf{n}} + \beta_1(H - H_0) = 0 \quad \text{on } \Gamma_\tau, \quad (3.40)$$

$$\frac{\partial F}{\partial \mathbf{n}} + \beta_2 F = 0 \quad \text{on } \Gamma_\tau, \quad (3.41)$$

$$p = \kappa \quad \text{on } \Gamma_\tau. \quad (3.42)$$

The existence and uniqueness of such a solution is guaranteed in [114]. We then define function \mathcal{F} by

$$\mathcal{F}(\tau S, \mu) = -\frac{\partial p}{\partial \mathbf{n}} \Big|_{\Gamma_\tau}, \quad (3.43)$$

We know 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:

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

$$X_1^{l+\alpha} = \text{closure of the linear space spanned by } \{\cos(n\theta), n = 0, 1, 2, \dots\} \text{ in } X^{l+\alpha}. \quad (3.44)$$

It has been shown in [114] that the mapping $\mathcal{F}(\cdot, \mu) : X_1^{l+4+\alpha} \rightarrow X_1^{l+1+\alpha}$ is bounded for any $l > 0$.

In order to apply the Crandall-Rabinowitz theorem, we need to compute the Fréchet derivatives of \mathcal{F} . For a fixed small ε , we write the expansion of (L, H, F, p) of order τ as follows:

$$L = L_* + \tau L_1 + O(\tau^2), \quad (3.45)$$

$$H = H_* + \tau H_1 + O(\tau^2), \quad (3.46)$$

$$F = F_* + \tau F_1 + O(\tau^2), \quad (3.47)$$

$$p = p_* + \tau p_1 + O(\tau^2). \quad (3.48)$$

The rigorous justification for (3.45) — (3.48) can be found in [114]. Substituting (3.45) — (3.48) into (3.35) — (3.42), and dropping all the higher order terms in τ , we obtain the system for (L_1, H_1, F_1, p_1) , which is also called the linearized system of (3.35) — (3.42).

Since the set $\{\cos(n\theta)\}_{n=0}^\infty$ is clearly a basis for the Banach space $X_1^{l+\alpha}$ defined in (3.44), we set the perturbation as $S(\theta) = \cos(n\theta)$, and we are seeking solutions of the form

$$L_1 = L_1^n \cos(n\theta), \quad H_1 = H_1^n \cos(n\theta), \quad (3.49)$$

$$F_1 = F_1^n \cos(n\theta), \quad p_1 = p_1^n \cos(n\theta). \quad (3.50)$$

From [114, (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 Ω_* denotes the annulus $1 - \varepsilon \leq r \leq 1$):

$$-\frac{\partial^2 L_1^n}{\partial r^2} - \frac{1}{r} \frac{\partial L_1^n}{\partial r} + \frac{n^2}{r^2} L_1^n = f_5(L_1^n, H_1^n, F_1^n) \quad \text{in } \Omega_*, \quad (3.51)$$

$$-\frac{\partial^2 H_1^n}{\partial r^2} - \frac{1}{r} \frac{\partial H_1^n}{\partial r} + \frac{n^2}{r^2} H_1^n = f_6(L_1^n, H_1^n, F_1^n) \quad \text{in } \Omega_*, \quad (3.52)$$

$$-\frac{\partial^2 F_1^n}{\partial r^2} - \frac{1}{r} \frac{\partial F_1^n}{\partial r} + \frac{n^2}{r^2} F_1^n = \frac{1}{D} \left(f_7(L_1^n, H_1^n, F_1^n) + \frac{\partial F_1^n}{\partial r} \frac{\partial p_1^n}{\partial r} + \frac{\partial F_1^n}{\partial r} \frac{\partial p_1^n}{\partial r} \right) \quad \text{in } \Omega_*, \quad (3.53)$$

$$-\frac{\partial^2 p_1^n}{\partial r^2} - \frac{1}{r} \frac{\partial p_1^n}{\partial r} + \frac{n^2}{r^2} p_1^n = f_8(L_1^n, H_1^n, F_1^n) \quad \text{in } \Omega_*, \quad (3.54)$$

with boundary conditions:

$$\frac{\partial L_1^n}{\partial r} = \frac{\partial H_1^n}{\partial r} = \frac{\partial F_1^n}{\partial r} = \frac{\partial p_1^n}{\partial r} = 0 \quad r = 1, \quad (3.55)$$

$$-\frac{\partial L_1^n}{\partial r} + \beta_1 L_1^n = \left(\frac{\partial^2 L_*}{\partial r^2} - \beta_1 \frac{\partial L_*}{\partial r} \right) \Big|_{r=1-\varepsilon} \quad r = 1 - \varepsilon, \quad (3.56)$$

$$-\frac{\partial H_1^n}{\partial r} + \beta_1 H_1^n = \left(\frac{\partial^2 H_*}{\partial r^2} - \beta_1 \frac{\partial H_*}{\partial r} \right) \Big|_{r=1-\varepsilon} \quad r = 1 - \varepsilon, \quad (3.57)$$

$$-\frac{\partial F_1^n}{\partial r} + \beta_2 F_1^n = \left(\frac{\partial^2 F_*}{\partial r^2} - \beta_2 \frac{\partial F_*}{\partial r} \right) \Big|_{r=1-\varepsilon} \quad r = 1 - \varepsilon, \quad (3.58)$$

$$p_1^n = \frac{1-n^2}{(1-\varepsilon)^2} \quad r = 1 - \varepsilon, \quad (3.59)$$

In equations (3.51) — (3.54), the terms f_5, f_6, f_7 , and f_8 can all be bounded by linear functions of $|L_1^n|$, $|H_1^n|$, and $|F_1^n|$. In particular, f_8 is expressed as

$$f_8(L_1^n, H_1^n, F_1^n) = \frac{1}{M_0} \left[\lambda \frac{(M_0 - F_*)L_1^n}{\gamma + H_*} - \lambda \frac{L_* F_1^n}{\gamma + H_*} - \lambda \frac{(M_0 - F_*)L_* H_1^n}{(\gamma + H_*)^2} + (\rho_3 - \rho_4)F_1^n \right], \quad (3.60)$$

which will be used in future calculations.

Based on the expansions (3.45) — (3.48), we are able to compute the Fréchet derivative of \mathcal{F} , which is crucial in applying the Crandall-Rabinowitz Theorem.

Lemma 3.3. *The Fréchet derivative of $\mathcal{F}(\tilde{R}, \mu)$ at the point $(0, \mu)$ is given by*

$$\left[\mathcal{F}_{\tilde{R}}(0, \mu) \right] S(\theta) = \left[\frac{\partial^2 p_*}{\partial r^2} \Big|_{r=1-\varepsilon} + \frac{\partial p_1^n}{\partial r} \Big|_{r=1-\varepsilon} \right] S(\theta). \quad (3.61)$$

Proof. From (3.23), we know that

$$\frac{\partial p_*}{\partial r} \Big|_{r=1-\varepsilon} = 0,$$

which implies $\mathcal{F}(0, \mu) = 0$. For $\tilde{R} = \tau S$, it then follows from (3.48) and (3.50) that

$$\begin{aligned} \mathcal{F}(\tau S, \mu) &= -\frac{\partial p}{\partial \mathbf{n}} \Big|_{\Gamma_\tau} = \frac{\partial(p_* + \tau p_1)}{\partial r} \Big|_{r=1-\varepsilon+\tau S} + O(|\tau|^2 \|S\|_{C^{4+\alpha}(\Sigma)}) \\ &= \tau \left[\frac{\partial^2 p_*}{\partial r^2} \Big|_{r=1-\varepsilon} S(\theta) + \frac{\partial p_1}{\partial r} \Big|_{r=1-\varepsilon} \right] + O(|\tau|^2 \|S\|_{C^{4+\alpha}(\Sigma)}), \\ &= \tau \left[\frac{\partial^2 p_*}{\partial r^2} \Big|_{r=1-\varepsilon} S(\theta) + \frac{\partial p_1^n}{\partial r} \Big|_{r=1-\varepsilon} S(\theta) \right] + O(|\tau|^2 \|S\|_{C^{4+\alpha}(\Sigma)}), \end{aligned}$$

which leads to the expression of the Fréchet derivative in (3.61). \square

Based on the second assumption in the Crandall-Rabinowitz Theorem (Appendix B), we shall consider the Kernel of $\mathcal{F}_{\tilde{R}}(0, \mu)$, hence we let

$$\frac{\partial^2 p_*(1-\varepsilon)}{\partial r^2} + \frac{\partial p_1^n(1-\varepsilon)}{\partial r} = 0, \quad (3.62)$$

and denote its solution by μ_n . In the following sections, we shall prove that for $n \geq 1$, $\mu = \mu_n$ is a bifurcation point by verifying the four conditions in the Crandall-Rabinowitz Theorem. However, unlike [24, 32, 45, 52, 73, 78, 88, 101–103], we cannot solve p_* and p_1^n explicitly since our model is highly nonlinear and coupled. To meet the challenges, we need to derive various sharp estimates on p_* and p_1^n .

3.4.1 Estimates for p_*

In order to estimate $\frac{\partial^2 p_*(1-\varepsilon)}{\partial r^2}$ in (3.61), we start with evaluating (3.18) at $r = 1 - \varepsilon$ and substituting the boundary condition (3.23), hence we obtain

$$-\frac{\partial^2 p_*(1-\varepsilon)}{\partial r^2} = \frac{1}{M_0} \left(\lambda \frac{(M_0 - F_*)L_*}{\gamma + H_*} - \rho_3(M_0 - F_*) - \rho_4 F_* \right) \Big|_{r=1-\varepsilon}. \quad (3.63)$$

Similar to the proof of Theorem 3.3, we substitute (3.26) — (3.28) into the above formula and combine with (3.33), we find that both $O(1)$ and $O(\varepsilon)$ terms cancel out, thus

$$\frac{\partial^2 p_*(1-\varepsilon)}{\partial r^2} = \frac{\varepsilon}{M_0} \left(\frac{M_0}{\gamma + H_0} (\mu - \mu_c) - \rho_4 F_*^1 \right) + O(\varepsilon^2) = O(\varepsilon^2). \quad (3.64)$$

Denote

$$J_1(\mu, \rho_4) = \frac{1}{\varepsilon^2} \frac{\partial^2 p_*(1-\varepsilon)}{\partial r^2}, \quad \text{i.e.,} \quad \frac{\partial^2 p_*(1-\varepsilon)}{\partial r^2} = \varepsilon^2 J_1(\mu, \rho_4), \quad (3.65)$$

it follows from (3.64) that $J_1(\mu, \rho_4) = O(1)$ is bounded. Besides, we claim that $\frac{dJ_1}{d\mu} = \frac{\partial J_1}{\partial \mu} + \frac{\partial J_1}{\partial \rho_4} \frac{\partial \rho_4}{\partial \mu} = O(1)$ is also bounded. To prove it, we take μ derivative of equation (3.64), and derive

$$\frac{\partial^2}{\partial r^2} \left(\frac{\partial p_*}{\partial \mu} \right) \Big|_{r=1-\varepsilon} = \varepsilon \left(\frac{1}{\gamma + H_0} - \frac{F_*^1}{M_0} \frac{\partial \rho_4}{\partial \mu} \right) + O(\varepsilon^2).$$

By substituting the formula of $\frac{\partial \rho_4}{\partial \mu}$ in (3.32), we find that the $O(\varepsilon)$ terms in the above equation cancel out, hence

$$\frac{dJ_1(\mu, \rho_4(\mu))}{d\mu} = \frac{1}{\varepsilon^2} \frac{\partial^2}{\partial r^2} \left(\frac{\partial p_*}{\partial \mu} \right) \Big|_{r=1-\varepsilon} = \frac{1}{\varepsilon^2} O(\varepsilon^2) = O(1).$$

To sum up, the properties of J_1 are listed in the following lemma:

Lemma 3.4. *For function $J_1(\mu, \rho_4)$ defined in (3.65), there exists a constant C which is independent of ε such that*

$$|J_1(\mu, \rho_4(\mu))| \leq C, \quad \left| \frac{dJ_1(\mu, \rho_4(\mu))}{d\mu} \right| \leq C. \quad (3.66)$$

3.4.2 Estimates for p_1^n

In order to estimate p_1^n , we need to consider L_1^n , H_1^n , and F_1^n . Recall their equations in (3.51) — (3.53) with boundary conditions (3.56) — (3.58). To make the boundary conditions homogeneous, let us instead work with

$$\widetilde{L}_1^n(r) = L_1^n(r) - \frac{1}{\beta_1} \left(\frac{\partial^2 L_*}{\partial r^2} - \beta_1 \frac{\partial L_*}{\partial r} \right) \Big|_{r=1-\varepsilon}, \quad (3.67)$$

$$\widetilde{H}_1^n(r) = H_1^n(r) - \frac{1}{\beta_1} \left(\frac{\partial^2 H_*}{\partial r^2} - \beta_1 \frac{\partial H_*}{\partial r} \right) \Big|_{r=1-\varepsilon}, \quad (3.68)$$

$$\widetilde{F}_1^n(r) = F_1^n(r) - \frac{1}{\beta_2} \left(\frac{\partial^2 F_*}{\partial r^2} - \beta_2 \frac{\partial F_*}{\partial r} \right) \Big|_{r=1-\varepsilon}. \quad (3.69)$$

Accordingly, $\widetilde{L}_1^n(r)$, $\widetilde{H}_1^n(r)$, $\widetilde{F}_1^n(r)$ satisfy the following equations:

$$-\frac{\partial^2 \widetilde{L}_1^n}{\partial r^2} - \frac{1}{r} \frac{\partial \widetilde{L}_1^n}{\partial r} + \frac{n^2}{r^2} \widetilde{L}_1^n = \widetilde{f}_5 \triangleq f_5 - \frac{n^2}{\beta_1 r^2} \left(\frac{\partial^2 L_*}{\partial r^2} - \beta_1 \frac{\partial L_*}{\partial r} \right) \Big|_{r=1-\varepsilon} \quad \text{in } \Omega_*, \quad (3.70)$$

$$-\frac{\partial^2 \widetilde{H}_1^n}{\partial r^2} - \frac{1}{r} \frac{\partial \widetilde{H}_1^n}{\partial r} + \frac{n^2}{r^2} \widetilde{H}_1^n = \widetilde{f}_6 \triangleq f_6 - \frac{n^2}{\beta_1 r^2} \left(\frac{\partial^2 H_*}{\partial r^2} - \beta_1 \frac{\partial H_*}{\partial r} \right) \Big|_{r=1-\varepsilon} \quad \text{in } \Omega_*, \quad (3.71)$$

$$-D \frac{\partial^2 \widetilde{F}_1^n}{\partial r^2} - \frac{D}{r} \frac{\partial \widetilde{F}_1^n}{\partial r} + \frac{D n^2}{r^2} \widetilde{F}_1^n - \frac{\partial \widetilde{F}_1^n}{\partial r} \frac{\partial p_*}{\partial r} = \widetilde{f}_7 \quad \text{in } \Omega_*, \quad (3.72)$$

$$\frac{\partial \widetilde{L}_1^n}{\partial r} = \frac{\partial \widetilde{H}_1^n}{\partial r} = \frac{\partial \widetilde{F}_1^n}{\partial r} = 0 \quad r = 1, \quad (3.73)$$

$$-\frac{\partial \widetilde{L}_1^n}{\partial r} + \beta_1 \widetilde{L}_1^n = 0 \quad r = 1 - \varepsilon, \quad (3.74)$$

$$-\frac{\partial \widetilde{H}_1^n}{\partial r} + \beta_1 \widetilde{H}_1^n = 0 \quad r = 1 - \varepsilon, \quad (3.75)$$

$$-\frac{\partial \widetilde{F}_1^n}{\partial r} + \beta_2 \widetilde{F}_1^n = 0 \quad r = 1 - \varepsilon, \quad (3.76)$$

where

$$\widetilde{f}_7 \triangleq f_7 + \frac{\partial F_*}{\partial r} \frac{\partial p_1^n}{\partial r} - \frac{Dn^2}{\beta_2 r^2} \left(\frac{\partial^2 F_*}{\partial r^2} - \beta_2 \frac{\partial F_*}{\partial r} \right) \Big|_{r=1-\varepsilon}, \quad (3.77)$$

and p_1^n is defined by (3.54) and (3.59).

Notice that equations (3.70) — (3.72) are of a similar structure, we denote this left-hand side operator by $\mathcal{L}_n \triangleq -\frac{\partial^2}{\partial r^2} - \frac{1}{r} \frac{\partial}{\partial r} + \frac{n^2}{r^2}$. For this special operator, one can easily verify the following lemmas.

Lemma 3.5. *The general solution of (η is a constant)*

$$\begin{aligned} \mathcal{L}_n[\psi] &\triangleq -\psi'' - \frac{1}{r}\psi' + \frac{n^2}{r^2}\psi = \eta + f(r), \quad 1 - \varepsilon < r < 1, \\ \psi'(1) &= 0, \end{aligned} \quad (3.78)$$

is given by

$$\psi - \psi_1 = \begin{cases} Ar^n + Br^{-n} + K[f](r), \text{ where } B = A + \frac{1}{n}K[f]'(1) & n \neq 0, \\ A + K[f](r) & n = 0, \end{cases} \quad (3.79)$$

where

$$K[f](r) = \begin{cases} \frac{r^n}{2n} \int_r^1 s^{-n+1} f(s) ds + \frac{r^{-n}}{2n} \int_{1-\varepsilon}^r s^{n+1} f(s) ds & n \neq 0, \\ - \int_r^1 \left(\log \frac{s}{r} \right) s f(s) ds & n = 0; \end{cases} \quad (3.80)$$

in addition, $\psi_1(r)$ satisfies

$$\begin{aligned} L_n[\psi_1] &= -\psi_1'' - \frac{1}{r}\psi_1' + \frac{n^2}{r^2}\psi_1 = \eta \quad 1 - \varepsilon < r < 1, \\ \psi_1'(1) &= 0, \quad \psi_1(1) = 0, \end{aligned} \quad (3.81)$$

and is given by

$$\psi_1 = \begin{cases} \frac{\eta}{n^2 - 4} \left(r^2 - \frac{n+2}{2n} r^n - \frac{n-2}{2n} r^{-n} \right) & n \neq 0, 2, \\ \eta \left(\frac{1-r^2}{4} + \frac{1}{2} \log r \right) & n = 0, \\ \eta \left(-\frac{1}{16} \frac{1}{r^2} + \frac{r^2}{16} - \frac{1}{4} r^2 \log r \right) & n = 2. \end{cases} \quad (3.82)$$

The special solution $K[f]$ satisfies

$$|K[f](r)| \leq \min \left(\frac{\varepsilon}{2n}, \frac{1}{n^2} \right) \|f\|_{L^\infty}, \quad |K[f]'(r)| \leq \min \left(\frac{\varepsilon}{2}, \frac{1}{n} \right) \|f\|_{L^\infty}, \quad n \geq 1, \quad (3.83)$$

and

$$|K[f](r)| \leq \varepsilon \|f\|_{L^\infty}, \quad |K[f]'(r)| \leq \varepsilon \|f\|_{L^\infty}, \quad n = 0. \quad (3.84)$$

Proof. Using the expression in (3.80), we clearly have, for $1 - \varepsilon \leq r \leq 1$ and $n \geq 1$,

$$|K[f](r)| \leq \|f\|_{L^\infty} \left[\frac{1}{2n} \int_r^1 \left(\frac{r}{s} \right)^n s \, ds + \frac{1}{2n} \int_{1-\varepsilon}^r \left(\frac{s}{r} \right)^n s \, ds \right] \leq \frac{\varepsilon}{2n} \|f\|_{L^\infty}. \quad (3.85)$$

We can also integrate the expression to obtain

$$\begin{aligned} \int_r^1 \left(\frac{r}{s} \right)^n s \, ds + \int_{1-\varepsilon}^r \left(\frac{s}{r} \right)^n s \, ds &\leq \int_r^1 r^n s^{-n-1} \, ds + \int_{1-\varepsilon}^r r^{-n} s^{n-1} \, ds \\ &\leq r^n \frac{r^{-n}}{n} + r^{-n} \frac{r^n}{n} = \frac{2}{n}; \end{aligned}$$

combining it with (3.85), we deduce

$$|K[f](r)| \leq \min\left(\frac{\varepsilon}{2n}, \frac{1}{n^2}\right) \|f\|_{L^\infty}.$$

Furthermore, it follows from (3.80) that

$$K[f]'(r) = \frac{r^{n-1}}{2} \int_r^1 s^{-n+1} f(s) \, ds - \frac{r^{-n-1}}{2} \int_{1-\varepsilon}^r s^{n+1} f(s) \, ds;$$

similarly, we shall obtain

$$|K[f]'(r)| \leq \|f\|_{L^\infty} \left[\frac{1}{2} \int_r^1 \left(\frac{r}{s}\right)^{n-1} ds + \frac{1}{2} \int_{1-\varepsilon}^r \left(\frac{s}{r}\right)^{n+1} ds \right] \leq \min\left(\frac{\varepsilon}{2}, \frac{1}{n}\right) \|f\|_{L^\infty}.$$

The case $n = 0$ is similar. □

Remark 3.6. For the particular solution ψ_1 defined by (3.81), it is easy to derive from (3.82) that $\psi_1''(1) = -\eta$ and $\psi_1'''(1) = \eta$ for each non-negative integer n , and hence

$$\begin{aligned} \psi_1(r) &= \psi_1(1) + \psi_1'(1)(r-1) + \frac{\psi_1''(1)}{2}(r-1)^2 + \cdots = -\frac{\eta}{2}(r-1)^2 + O(\varepsilon^3), \\ \psi_1'(r) &= \psi_1'(1) + \psi_1''(1)(r-1) + \frac{\psi_1'''(1)}{2}(r-1)^2 + \cdots \\ &= -\eta(r-1) + \frac{\eta}{2}(r-1)^2 + O(\varepsilon^3). \end{aligned}$$

In particular, when evaluating at $r = 1 - \varepsilon$, we have

$$\psi_1(1 - \varepsilon) = -\frac{\eta}{2}\varepsilon^2 + O(\varepsilon^3), \tag{3.86}$$

$$\psi_1'(1 - \varepsilon) = \varepsilon\eta + \frac{\eta}{2}\varepsilon^2 + O(\varepsilon^3). \tag{3.87}$$

Lemma 3.6. If in addition to (3.78), we further assume $\psi(1 - \varepsilon) = G$, then, for

$n \geq 1$, the coefficients A and B in (3.79) take the form:

$$A = \frac{1}{1+(1-\varepsilon)^{2n}} \left((1-\varepsilon)^n [G - \psi_1(1-\varepsilon)] - (1-\varepsilon)^n K[f](1-\varepsilon) - \frac{1}{n} K[f]'(1) \right), \quad (3.88)$$

$$B = \frac{1}{1+(1-\varepsilon)^{2n}} \left((1-\varepsilon)^n [G - \psi_1(1-\varepsilon)] - (1-\varepsilon)^n K[f](1-\varepsilon) + \frac{(1-\varepsilon)^{2n}}{n} K[f]'(1) \right); \quad (3.89)$$

in particular, for $n = 0$,

$$A = G - \psi_1(1-\varepsilon) - K[f](1-\varepsilon). \quad (3.90)$$

Lemma 3.7. For $n \geq 0$ and $0 < \varepsilon < 1$,

$$1 - n\varepsilon \leq (1-\varepsilon)^n \leq 1 - n\varepsilon + \frac{1}{2}n^2\varepsilon^2. \quad (3.91)$$

Proof. The function $f(\varepsilon) \triangleq (1-\varepsilon)^n - 1 + n\varepsilon$ satisfies $f(0) = 0$ and $f'(\varepsilon) = -n(1-\varepsilon)^{n-1} + n \geq 0$ for $0 < \varepsilon < 1$, so that $f(\varepsilon) \geq 0$ for $0 < \varepsilon < 1$.

Similarly, the function $f(\varepsilon) \triangleq (1-\varepsilon)^n - 1 + n\varepsilon - \frac{1}{2}n^2\varepsilon^2$ satisfies $f(0) = f'(0) = 0$ and $f''(\varepsilon) = n(n-1)(1-\varepsilon)^{n-2} - n^2 \leq 0$ for $0 < \varepsilon < 1$, so that $f(\varepsilon) \leq 0$ for $0 < \varepsilon < 1$. \square

Using these lemmas, we can derive from system (3.70) — (3.76) that the following estimates hold:

Lemma 3.8. For sufficiently small ε , there exist a constant C which does not depend on ε and n such that the following inequalities are valid for system (3.70) — (3.76),

$$\|\widetilde{L}_1^n\|_{L^\infty(1-\varepsilon,1)} + \|\widetilde{H}_1^n\|_{L^\infty(1-\varepsilon,1)} + \|\widetilde{F}_1^n\|_{L^\infty(1-\varepsilon,1)} \leq C(n^2 + 1)\varepsilon, \quad (3.92)$$

$$\|(p_1^n)'\|_{L^\infty(1-\varepsilon,1)} \leq 2(n^3 + 1). \quad (3.93)$$

Proof. To prove (3.92) and (3.93), we use the idea of continuation (Lemma C.2 in Appendix C). We multiply the right-hand sides of (3.70) — (3.72) and (3.54) by δ with $0 \leq \delta \leq 1$. When $\delta = 0$, it follows from the maximum principle that $\widetilde{L}_1^n = \widetilde{H}_1^n = \widetilde{F}_1^n = 0$, hence (3.92) clearly holds in this case. Furthermore, it can be solved from

$$-\frac{\partial^2 p_1^n}{\partial r^2} - \frac{1}{r} \frac{\partial p_1^n}{\partial r} + \frac{n^2}{r^2} p_1^n = 0 \quad 1 - \varepsilon < r < 1, \quad (3.94)$$

$$\frac{\partial p_1^n(1)}{\partial r} = 0, \quad p_1^n(1 - \varepsilon) = \frac{1 - n^2}{(1 - \varepsilon)^2}, \quad (3.95)$$

that

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

and hence for $0 < \varepsilon \ll 1$,

$$\begin{aligned} \|(p_1^n)'\|_{L^\infty(1-\varepsilon,1)} &= \max_{1-\varepsilon \leq r \leq 1} \left| \frac{1 - n^2}{(1 - \varepsilon)^2[(1 - \varepsilon)^n + (1 - \varepsilon)^{-n}]} n (r^{n-1} - r^{-n-1}) \right| \\ &\leq n(n^2 - 1) \left| \frac{1}{(1 - \varepsilon)^3} \frac{(1 - \varepsilon)^n - (1 - \varepsilon)^{-n}}{(1 - \varepsilon)^n + (1 - \varepsilon)^{-n}} \right| \leq 2(n^3 + 1). \end{aligned}$$

Next we consider the case when $0 < \delta \leq 1$. We first assume that

$$\|\widetilde{L}_1^n\|_{L^\infty(1-\varepsilon,1)} + \|\widetilde{H}_1^n\|_{L^\infty(1-\varepsilon,1)} + \|\widetilde{F}_1^n\|_{L^\infty(1-\varepsilon,1)} \leq n^2 + 1, \quad (3.96)$$

$$\|(p_1^n)'\|_{L^\infty(1-\varepsilon,1)} \leq 3(n^3 + 1), \quad (3.97)$$

and on the basis of these two assumptions, we shall derive smaller bounds for \widetilde{L}_1^n , \widetilde{H}_1^n , \widetilde{F}_1^n , and $(\widetilde{p}_1^n)'$ so that the second condition in Lemma C.2 is satisfied. By (3.96) and (3.97), we clearly have $|\widetilde{f}_5| \leq C(n^2 + 1)$, and $K[\widetilde{f}_5](r) + |K[\widetilde{f}_5]'(1)|(r + \frac{1}{\beta_1}) + \frac{1}{\beta_1} |K[\widetilde{f}_5]'(1 - \varepsilon) - \beta_1 K[\widetilde{f}_5](1 - \varepsilon)|$ is a supersolution for $\widetilde{L}_1^n(r)$ when $n \geq 1$. It follows

that, by Lemma 3.5,

$$\begin{aligned} |\widetilde{L}_1^n(r)| &\leq K[\widetilde{f}_5](r) + |K[\widetilde{f}_5]'(1)|\left(r + \frac{1}{\beta_1}\right) + \frac{1}{\beta_1}|K[\widetilde{f}_5]'(1 - \varepsilon) - \beta_1 K[\widetilde{f}_5](1 - \varepsilon)| \\ &\leq C(n^2 + 1)\varepsilon. \end{aligned}$$

The case when $n = 0$ can be easily proved. Similarly, we have $|\widetilde{H}_1^n(r)| \leq C(n^2 + 1)\varepsilon$.

Next we prove the estimate for \widetilde{F}_1^n . Under our assumptions, by (3.34), (3.96), and (3.97),

$$\|\widetilde{f}_7\|_{L^\infty} \leq C(n^2 + 1) + C\varepsilon(n^3 + 1),$$

and we can use (3.83) to derive

$$|K[\widetilde{f}_7](r)| \leq C(n + 1)\varepsilon, \quad |K[\widetilde{f}_7]'(r)| \leq C(n^2 + 1)\varepsilon.$$

The function $\phi = \frac{1}{D}\{K[\widetilde{f}_7](r) + |K[\widetilde{f}_7]'(1)|\left(r + \frac{1}{\beta_2}\right) + \frac{1}{\beta_2}|K[\widetilde{f}_7]'(1 - \varepsilon) - \beta_2 K[\widetilde{f}_7](1 - \varepsilon)| + \varepsilon\}$ satisfies,

$$\begin{aligned} &DL[\phi] + \frac{\partial \phi}{\partial r} \frac{\partial p_*}{\partial r} \\ &= \widetilde{f}_7 + \frac{1}{D}\left(K[\widetilde{f}_7]'(r) + |K[\widetilde{f}_7]'(1)|\right) \frac{\partial p_*}{\partial r} - \frac{1}{Dr}|K[\widetilde{f}_7]'(1)| + \frac{n^2}{Dr^2}|K[\widetilde{f}_7]'(1)|\left(r + \frac{1}{\beta_2}\right) \\ &\quad + \frac{n^2}{Dr^2}\left(\frac{1}{\beta_2}|K[\widetilde{f}_7]'(1 - \varepsilon) - \beta_2 K[\widetilde{f}_7](1 - \varepsilon)| + \varepsilon\right) \\ &\geq \widetilde{f}_7 - C\varepsilon\|K[\widetilde{f}_7]'\|_{L^\infty} + n^2\varepsilon \geq \widetilde{f}_7 - C(n^2 + 1)\varepsilon^2 + n^2\varepsilon \geq \widetilde{f}_7, \end{aligned}$$

for $n \geq 1$, where we also make use of (3.34) in deriving the above estimate. Therefore, it follows from the maximum principle that

$$|\widetilde{F}_1^n(r)| \leq \phi \leq C(n^2 + 1)\varepsilon.$$

Finally, in order to estimate $(p_1^n)'$, we use the explicit formula from Lemma 3.5.

Taking $\eta = 0$ and $G = (1 - n^2)/(1 - \varepsilon)^2$, we obtain from Lemma 3.5 that

$$(p_1^n)' = Anr^{n-1} - Bnr^{-n-1} + K[f_8]'(r), \quad (3.98)$$

where A and B are defined in Lemma 3.6. Recall f_8 is defined in (3.60), by (3.96),

$$\|f_8\|_{L^\infty} \leq C(n^2 + 1),$$

and together with (3.83) in Lemma 3.5, we have

$$|K[f_8](r)| \leq C \frac{n^2 + 1}{n} \varepsilon, \quad |K[f_8]'(r)| \leq C(n^2 + 1) \varepsilon. \quad (3.99)$$

Combining (3.98) with (3.88) (3.89) and (3.99), we then obtain

$$\begin{aligned} |(p_1^n)'| &\leq \max_{1-\varepsilon \leq r \leq 1} \left| \frac{n(r^{n-1} - r^{-n-1})}{(1-\varepsilon)^n + (1-\varepsilon)^{-n}} [G - k[f_8](1-\varepsilon)] \right| \\ &\quad + \max_{1-\varepsilon \leq r \leq 1} \left| \frac{r^{n-1} + (1-\varepsilon)^{2n} r^{-n-1}}{1 + (1-\varepsilon)^{2n}} K[f_8]'(1) \right| + \max_{1-\varepsilon \leq r \leq 1} |K[f_8]'(r)| \\ &\leq \left| \frac{nG}{1-\varepsilon} \frac{(1-\varepsilon)^n - (1-\varepsilon)^{-n}}{(1-\varepsilon)^n + (1-\varepsilon)^{-n}} \right| + Cn \|K[f_8]\|_{L^\infty} + C \|K[f_8]'\|_{L^\infty} \\ &\leq \left| \frac{n(n^2 - 1)}{(1-\varepsilon)^3} \frac{(1-\varepsilon)^n - (1-\varepsilon)^{-n}}{(1-\varepsilon)^n + (1-\varepsilon)^{-n}} \right| + C(n^2 + 1) \varepsilon \\ &\leq 2(n^3 + 1), \end{aligned}$$

hence $\|(p_1^n)'\|_{L^\infty(1-\varepsilon, 1)} \leq 2(n^3 + 1)$ is valid for sufficiently small ε . \square

Based on (3.92) and (3.93), the existence and uniqueness of such a solution $(L_1^n, H_1^n, F_1^n, p_1^n)$ to the system (3.51) — (3.59) can be justified through the contraction mapping principle, hence we have the following lemma.

Lemma 3.9. *For each nonnegative n and sufficiently small ε , the system (3.51) — (3.59) admits a unique solution $(L_1^n, H_1^n, F_1^n, p_1^n)$.*

By (3.93) we already derived the estimate

$$\left| \frac{\partial p_1^n(r)}{\partial r} \right| \leq 2(n^3 + 1), \quad 1 - \varepsilon \leq r \leq 1.$$

This estimate, however, is not enough; we need a sharper bound for $\frac{\partial p_1^n(1-\varepsilon)}{\partial r}$. To do that, we start with rewriting (3.67) — (3.69) in the same way as in (3.26) — (3.28).

Evaluating (3.15) at $r = 1 - \varepsilon$, and using (3.26) — (3.28), we obtain

$$\begin{aligned} \frac{\partial^2 L_*(1-\varepsilon)}{\partial r^2} &= \left(k_1 \frac{(M_0 - F_*)L_*}{K_1 + L_*} + \rho_1 L_* \right) \Big|_{r=1-\varepsilon} - \frac{1}{1-\varepsilon} \frac{\partial L_*(1-\varepsilon)}{\partial r} \\ &= \rho_3(\gamma + H_0) \left(\frac{k_1 M_0}{\lambda K_1 + \rho_3(\gamma + H_0)} + \frac{\rho_1}{\lambda} \right) - \frac{1}{1-\varepsilon} \frac{\partial L_*(1-\varepsilon)}{\partial r} + O(\varepsilon). \end{aligned}$$

Recall that the boundary condition for L_* is

$$\frac{\partial L_*(1-\varepsilon)}{\partial r} = \beta_1(L_*(1-\varepsilon) - L_0) = \beta_1 \left(\frac{\rho_3(\gamma + H_0)}{\lambda} + O(\varepsilon) - \frac{\rho_3(\gamma + H_0)}{\lambda} - \frac{\varepsilon \mu}{\lambda} \right) = O(\varepsilon).$$

We combine the above two equations to derive

$$\frac{1}{\beta_1} \left(\frac{\partial^2 L_*}{\partial r^2} - \beta_1 \frac{\partial L_*}{\partial r} \right) \Big|_{r=1-\varepsilon} = \frac{\rho_3(\gamma + H_0)}{\beta_1} \left(\frac{k_1 M_0}{\lambda K_1 + \rho_3(\gamma + H_0)} + \frac{\rho_1}{\lambda} \right) + O(\varepsilon).$$

Similarly, we can also get

$$\begin{aligned} \frac{1}{\beta_1} \left(\frac{\partial^2 H_*}{\partial r^2} - \beta_1 \frac{\partial H_*}{\partial r} \right) \Big|_{r=1-\varepsilon} &= \frac{\rho_2 H_0}{\beta_1} + O(\varepsilon), \\ \frac{1}{\beta_2} \left(\frac{\partial^2 F_*}{\partial r^2} - \beta_2 \frac{\partial F_*}{\partial r} \right) \Big|_{r=1-\varepsilon} &= -\frac{\rho_3(\gamma + H_0)}{\beta_2 D} \frac{k_1 M_0}{\lambda K_1 + \rho_3(\gamma + H_0)} + O(\varepsilon). \end{aligned}$$

Comparing with the definitions of L_*^1 , H_*^1 and F_*^1 in (3.26) — (3.28), we find that

$$\begin{aligned} \frac{\rho_3(\gamma + H_0)}{\beta_1} \left(\frac{k_1 M_0}{\lambda K_1 + \rho_3(\gamma + H_0)} + \frac{\rho_1}{\lambda} \right) &= \frac{\mu}{\lambda} - L_*^1, \\ \frac{\rho_2 H_0}{\beta_1} &= -H_*^1, \quad -\frac{\rho_3(\gamma + H_0)}{\beta_2 D} \frac{k_1 M_0}{\lambda K_1 + \rho_3(\gamma + H_0)} = -F_*^1. \end{aligned}$$

Therefore, the above equations indicate

$$\frac{1}{\beta_1} \left(\frac{\partial^2 L_*}{\partial r^2} - \beta_1 \frac{\partial L_*}{\partial r} \right) \Big|_{r=1-\varepsilon} = \frac{\mu}{\lambda} - L_*^1 + O(\varepsilon), \quad (3.100)$$

$$\frac{1}{\beta_1} \left(\frac{\partial^2 H_*}{\partial r^2} - \beta_1 \frac{\partial H_*}{\partial r} \right) \Big|_{r=1-\varepsilon} = -H_*^1 + O(\varepsilon), \quad (3.101)$$

$$\frac{1}{\beta_2} \left(\frac{\partial^2 F_*}{\partial r^2} - \beta_2 \frac{\partial F_*}{\partial r} \right) \Big|_{r=1-\varepsilon} = -F_*^1 + O(\varepsilon). \quad (3.102)$$

After we show (3.100) — (3.102), we can combine them with (3.67) — (3.69) as well as (3.92) to claim that

$$L_1^n = \mu/\lambda - L_*^1 + O((n^2 + 1)\varepsilon), \quad (3.103)$$

$$H_1^n = -H_*^1 + O((n^2 + 1)\varepsilon), \quad (3.104)$$

$$F_1^n = -F_*^1 + O((n^2 + 1)\varepsilon). \quad (3.105)$$

With (3.103) — (3.105), we are able to derive a more delicate estimate for $\frac{\partial p_1^n(1-\varepsilon)}{\partial r}$. Substituting (3.26) — (3.28) and (3.103) — (3.105) all into (3.60), recalling also (3.30) and (3.31), we obtain

$$f_8 = \frac{\mu}{\gamma + H_0} - \frac{1}{M_0} \left(\frac{M_0(\lambda L_*^1 - \rho_3 H_*^1)}{\gamma + H_0} - \rho_4 F_*^1 \right) + O((n^2 + 1)\varepsilon) = \frac{\mu}{\gamma + H_0} + O((n^2 + 1)\varepsilon), \quad (3.106)$$

and we are ready to establish the following lemma.

Lemma 3.10. *For each nonnegative n and small $0 < \varepsilon \ll 1$, the following inequality holds:*

$$\left| \frac{\partial p_1^n(1-\varepsilon)}{\partial r} - \frac{\varepsilon\mu}{\gamma + H_0} - \frac{n[(1-\varepsilon)^{2n} - 1]}{(1-\varepsilon)[(1-\varepsilon)^{2n} + 1]} G \right| \leq C(n^2 + 1)\varepsilon^2, \quad (3.107)$$

where $G = (1 - n^2)/(1 - \varepsilon)^2$, and the constant C is independent of ε and n .

Proof. The estimate (3.107) shall be established by using the explicit formula from

Lemma 3.5. Specifically, we take $\eta = \frac{\mu}{\gamma + H_0}$ and $f(r) = f_8 - \eta$. From (3.106), we have

$$\|f\|_{L^\infty} = \|f_8 - \eta\|_{L^\infty} \leq C(n^2 + 1)\varepsilon;$$

we then combine it with Lemma 3.5 to derive

$$|K[f](r)| \leq C(n+1)\varepsilon^2, \quad |K[f]'(r)| \leq C(n^2+1)\varepsilon^2. \quad (3.108)$$

Following Lemmas 3.5 and 3.6, we can explicitly solve p_1^n as

$$p_1^n(r) = \psi_1(r) + Ar^n + Br^{-n} + K[f](r).$$

Recall the properties of $\psi_1(r)$ in Remark 3.6, we have,

$$\psi_1(1-\varepsilon) = -\frac{\eta}{2}\varepsilon^2 + O(\varepsilon^3), \quad \psi_1'(1-\varepsilon) = \varepsilon\eta + \frac{\eta}{2}\varepsilon^2 + O(\varepsilon^3).$$

Together with (3.88) (3.89) as well as (3.108) the first derivative of p_1^n at $r = 1 - \varepsilon$ evaluates to

$$\begin{aligned} \frac{\partial p_1^n(1-\varepsilon)}{\partial r} &= \psi_1'(1-\varepsilon) + An(1-\varepsilon)^{n-1} - Bn(1-\varepsilon)^{-n-1} + K[f]'(1-\varepsilon) \\ &= \psi_1'(1-\varepsilon) + \frac{n[(1-\varepsilon)^{2n} - 1]}{(1-\varepsilon)[(1-\varepsilon)^{2n} + 1]} \left(G - \psi_1(1-\varepsilon) \right) + O((n^2+1)\varepsilon^2) \\ &= \eta\varepsilon + \frac{n[(1-\varepsilon)^{2n} - 1]}{(1-\varepsilon)[(1-\varepsilon)^{2n} + 1]} G + O((n^2+1)\varepsilon^2), \quad n \neq 0, \end{aligned}$$

which is equivalent to (3.107). □

Like in (3.65), we denote

$$J_2^n(\mu, \rho_4) = \frac{1}{\varepsilon^2} \left[\frac{\partial p_1^n(1-\varepsilon)}{\partial r} - \frac{\varepsilon\mu}{\gamma + H_0} - \frac{n(1-n^2)[(1-\varepsilon)^{2n} - 1]}{(1-\varepsilon)^3[(1-\varepsilon)^{2n} + 1]} \right], \quad (3.109)$$

which indicates

$$\frac{\partial p_1^n(1-\varepsilon)}{\partial r} = \frac{\varepsilon\mu}{\gamma + H_0} + \frac{n(1-n^2)[(1-\varepsilon)^{2n}-1]}{(1-\varepsilon)^3[(1-\varepsilon)^{2n}+1]} + \varepsilon^2 J_2^n(\mu, \rho_4). \quad (3.110)$$

From Lemma 3.10, we immediately obtain that there exists a constant C which is independent of n and ε such that

$$|J_2^n(\mu, \rho_4)| \leq C(n^2 + 1).$$

In addition, we also need to estimate $\frac{dJ_2^n}{d\mu}$. To do that, we take μ derivative of equation (3.110) to obtain

$$\frac{dJ_2^n}{d\mu} = \frac{\partial J_2^n}{\partial \mu} + \frac{\partial J_2^n}{\partial \rho_4} \frac{\partial \rho_4}{\partial \mu} = \frac{1}{\varepsilon^2} \left[\frac{\partial}{\partial r} \left(\frac{\partial p_1^n}{\partial \mu} \right) \Big|_{r=1-\varepsilon} - \frac{\varepsilon}{\gamma + H_0} \right]. \quad (3.111)$$

In order to estimate the right-hand side of (3.111), we differentiate the whole system (3.51) — (3.59) in μ and follow the same procedures as in Lemmas 3.8 and 3.10. Consequently, a similar result as (3.107) can be obtained, i.e.,

$$\left| \frac{\partial}{\partial r} \left(\frac{\partial p_1^n}{\partial \mu} \right) \Big|_{r=1-\varepsilon} - \frac{\varepsilon}{\gamma + H_0} \right| \leq C(n^2 + 1)\varepsilon^2.$$

Combined with (3.111), it follows that $\left| \frac{dJ_2^n}{d\mu} \right| \leq C(n^2 + 1)$. Therefore we have the following lemma.

Lemma 3.11. *For function $J_2^n(\mu, \rho_4)$ defined in (3.109), there exists a constant C which is independent of ε and n such that*

$$|J_2^n(\mu, \rho_4(\mu))| \leq C(n^2 + 1), \quad \left| \frac{dJ_2^n(\mu, \rho_4(\mu))}{d\mu} \right| \leq C(n^2 + 1). \quad (3.112)$$

At this point, we are finally ready to prove our main result Theorem 3.1.

3.5 Proof of Theorem 3.1

Proof. Substituting (3.50) into (3.61), we obtain the Fréchet derivative of $\mathcal{F}(\tilde{R}, \mu)$ in \tilde{R} at the point $(0, \mu)$, namely,

$$[\mathcal{F}_{\tilde{R}}(0, \mu)] \cos(n\theta) = \left(\frac{\partial^2 p_*(1-\varepsilon)}{\partial r^2} + \frac{\partial p_1^n(1-\varepsilon)}{\partial r} \right) \cos(n\theta);$$

we then combine the above formula with (3.65) and (3.110) to derive

$$[\mathcal{F}_{\tilde{R}}(0, \mu)] \cos(n\theta) = \left(\frac{\varepsilon\mu}{\gamma + H_0} + \frac{n(1-n^2)[(1-\varepsilon)^{2n}-1]}{(1-\varepsilon)^3[(1-\varepsilon)^{2n}+1]} + \varepsilon^2(J_1 + J_2^n) \right) \cos(n\theta). \quad (3.113)$$

For a fixed nonnegative n ,

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

when ε is sufficiently small so that $n\varepsilon < 1$. In this case, the equation $[\mathcal{F}_{\tilde{R}}(0, \mu)] \cos(n\theta) = 0$ is satisfied if and only if

$$U(\mu, \varepsilon) \triangleq \frac{\mu}{\gamma + H_0} - n^2(1-n^2) + \varepsilon(J_1 + J_2^n) + O(n^5\varepsilon) = 0. \quad (3.114)$$

Notice that both J_1 and J_2^n contain μ , it is impossible to solve μ explicitly from equation (3.114). However, we are able to claim that for each n , (3.114) admits a unique solution when ε is small. To prove it, we first find that $U((\gamma + H_0)n^2(1-n^2), 0) = 0$; in addition, if we take partial μ derivative on both sides of (3.114) and evaluate the value at $(\mu, 0)$, we have

$$\frac{\partial}{\partial \mu} U(\mu, 0) = \left[\frac{1}{\gamma + H_0} + \varepsilon \left(\frac{dJ_1}{d\mu} + \frac{dJ_2^n}{d\mu} \right) \right] \Big|_{\varepsilon=0} = \frac{1}{\gamma + H_0} > 0.$$

Therefore, it follows from the implicit function theorem that, for each small ε , there exists a unique solution, which is close to $(\gamma + H_0)n^2(1 - n^2)$, such that equation (3.114) is satisfied; we denote the unique solution by μ_n . In what follows, we shall justify that $\mu = \mu_n$ with $n \geq 2$ and $\mu_n > \mu_c$ is a bifurcation point for the System (P) when ε is sufficiently small.

What we need to do is to verify the four assumptions of the Crandall-Rabinowitz theorem (Theorem B.1) at the point $\mu = \mu_n$. To begin with, the assumption (1) is naturally satisfied due to Theorem 3.3. To be more specific, for each $\mu_n > \mu_c$, we can find a small $\varepsilon^* > 0$, such that for $0 < \varepsilon < \varepsilon^*$, there exists a unique radially symmetric stationary solution, hence $\mathcal{F}(0, \mu_n) = 0$. Next let us proceed to verify the assumption (2) and (3) for a fixed $n \geq 2$. It suffices to show that for every m , $m \neq n$,

$$[\mathcal{F}_{\bar{R}}(0, \mu_n)] \cos(m\theta) \neq 0, \quad (3.115)$$

or equivalently,

$$W(m) \triangleq \frac{\varepsilon \mu_n}{\gamma + H_0} + \frac{m(m^2 - 1)[1 - (1 - \varepsilon)^{2m}]}{(1 - \varepsilon)^3[(1 - \varepsilon)^{2m} + 1]} + \varepsilon^2 \left(J_1(\mu_n, \rho_4) + J_2^m(\mu_n, \rho_4) \right) \neq 0, \quad (3.116)$$

To establish statement (3.115) (or statement (3.116)), we split the proof into three cases:

Case (i) $m > \max\{2n, m_0\}$ and $m\varepsilon \leq \frac{1}{2}$, where m_0 will be determined later. Using the inequality $m\varepsilon \leq \frac{1}{2}$, together with Lemma 3.7, we deduce that

$$(1 - \varepsilon)^{2m} \leq 1 - 2m\varepsilon + 2m^2\varepsilon^2 \leq 1 - 2m\varepsilon + m\varepsilon \leq 1 - m\varepsilon,$$

hence (recall that $n \geq 2$ so that $m > 4$ in this case)

$$\frac{m(m^2 - 1)[1 - (1 - \varepsilon)^{2m}]}{(1 - \varepsilon)^3[(1 - \varepsilon)^{2m} + 1]} \geq \frac{\varepsilon}{2} m^2 (m^2 - 1). \quad (3.117)$$

In addition, by Lemma 3.4 and Lemma 3.11, there exists a constant C which does not depend on ε and m such that,

$$|J_1 + J_2^m| \leq |J_1| + |J_2^m| \leq C(m^2 + 1). \quad (3.118)$$

Substituting (3.117) and (3.118) into (3.116), we derive

$$\begin{aligned} W(m) &\geq \frac{\varepsilon\mu_n}{\gamma + H_0} + \frac{\varepsilon}{2}m^2(m^2 - 1) - C\varepsilon^2(m^2 + 1) \\ &= \varepsilon \left[\frac{\mu_n}{\gamma + H_0} + \frac{1}{2}m^2(m^2 - 1) - C\varepsilon(m^2 + 1) \right]. \end{aligned}$$

It is clear that $W(m) > 0$ for large m as the leading order term in the brackets is $\frac{m^4}{2}$; hence we can find $m_0 > 0$ such that when $m > m_0$,

$$W(m) > 0.$$

Case (ii) $m > \max\{2n, m_0\}$ and $m\varepsilon > \frac{1}{2}$. In this case, we have

$$(1 - \varepsilon)^{2m} \leq \left(1 - \frac{1}{2m}\right)^{2m} \leq e^{-1},$$

and hence (since $m > \max\{2n, m_0\}$, we also have $m > 4$ in this case)

$$\frac{m(m^2 - 1)[1 - (1 - \varepsilon)^{2m}]}{(1 - \varepsilon)^3[(1 - \varepsilon)^{2m} + 1]} \geq \frac{1 - e^{-1}}{2}m(m^2 - 1).$$

Similar as in Case (i), we substitute the above inequality as well as (3.118) into (3.116), and derive

$$W(m) \geq \frac{\varepsilon\mu_n}{\gamma + H_0} + \frac{1 - e^{-1}}{2}m(m^2 - 1) - C\varepsilon^2(m^2 + 1);$$

notice that the leading order term is $\frac{1 - e^{-1}}{2}m^3$, we can easily find a bound for ε ,

denoted by E_1 , such that when $\varepsilon < E_1$,

$$W(m) \geq \frac{1 - e^{-1}}{4} m(m^2 - 1) > 0.$$

Case (iii) $0 \leq m \leq \max\{2n, m_0\}$. From our previous analysis, we know that μ_n is close to $(\gamma + H_0)n^2(1 - n^2)$. Since $\max\{2n, m_0\}$ is a finite number, we can choose ε small and similarly define all μ_m for $m \leq \max\{2n, m_0\}$ so that μ_m is close to $(\gamma + H_0)m^2(1 - m^2)$; in this case $W(m) \neq 0$ if and only if $\mu_n \neq \mu_m$. To be more specific, we have

$$\lim_{\varepsilon \rightarrow 0} \mu_n = (\gamma + H_0)n^2(1 - n^2), \quad \lim_{\varepsilon \rightarrow 0} \mu_m = (\gamma + H_0)m^2(1 - m^2).$$

Since $m \neq n$ and $n \geq 2$, it follows that

$$\begin{aligned} \lim_{\varepsilon \rightarrow 0} |\mu_n - \mu_m| &\geq \min\left\{\lim_{\varepsilon \rightarrow 0} |\mu_n - \mu_{n-1}|, \lim_{\varepsilon \rightarrow 0} |\mu_n - \mu_{n+1}|\right\} \\ &= (\gamma + H_0)(4n^3 - 6n^2 + 2n) \geq 12(\gamma + H_0). \end{aligned} \tag{3.119}$$

Recall again m is bounded in this case, we can find a bound for ε , denoted by E_2 , such that when $\varepsilon < E_2$,

$$\left| \mu_n - \lim_{\varepsilon \rightarrow 0} \mu_n \right| + \max_{0 \leq m \leq \max\{2n, m_0\}} \left| \mu_m - \lim_{\varepsilon \rightarrow 0} \mu_m \right| \leq 6(\gamma + H_0),$$

together with (3.119), we obtain

$$\left| \mu_n - \mu_m \right| \geq \left| \lim_{\varepsilon \rightarrow 0} \mu_n - \lim_{\varepsilon \rightarrow 0} \mu_m \right| - \left| \mu_n - \lim_{\varepsilon \rightarrow 0} \mu_n \right| - \left| \mu_m - \lim_{\varepsilon \rightarrow 0} \mu_m \right| \geq 6(\gamma + H_0) > 0.$$

By combining all three cases, the assumptions (2) and (3) in Theorem B.1 are

satisfied when ε is sufficiently small, i.e.,

$$\begin{aligned}\text{Ker } \mathcal{F}_{\tilde{R}}(0, \mu_n) &= \text{span}\{\cos(n\theta)\}, \\ Y_1 &= \text{span}\{1, \cos(\theta), \dots, \cos((n-1)\theta), \cos((n+1)\theta), \dots\}, \\ \text{and } Y_1 \oplus \text{Ker } \mathcal{F}_{\tilde{R}}(0, \mu_n) &= X_1^{l+\alpha},\end{aligned}$$

such that the spaces listed here (codimension space, non-tangential space) meet the requirements of the Crandall-Rabinowitz Theorem. To finish the whole proof, it remains to show the last assumption. Differentiating (3.113) in μ , we derive

$$\begin{aligned}[\mathcal{F}_{\mu\tilde{R}}(0, \mu)] \cos(n\theta) &= \left(\frac{\varepsilon}{\gamma + H_0} + \varepsilon^2 \left(\frac{dJ_1}{d\mu} + \frac{dJ_2^n}{d\mu} \right) \right) \cos(n\theta) \\ &= \varepsilon \left(\frac{1}{\gamma + H_0} + \varepsilon \left(\frac{dJ_1}{d\mu} + \frac{dJ_2^n}{d\mu} \right) \right) \cos(n\theta).\end{aligned}\tag{3.120}$$

By Lemma 3.4 and Lemma 3.11, there exists a constant C independent of ε and n such that

$$\left| \frac{dJ_1}{d\mu} + \frac{dJ_2^n}{d\mu} \right| \leq \left| \frac{dJ_1}{d\mu} \right| + \left| \frac{dJ_2^n}{d\mu} \right| \leq C(n^2 + 1).\tag{3.121}$$

Based on (3.121), we can find a bound E_3 (depending on n), such that when $\varepsilon < E_3$,

$$\frac{1}{\gamma + H_0} + \varepsilon \left(\frac{dJ_1}{d\mu} + \frac{dJ_2^n}{d\mu} \right) > \frac{1}{\gamma + H_0} - CE_3(n^2 + 1) > 0,$$

and hence $[\mathcal{F}_{\mu\tilde{R}}(0, \mu)] \cos(n\theta) \notin Y_1$, i.e., the assumption (4) is satisfied.

Combining all pieces together, we take $E = \min\{\varepsilon^*, E_1, E_2, E_3\}$, then we know that all the assumptions of the Crandall-Rabinowitz theorem are satisfied when $\varepsilon \in (0, E)$. Hence we conclude that $\mu = \mu_n$ with $n \geq 2$ is a symmetry-breaking bifurcation point. \square

3.6 Proof of Theorem 3.2

Notice that in the last section, we derived an approximation of the bifurcation points μ_n as

$$\mu_n = (\gamma + H_0)n^2(1 - n^2) + O(n^5\varepsilon). \quad (3.122)$$

It is clear that when $n = 0, 1$, the first term in the above equation is 0, hence $\mu_0 = \mu_1 = O(\varepsilon)$. To prove the first bifurcation point μ_1 , the key is to show $\mu_0 \neq \mu_1$, which requires higher order approximations for μ_0 and μ_1 . With this aim, we introduce the following lemmas (note that we only consider the cases $n = 0$ and 1):

Lemma 3.12. *If in addition to (3.78), we further assume the boundary condition*

$$-\psi'(1 - \varepsilon) + \beta\psi(1 - \varepsilon) = G, \quad (3.123)$$

then the coefficients A and B in (3.79) can be explicitly computed as: for $n = 1$

$$A = \frac{1}{-1 + \frac{1}{(1-\varepsilon)^2} + \beta(1 - \varepsilon) + \frac{\beta}{1-\varepsilon}} \left[G + \psi'_1(1 - \varepsilon) - \beta\psi_1(1 - \varepsilon) - \beta K[f](1 - \varepsilon) + K[f]'(1 - \varepsilon) - \frac{1}{(1-\varepsilon)^2} K[f]'(1) - \frac{\beta}{1-\varepsilon} K[f]'(1) \right], \quad (3.124)$$

$$B = A + K[f]'(1); \quad (3.125)$$

and for $n = 0$,

$$A = \frac{1}{\beta} \left[G + \psi'_1(1 - \varepsilon) - \beta\psi_1(1 - \varepsilon) - \beta K[f](1 - \varepsilon) + K[f]'(1 - \varepsilon) \right]. \quad (3.126)$$

Lemma 3.13. *If $f(r) = O(\varepsilon)$ in (3.78), and the assumptions in Lemma 3.12 hold, then for $1 - \varepsilon \leq r \leq 1$,*

$$\psi(r) = \frac{G}{\beta} + \varepsilon \left(\frac{\eta}{\beta} - \frac{G}{\beta^2} \right) + O(\varepsilon^2) \quad n = 1, \quad (3.127)$$

$$\psi(r) = \frac{G}{\beta} + \varepsilon \frac{\eta}{\beta} + O(\varepsilon^2) \quad n = 0. \quad (3.128)$$

Proof. Based on Lemma 3.5, if $f(r) = O(\varepsilon)$ in (3.78), we have in either $n = 0$ or $n = 1$ case,

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

Substituting into (3.124) — (3.126), recalling also (3.86) and (3.87), we obtain, for $n = 1$

$$\begin{aligned} A &= \frac{G + \varepsilon\eta + O(\varepsilon^2)}{2(\beta + \varepsilon) + O(\varepsilon^2)} = \frac{G}{2\beta} + \varepsilon\left(\frac{\eta}{2\beta} - \frac{G}{2\beta^2}\right) + O(\varepsilon^2), \\ B &= A + K[f]'(1) = \frac{G}{2\beta} + \varepsilon\left(\frac{\eta}{2\beta} - \frac{G}{2\beta^2}\right) + O(\varepsilon^2); \end{aligned}$$

and for $n = 0$,

$$A = \frac{G + \varepsilon\eta + O(\varepsilon^2)}{\beta} = \frac{G}{\beta} + \varepsilon\frac{\eta}{\beta} + O(\varepsilon^2).$$

We further substitute the above coefficients into (3.79) to derive, for $1 - \varepsilon \leq r \leq 1$,

$$\begin{aligned} \psi(r) &= Ar + B\frac{1}{r} + O(\varepsilon^2) = A + B + O(\varepsilon^2) = \frac{G}{\beta} + \varepsilon\left(\frac{\eta}{\beta} - \frac{G}{\beta^2}\right) + O(\varepsilon^2) \quad n = 1, \\ \psi(r) &= A + O(\varepsilon^2) = \frac{G}{\beta} + \varepsilon\frac{\eta}{\beta} + O(\varepsilon^2) \quad n = 0. \end{aligned}$$

This completes the proof. □

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 $\varepsilon\frac{G}{\beta^2}$, which is determined only by G and β .

Lemma 3.5, together with Lemmas 3.12 and 3.13, are 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 (3.123), we hence need the following lemmas that can be easily verified:

Lemma 3.14. *If in addition to (3.78), we further assume the boundary condition for ψ as*

$$\psi(1 - \varepsilon) = \frac{1 - n^2}{(1 - \varepsilon)^2}, \quad (3.129)$$

then the coefficients A and B in (3.79) is solved as

$$\begin{aligned} A &= \frac{-\psi_1(1 - \varepsilon) - K[f](1 - \varepsilon) - \frac{1}{1 - \varepsilon}K[f]'(1)}{1 - \varepsilon + \frac{1}{1 - \varepsilon}}, \quad B = A + K[f]'(1) & n = 1, \\ A &= -\psi_1(1 - \varepsilon) - K[f](1 - \varepsilon) & n = 0. \end{aligned}$$

Lemma 3.15. *If $f(r) = O(\varepsilon^2)$ in (3.78), and the assumptions in Lemma 3.14 hold, then for $n = 0$ and 1 , and $1 - \varepsilon \leq r \leq 1$,*

$$\psi'(1 - \varepsilon) = \varepsilon\eta + \varepsilon^2\frac{\eta}{2} + O(\varepsilon^3). \quad (3.130)$$

Proof. If $f = O(\varepsilon^2)$ in (3.78), by Lemma 3.5 we have

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

In order to estimate $\psi'(1 - \varepsilon)$, we differentiate (3.79) and evaluate the derivative at $r = 1 - \varepsilon$,

$$\begin{aligned} \psi'(1 - \varepsilon) &= \psi'_1(1 - \varepsilon) + A - \frac{B}{(1 - \varepsilon)^2} + K[f]'(1 - \varepsilon) & n = 1, \\ \psi'(1 - \varepsilon) &= \psi'_1(1 - \varepsilon) + K[f]'(1 - \varepsilon) & n = 0. \end{aligned}$$

Combining with the expression of A and B in Lemma 3.14, recalling also (3.86) — (3.87), we further derive $A = O(\varepsilon^2)$, $B = O(\varepsilon^2)$, and in both cases,

$$\psi'(1 - \varepsilon) = \varepsilon\eta + \varepsilon^2\frac{\eta}{2} + O(\varepsilon^3) \quad n = 0, 1,$$

which completes the proof. □

With the above lemmas, we are able to derive more sophisticated estimates. To get more information about the higher order ε terms for L_1^n , H_1^n , and F_1^n , we denote

$$L_1^n = \frac{\mu}{\lambda} - L_*^1 + \varepsilon L_{11}^n + O(\varepsilon^2), \quad (3.131)$$

$$H_1^n = -H_*^1 + \varepsilon H_{11}^n + O(\varepsilon^2), \quad (3.132)$$

$$F_1^n = -F_*^1 + \varepsilon F_{11}^n + O(\varepsilon^2). \quad (3.133)$$

Notice that the $O(1)$ terms are based on the estimates (3.103) — (3.105). Next we proceed to estimate L_{11}^n , H_{11}^n and F_{11}^n based on Lemmas 3.5, 3.12 and 3.13.

Recall first the equations for L_1^n , H_1^n , and F_1^n in (3.51) — (3.59). For the right-hand sides of (3.51) — (3.53), we can write them as the form $\eta + O(\varepsilon)$, and we shall claim that η is independent of n . In fact, we notice that the $O(1)$ terms of $L_1^n(r)$, $H_1^n(r)$, and $F_1^n(r)$ in (3.131) — (3.133) are constants, and are independent of n . Moreover, it has been proved before that $\frac{\partial F_*}{\partial r}, \frac{\partial p_*}{\partial r} = O(\varepsilon)$, and $\frac{\partial p_1^n}{\partial r}, \frac{\partial F_1^n}{\partial r}$ are both bounded. Hence the extra two terms in (3.53), $\frac{\partial F_*}{\partial r} \frac{\partial p_1^n}{\partial r}$ and $\frac{\partial F_1^n}{\partial r} \frac{\partial p_*}{\partial r}$, do not affect the $O(1)$ term η .

Using Lemma 3.13, we find that the difference between $L_1^1(r)$ and $L_1^0(r)$ starts from $O(\varepsilon)$ terms. As a matter of fact, by (3.127), (3.128), and (3.100),

$$L_1^1 - L_1^0 = -\frac{\varepsilon}{\beta_1^2} \left(\frac{\partial^2 L_*}{\partial r^2} - \beta_1 \frac{\partial L_*}{\partial r} \right) \Big|_{r=1-\varepsilon} + O(\varepsilon^2) = \frac{\varepsilon}{\beta_1} \left(L_*^1 - \frac{\mu}{\lambda} \right) + O(\varepsilon^2).$$

From (3.131), $L_1^1 = \frac{\mu}{\lambda} - L_*^1 + \varepsilon L_{11}^1 + O(\varepsilon^2)$, and $L_1^0 = \frac{\mu}{\lambda} - L_*^1 + \varepsilon L_{11}^0 + O(\varepsilon^2)$; combining with the above equation, we further have

$$L_{11}^1 - L_{11}^0 = \frac{1}{\beta_1} \left(L_*^1 - \frac{\mu}{\lambda} \right). \quad (3.134)$$

Similarly, we can derive

$$H_{11}^1 - H_{11}^0 = \frac{1}{\beta_1} H_*^1, \quad (3.135)$$

$$F_{11}^1 - F_{11}^0 = \frac{1}{\beta_2} F_*^1. \quad (3.136)$$

Next we consider the equation for p_1^n from (3.54) and (3.59). Recall from (3.60) that the right-hand side of the equation for p_1^n is

$$f_8(L_1^n, H_1^n, F_1^n) = \frac{1}{M_0} \left[\lambda \frac{(M_0 - F_*)L_1^n}{\gamma + H_*} - \lambda \frac{L_* F_1^n}{\gamma + H_*} - \lambda \frac{(M_0 - F_*)L_* H_1^n}{(\gamma + H_*)^2} + (\rho_3 - \rho_4)F_1^n \right].$$

In order to apply Lemmas 3.5, 3.14 and 3.15, we shall rewrite f_8 in the form $f_8 = \eta + f(r)$, where $f(r) = O(\varepsilon^2)$. More specifically, we denote,

$$f_8(L_1^n, H_1^n, F_1^n) = \eta_n + O(\varepsilon^2),$$

and we now proceed a long and tedious journal to compute $\eta_n = \eta_n(\varepsilon)$. Substituting (3.26) — (3.28) and (3.131) — (3.133) all into f_8 , we have

$$\begin{aligned} M_0 f_8 &= \lambda \frac{(M_0 - \varepsilon F_*^1)(\frac{\mu}{\lambda} - L_*^1 + \varepsilon L_{11}^n)}{\gamma + H_0 + \varepsilon H_*^1} - \lambda \frac{(\frac{\rho_3(\gamma + H_0)}{\lambda} + \varepsilon L_*^1)(-F_*^1 + \varepsilon F_{11}^n)}{\gamma + H_0 + \varepsilon H_*^1} + (\rho_3 \\ &\quad - \rho_4)(-F_*^1 + \varepsilon F_{11}^n) - \lambda \frac{(M_0 - \varepsilon F_*^1)(\frac{\rho_3(\gamma + H_0)}{\lambda} + \varepsilon L_*^1)(-H_*^1 + \varepsilon H_{11}^n)}{(\gamma + H_0 + \varepsilon H_*^1)^2} + O(\varepsilon^2) \\ &= \left(\frac{M_0(\mu - \lambda L_*^1)}{\gamma + H_0} + \frac{(-\varepsilon F_*^1)(\mu - \lambda L_*^1)}{\gamma + H_0} + \frac{\lambda M_0 \varepsilon L_{11}^n}{\gamma + H_0} - \frac{M_0(\mu - \lambda L_*^1) \varepsilon H_*^1}{(\gamma + H_0)^2} \right) \\ &\quad - \left(-\rho_3 F_*^1 - \frac{\lambda \varepsilon L_*^1 F_*^1}{\gamma + H_0} + \rho_3 \varepsilon F_{11}^n + \frac{\rho_3 F_*^1 \varepsilon H_*^1}{\gamma + H_0} \right) + (\rho_3 - \rho_4)(-F_*^1 + \varepsilon F_{11}^n) \\ &\quad - \left(-\frac{M_0 \rho_3 H_*^1}{\gamma + H_0} + \frac{\varepsilon F_*^1 \rho_3 H_*^1}{\gamma + H_0} - \frac{\lambda M_0 \varepsilon L_*^1 H_*^1}{(\gamma + H_0)^2} + \frac{M_0 \rho_3 \varepsilon H_{11}^n}{\gamma + H_0} + \frac{2M_0 \rho_3 H_*^1 \varepsilon H_*^1}{(\gamma + H_0)^2} \right) \\ &\quad + O(\varepsilon^2) \\ &= \left(\frac{M_0 \mu}{\gamma + H_0} - \frac{M_0(\lambda L_*^1 - \rho_3 H_*^1)}{\gamma + H_0} + \rho_4 F_*^1 \right) + \varepsilon \left(-\frac{F_*^1 \mu}{\gamma + H_0} - \frac{M_0 H_*^1 \mu}{(\gamma + H_0)^2} \right) \end{aligned}$$

$$\begin{aligned}
& + 2 \frac{\lambda L_*^1 F_*^1}{\gamma + H_0} + 2 \frac{\lambda M_0 L_*^1 H_*^1}{(\gamma + H_0)^2} - 2 \frac{\rho_3 F_*^1 H_*^1}{\gamma + H_0} - 2 \frac{M_0 \rho_3 (H_*^1)^2}{(\gamma + H_0)^2} \Big) + \varepsilon \Big(\frac{\lambda M_0 L_{11}^n}{\gamma + H_0} \\
& - \frac{M_0 \rho_3 H_{11}^n}{\gamma + H_0} - \rho_4 F_{11}^n \Big) + O(\varepsilon^2),
\end{aligned}$$

hence

$$\begin{aligned}
\eta_n = & \frac{1}{M_0} \Big[\Big(\frac{M_0 \mu}{\gamma + H_0} - \frac{M_0 (\lambda L_*^1 - \rho_3 H_*^1)}{\gamma + H_0} + \rho_4 F_*^1 \Big) + \varepsilon \Big(- \frac{F_*^1 \mu}{\gamma + H_0} - \frac{M_0 H_*^1 \mu}{(\gamma + H_0)^2} \\
& + 2 \frac{\lambda L_*^1 F_*^1}{\gamma + H_0} + 2 \frac{\lambda M_0 L_*^1 H_*^1}{(\gamma + H_0)^2} - 2 \frac{\rho_3 F_*^1 H_*^1}{\gamma + H_0} - 2 \frac{M_0 \rho_3 (H_*^1)^2}{(\gamma + H_0)^2} \Big) \Big] + \frac{\varepsilon}{M_0} \Big(\frac{\lambda M_0 L_{11}^n}{\gamma + H_0} \\
& - \frac{M_0 \rho_3 H_{11}^n}{\gamma + H_0} - \rho_4 F_{11}^n \Big).
\end{aligned} \tag{3.137}$$

We notice that all the terms in the first bracket [...] of (3.137) are independent of n , hence if we calculate $\eta_1 - \eta_0$, these terms are cancelled out. As a result,

$$\eta_1 - \eta_0 = \frac{\varepsilon}{M_0} \Big[\frac{\lambda M_0}{\gamma + H_0} (L_{11}^1 - L_{11}^0) - \frac{M_0 \rho_3}{\gamma + H_0} (H_{11}^1 - H_{11}^0) - \rho_4 (F_{11}^1 - F_{11}^0) \Big]. \tag{3.138}$$

In addition, by Lemma 3.15, we immediately have

$$\frac{\partial p_1^n (1 - \varepsilon)}{\partial r} = \varepsilon \eta_n + \varepsilon^2 \frac{\eta_n}{2} + O(\varepsilon^3). \tag{3.139}$$

Now we are ready to prove the first bifurcation point, Theorem 3.2.

Proof of Theorem 3.2. What we need to do is to verify the four assumptions of the Crandall-Rabinowitz Theorem (Theorem B.1) at the point $\mu = \mu_1$. Since assumptions (1) and (4) are clearly satisfied at $\mu = \mu_1$ due to Section 3.5, it suffices to show assumptions (2) and (3), and the key step is to prove the statement

$$[F_{\tilde{R}}(0, \mu_1)] \cos n\theta \neq 0, \quad \text{for } \forall n \neq 1. \tag{3.140}$$

From Section 3.5, it has been established that there exists a bound $E_2 > 0$, when $0 < \varepsilon < E_2$, we have (3.140) to be true for each $n \geq 2$. Hence it remains to show

$$[F_{\tilde{R}}(0, \mu_1)]1 \neq 0, \quad i.e., \quad \mu_0 \neq \mu_1, \quad (3.141)$$

and we shall prove it by contradiction.

Recall that μ_n is the solution to the equation

$$\frac{\partial^2 p_*(1 - \varepsilon)}{\partial r^2} + \frac{\partial p_1^n(1 - \varepsilon)}{\partial r} = 0.$$

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

$$\frac{\partial p_1^1(1 - \varepsilon)}{\partial r} - \frac{\partial p_1^0(1 - \varepsilon)}{\partial r} = 0. \quad (3.142)$$

On the other hand, it follows from (3.139) and (3.138) that

$$\begin{aligned} & \frac{\partial p_1^1(1 - \varepsilon)}{\partial r} - \frac{\partial p_1^0(1 - \varepsilon)}{\partial r} \\ &= \varepsilon(\eta_1 - \eta_0) + \frac{\varepsilon^2}{2}(\eta_1 - \eta_0) + O(\varepsilon^3) \\ &= \frac{\varepsilon^2}{M_0} \left[\frac{\lambda M_0}{\gamma + H_0} (L_{11}^1 - L_{11}^0) - \frac{\rho_3 M_0}{\gamma + H_0} (H_{11}^1 - H_{11}^0) - \rho_4 (F_{11}^1 - F_{11}^0) \right] + O(\varepsilon^3). \end{aligned}$$

Substituting into the estimates for $L_{11}^1 - L_{11}^0$, $H_{11}^1 - H_{11}^0$, and $F_{11}^1 - F_{11}^0$ in (3.134) — (3.136), recalling also (3.33) and the fact that $\mu_0, \mu_1 = O(\varepsilon)$ by (3.122), we further have

$$\begin{aligned} \frac{\partial p_1^1(1 - \varepsilon)}{\partial r} - \frac{\partial p_1^0(1 - \varepsilon)}{\partial r} &= \varepsilon^2 \left[\frac{\lambda}{\gamma + H_0} \frac{1}{\beta_1} (L_*^1 - \frac{\mu_0}{\lambda}) - \frac{\rho_3}{\gamma + H_0} \frac{H_*^1}{\beta_1} - \frac{\rho_4}{M_0} \frac{F_*^1}{\beta_2} \right] + O(\varepsilon^3) \\ &= \varepsilon^2 \left[\frac{1}{\beta_1} \frac{\lambda L_*^1 - \rho_3 H_*^1}{\gamma + H_0} - \frac{1}{\beta_2} \frac{\rho_4 F_*^1}{M_0} - \frac{\mu_0}{\beta_1(\gamma + H_0)} \right] + O(\varepsilon^3) \\ &= \varepsilon^2 \left(\frac{1}{\beta_1} - \frac{1}{\beta_2} \right) \frac{\rho_4 F_*^1}{M_0} + O(\varepsilon^3). \end{aligned}$$

We have assumed that $\beta_1 \neq \beta_2$. Since the sign of $\frac{\partial p_1^1(1-\varepsilon)}{\partial r} - \frac{\partial p_1^0(1-\varepsilon)}{\partial r}$ is dominated by $\left(\frac{1}{\beta_1} - \frac{1}{\beta_2}\right) \frac{\rho_4 F_*^1}{M_0}$, we can easily find $E_2 > 0$, such that when $0 < \varepsilon < E_2$,

$$\frac{\partial p_1^1(1-\varepsilon)}{\partial r} - \frac{\partial p_1^0(1-\varepsilon)}{\partial r} \neq 0,$$

which contradicts with the statement (3.142). Hence we have $\mu_1 \neq \mu_0$ when $\varepsilon < E_2$.

By taking $E = \min\{E_1, E_2\}$, we finish showing (3.140). With (3.140), we now have

$$\text{Ker } \mathcal{F}_{\tilde{R}}(0, \mu_1) = \text{span}\{\cos(\theta)\},$$

$$Y_1 = \text{Im } \mathcal{F}_{\tilde{R}}(0, \mu_1) = \text{span}\{1, \cos(2\theta), \cos(3\theta), \dots, \cos(n\theta), \dots\},$$

$$Y_1 \oplus \text{Ker } \mathcal{F}_{\tilde{R}}(0, \mu_1) = Y,$$

$$[\mathcal{F}_{\mu\tilde{R}}(0, \mu_1)] \cos \theta \in \text{span}\{\cos(\theta)\}, \text{ and hence } [\mathcal{F}_{\mu\tilde{R}}(0, \mu_1)] \cos(\theta) \notin Y_1.$$

In other words, all the spaces (kernel space, codimension space, non-tangential space) meet the requirements of the Crandall-Rabinowitz Theorem, and all the assumptions in the Crandall-Rabinowitz Theorem are satisfied. Therefore, $\mu = \mu_1$ is a bifurcation point for the system (3.1) — (3.13). \square

3.7 Biological implications

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 when $n = 1$. As some arterial plaque is often accumulated more on one side of the artery in real life, which resembles the pattern corresponding to the $n = 1$ bifurcation solutions. The bifurcation results can help to understand this phenomenon.

CHAPTER 4

SOLVING A FREE BOUNDARY SYSTEM BY USING MACHINE LEARNING

Due to the existing theories and tools, theoretical analysis for free boundary problems is often limited to local solution structures. In fact, most theoretical studies [44, 45, 111–114] are based on and carried out in a small neighborhood of the radially symmetric solutions. In order to obtain the global solution structure, we need numerical methods to compute approximations of solutions.

Recently, there are several numerical methods developed for studying free boundary problems, e.g., computing multiple steady-states by coupling multi-grid and domain decomposition techniques with numerical algebraic geometry [62, 63, 67, 100]; detecting bifurcation points by using the adaptive homotopy tracking method [61, 64, 68]; and exploring global solution structures based on computations and PDE theories [61, 63, 65]. These numerical methods have also been successfully applied to some complex biological models including tumor growth model and cardiovascular disease risk evaluation [58, 60]. However, to the date, there are still several numerical challenges for solving free boundary problems:

- 1) there is lack of rigorous theoretical analysis of numerical methods for free boundary problems;
- 2) and steady-state solution patterns are hard to compute so that the global solution structure is unclear.

Therefore, efficient numerical methods, rigorous theoretical analysis of these numerical methods and global solution structures are needed to deeply study free boundary problems.

Since the late 2000s, machine learning techniques have been experiencing an extraordinary resurgence in many important artificial intelligence applications . In particular, it has been able to produce state-of-the-art accuracy in computer vision [93], video analysis [14], natural language processing [75] and speech recognition [4]. Recently, interests in machine-learning-based approaches in the applied mathematics community have increased rapidly [10, 91]. This growing enthusiasm for machine learning stems from massive amounts of data available from scientific computations [28] and other sources [29]; the design of efficient data analysis algorithms [109]; advances in high-performance computing; and the data-driven modeling [81]. In order to take advantage of machine learning, we will develop a new approach for solving free boundary problems and address the current challenges in this area; in particular, we will consider a Hele-Shaw model with surface tension term in the following discussion.

4.1 The model problem and bifurcation results

The classical Hele-Shaw problem seeks a fluid domain $\Omega(t) \in \mathbb{R}^2$ and the fluid pressure σ such that

$$\begin{cases} \Delta\sigma = 0 & \text{in } \Omega(t), \\ \sigma = \kappa & \text{on } \partial\Omega(t), \\ V_n = -\frac{\partial\sigma}{\partial\mathbf{n}} & \text{on } \partial\Omega(t), \end{cases} \quad (4.1)$$

where κ denotes the curvature of $\partial\Omega(t)$ ($\kappa = \frac{1}{R}$ if $\partial\Omega(t)$ is a circle of radius $R > 0$); V_n is the velocity of the fluid boundary $\partial\Omega(t)$ in the outward normal direction \mathbf{n} ; and $\frac{\partial\sigma}{\partial\mathbf{n}} = \nabla\sigma \cdot \mathbf{n}$ is the directional derivative of σ along the outer normal direction \mathbf{n} .

It is well-known that model (4.1) possesses only radially symmetric stationary solution. In order to investigate the complexity of free boundaries, we introduce a

modified Hele-Shaw model as below:

$$\begin{cases} -\Delta\sigma = c(-\sigma - \mu) & \text{in } \Omega(t), \\ \sigma = \kappa & \text{on } \partial\Omega(t), \\ V_n = -\frac{\partial\sigma}{\partial\mathbf{n}} + \beta & \text{on } \partial\Omega(t), \end{cases} \quad (4.2)$$

where c, μ, β are positive constants. The first equation on the right-hand side of (4.2) represents a sink of fluid, while the additional constant β represents the influx of fluid in addition to the balance of mass. When $c = \beta = 0$, (4.2) reverts to the classical Hele-Shaw problem. By introducing the non-dimensional length scale $L_D = \sqrt{c}$, we define:

$$\tilde{\mathbf{x}} = L_D \mathbf{x}, \quad \tilde{\sigma}(\tilde{\mathbf{x}}) = \sigma(\mathbf{x}) + \mu, \quad \tilde{\Omega}(t) = L_D \Omega(t), \quad \tilde{\beta} = \frac{\beta}{L_D}.$$

After dropping the \sim in the above variables, the dimensionless model takes the following form

$$\begin{cases} -\Delta\sigma = -\sigma & \text{in } \Omega(t), \\ \sigma = \mu + \kappa & \text{on } \partial\Omega(t), \\ V_n = -\frac{\partial\sigma}{\partial\mathbf{n}} + \beta & \text{on } \partial\Omega(t). \end{cases} \quad (4.3)$$

We consider the steady state system of (4.3) by setting $V_n = 0$ and obtain the following stationary system:

$$\begin{cases} -\Delta\sigma = -\sigma & \text{in } \Omega, \\ \sigma = \mu + \kappa & \text{on } \partial\Omega, \\ \frac{\partial\sigma}{\partial\mathbf{n}} = \beta & \text{on } \partial\Omega. \end{cases} \quad (4.4)$$

Theoretically, system (4.4) admits a unique radially symmetric solution $\sigma_S(r)$ with radius $r = R_S$:

$$\sigma_S(r) = \left(\mu + \frac{1}{R_S} \right) \frac{I_0(r)}{I_0(R_S)}, \quad (4.5)$$

provided that $\beta = \beta(\mu, R_S)$ is given by

$$\beta = \left(\mu + \frac{1}{R_S} \right) \frac{I_1(R_S)}{I_0(R_S)}. \quad (4.6)$$

Here $I_n(r)$ is the modified Bessel function for integer $n \geq 0$.

We are more interested in finding the non-radially symmetric solutions of system (4.4). Particularly, we would like to know what the boundaries look like in non-radially symmetric case. By applying similar techniques from the above chapters and using the Crandall-Rabinowitz Theorem (Theorem B.1 in Appendix B), we can establish the following theorem for the bifurcation solutions of system (4.4). The detailed proof of Theorem 4.1 can be found in [110].

Theorem 4.1. *For each even $n \geq 2$,*

$$\mu = \mu_n(R_S) \triangleq -\frac{1}{R_S} + \frac{I_0(R_S)}{R_S^2 I_1(R_S)} \cdot \frac{I'_n(R_S)}{I_n(R_S)} \Big/ \left[\frac{1}{n^2 - 1} \left(\frac{I'_n(R_S)}{I_n(R_S)} - \frac{I'_1(R_S)}{I_1(R_S)} \right) \right], \quad (4.7)$$

is a bifurcation point of the symmetry-breaking solution to the system (4.4) with free boundary

$$r = R_S + \varepsilon \cos(n\theta) + o(\varepsilon), \quad \mu = \mu(\varepsilon) = \mu_n(R_S) + o(1). \quad (4.8)$$

In equation (4.7), $I_n(r)$ denotes the modified Bessel function of integer n .

Remark 4.1. *The bifurcation result is actually valid for all $n \geq 2$ not restricting to even n only, however the proof is much more complicated.*

In the next section, we will propose a new method, which is a combination of boundary integral method (BIM) and machine learning approximation, to numerically derive the shapes of the boundaries of system (4.4) and compare with theoretical results.

4.2 The numerical method based on the neural network discretization

4.2.1 Boundary integral formulation

Using the boundary integral formulation [5, 22, 89, 90], we apply the standard representation formula [36] on system (4.4) to obtain

$$\sigma(\mathbf{x}) = \int_{\partial\Omega} \left[G_1(\mathbf{x}, \mathbf{y}) \frac{\partial \sigma(\mathbf{y})}{\partial \mathbf{n}_y} - \sigma(\mathbf{y}) \frac{\partial G_1(\mathbf{x}, \mathbf{y})}{\partial \mathbf{n}_y} \right] dS_y \quad \text{for } \mathbf{x} \in \Omega, \quad (4.9)$$

where G_1 is the Green function for the operator $-\Delta + 1$, namely, $G_1(\mathbf{x}, \mathbf{y}) = G_1(|\mathbf{x} - \mathbf{y}|) = \frac{i}{4} H_0^{(1)}(i|\mathbf{x} - \mathbf{y}|)$ for two dimensional case, and $H_0^{(1)}$ is a Hankel function. By using the “jump” relationship [77] as $\mathbf{x} \rightarrow \partial\Omega$, we derive

$$\frac{\sigma(\mathbf{x})}{2} = \int_{\partial\Omega} \left[G_1(\mathbf{x}, \mathbf{y}) \frac{\partial \sigma(\mathbf{y})}{\partial \mathbf{n}_y} - \sigma(\mathbf{y}) \frac{\partial G_1(\mathbf{x}, \mathbf{y})}{\partial \mathbf{n}_y} \right] dS_y \quad \text{for } \mathbf{x} \in \partial\Omega. \quad (4.10)$$

Combining with the boundary conditions in (4.4), we further obtain

$$\frac{\mu + \kappa(\mathbf{x})}{2} = \int_{\partial\Omega} \left[\beta G_1(\mathbf{x}, \mathbf{y}) - (\mu + \kappa(\mathbf{y})) \frac{\partial G_1(\mathbf{x}, \mathbf{y})}{\partial \mathbf{n}_y} \right] dS_y \quad \text{for } \mathbf{x} \in \partial\Omega. \quad (4.11)$$

Since the function $G_1(r)$ and $G_1'(r)$ are singular at $r = 0$, we introduce a new function $Q(r)$ defined as

$$Q(r) = \frac{1}{r} \left(G_1'(r) + \frac{1}{2\pi r} \right). \quad (4.12)$$

Then $Q(r) = O(|\ln r|)$, $Q'(r) = O(r^{-1})$, $Q''(r) = O(r^{-2})$ (see [66]). As in [66], if we replace G_1 in (4.10) by the fundamental solution for $-\Delta$ (which equals to $-\frac{1}{2\pi} \ln |\mathbf{x} - \mathbf{y}|$), and take $\sigma = 1$, we have, for $x \in \partial\Omega$,

$$\frac{1}{2} = - \int_{\partial\Omega} \frac{\partial}{\partial \mathbf{n}_y} \left(-\frac{1}{2\pi} \ln |\mathbf{x} - \mathbf{y}| \right) dS_y = \frac{1}{2\pi} \int_{\partial\Omega} \frac{\mathbf{y} - \mathbf{x}}{|\mathbf{x} - \mathbf{y}|^2} \cdot \mathbf{n}_y dS_y, \quad (4.13)$$

hence

$$\frac{\mu + \kappa(\mathbf{x})}{2} = \frac{1}{2\pi} \int_{\partial\Omega} (\mu + \kappa(\mathbf{x})) \frac{\mathbf{y} - \mathbf{x}}{|\mathbf{x} - \mathbf{y}|^2} \cdot \mathbf{n}_y dS_y. \quad (4.14)$$

Using (4.12), (4.13), as well as (4.14), we can rewrite (4.11) as

$$\int_{\partial\Omega} \left[\beta G_1(\mathbf{x}, \mathbf{y}) - \left((\mu + \kappa(\mathbf{y})) Q(|\mathbf{x} - \mathbf{y}|) - \frac{\kappa(\mathbf{y}) - \kappa(\mathbf{x})}{2\pi|\mathbf{x} - \mathbf{y}|^2} \right) (\mathbf{y} - \mathbf{x}) \cdot \mathbf{n}_y \right] dS_y = 0, \quad (4.15)$$

for $\forall x \in \partial\Omega$. Notice that the boundary $\partial\Omega$ is the only unknown in the equation.

Equation (4.15) determines the free boundary $\partial\Omega$. Due to the highly non-linear nature of (4.15), there might be multiple solutions of $\partial\Omega$, and these solutions are expected to be computed by the machine learning techniques.

4.2.2 The neural network discretization

We use $\partial\Omega : r = R(\theta)$, $\theta \in (-\infty, \infty)$ to represent the unknown boundary. Clearly, it satisfies the 2π -periodic boundary condition, namely,

$$R(\theta) = R(\theta + 2\pi). \quad (4.16)$$

For simplicity, we shall restrict θ to $[0, 2\pi]$. By denoting in the polar coordinates $\mathbf{x} = (R(\hat{\theta}) \cos(\hat{\theta}), R(\hat{\theta}) \sin(\hat{\theta}))$ and $\mathbf{y} = (R(\theta) \cos(\theta), R(\theta) \sin(\theta))$, we have

$$\begin{aligned} |\mathbf{x} - \mathbf{y}| &= \sqrt{[R(\hat{\theta}) \cos(\hat{\theta}) - R(\theta) \cos(\theta)]^2 + [R(\hat{\theta}) \sin(\hat{\theta}) - R(\theta) \sin(\theta)]^2} \\ &= \sqrt{R^2(\hat{\theta}) + R^2(\theta) - 2R(\hat{\theta})R(\theta) \cos(\hat{\theta} - \theta)} \\ &\triangleq D[R]. \end{aligned}$$

In addition,

$$\mathbf{n}_y = \frac{\left(R'(\theta) \sin(\theta) + R(\theta) \cos(\theta), -R'(\theta) \cos(\theta) + R(\theta) \sin(\theta) \right)}{\sqrt{[R'(\theta)]^2 + R^2(\theta)}},$$

$$dS_y = \sqrt{[R'(\theta)]^2 + R^2(\theta)} d\theta.$$

Using the mean-curvature formula in the 2-dimensional case for $r = R(\theta)$, we also have

$$\kappa_R = \frac{R^2 + 2(R')^2 - RR''}{[R^2 + (R')^2]^{\frac{3}{2}}}. \quad (4.17)$$

For notational convenience, we denote $\kappa_R(\hat{\theta}) = \kappa_R(\boldsymbol{x})$ and $\kappa_R(\theta) = \kappa_R(\boldsymbol{y})$. Both $\kappa_R(\hat{\theta})$ and $\kappa_R(\theta)$ can be computed by (4.17).

Based on the above calculations, we rewrite the left-hand side of (4.15) as a functional of $R(\theta)$ as follows

$$\begin{aligned} \mathcal{L}[R](\hat{\theta}) \triangleq & \int_0^{2\pi} \left[\beta G_1(D[R]) \sqrt{[R'(\theta)]^2 + R^2(\theta)} - \left((\mu + \kappa_R(\theta)) Q(D[R]) \right. \right. \\ & \left. \left. - \frac{\kappa_R(\theta) - \kappa_R(\hat{\theta})}{2\pi(D[R])^2} \right) \left(R^2(\theta) + R(\hat{\theta})R'(\theta) \sin(\hat{\theta} - \theta) - R(\hat{\theta})R(\theta) \cos(\hat{\theta} - \theta) \right) \right] d\theta, \end{aligned} \quad (4.18)$$

for $\hat{\theta} \in [0, 2\pi]$. Equation (4.15) implies that $\mathcal{L}[R](\hat{\theta}) \equiv 0$. To regularize the singularity of the kernel, we introduce a small constant $\tau > 0$ in $D[R]$, namely,

$$D_\tau[R] = \sqrt{R^2(\hat{\theta}) + R^2(\theta) - 2R(\hat{\theta})R(\theta) \cos(\hat{\theta} - \theta) + \tau^2}, \quad (4.19)$$

and define the corresponding functional for each $\hat{\theta} \in [0, 2\pi]$,

$$\begin{aligned} \mathcal{L}_\tau[R](\hat{\theta}) \triangleq & \int_0^{2\pi} \left[\beta G_1(D_\tau[R]) \sqrt{[R'(\theta)]^2 + R^2(\theta)} - \left((\mu + \kappa_R(\theta)) Q(D_\tau[R]) \right. \right. \\ & \left. \left. - \frac{\kappa_R(\theta) - \kappa_R(\hat{\theta})}{2\pi(D_\tau[R])^2} \right) \left(R^2(\theta) + R(\hat{\theta})R'(\theta) \sin(\hat{\theta} - \theta) - R(\hat{\theta})R(\theta) \cos(\hat{\theta} - \theta) \right) \right] d\theta. \end{aligned} \quad (4.20)$$

Hence we recover (4.18) when $\tau \rightarrow 0$ and have a non-singular kernel when $\tau > 0$. In the convergence analysis in Section 4.3, we shall prove that (4.20) is a good

approximation of (4.18).

Based on the machine learning techniques, an approximation of $R(\theta)$ by a single hidden layer neural network is written as

$$R(\theta) \approx \sum_{i=1}^N a_i \Psi(b_i \theta + c_i) + d \triangleq \rho(\theta; \mathcal{X}), \quad (4.21)$$

where N is the width, $\mathcal{X} = (a_1, \dots, a_N, b_1, \dots, b_N, c_1, \dots, c_N, d) \in \mathbb{R}^{3N+1}$ is the neural network's parameter, and Ψ is the nonlinear “activation” function such as sigmoid function. Note that for each ρ , the operator $\mathcal{L}_\tau[\rho](\hat{\theta}_i)$ can be calculated analytically, where $\hat{\theta}_i$ are m randomly sampled points, which are i.i.d. in $[0, 2\pi]$. We consider the loss function:

$$F(\mathcal{X}, \hat{\boldsymbol{\theta}}) \triangleq \frac{1}{m} \sum_{i=1}^m \left(\mathcal{L}_\tau[\rho](\hat{\theta}_i) \right)^2 + \sum_{\alpha=0}^2 \left(D^\alpha(\rho(0; \mathcal{X}) - \rho(2\pi; \mathcal{X})) \right)^2. \quad (4.22)$$

The reason why we choose up to second-order derivative in the second term is that the curvature term involves at most second-order derivative, hence we shall guarantee the continuity up to second-order. The loss function (4.22) measures how well the function $\rho(\theta; \mathcal{X})$ satisfies equation (4.15) as well as the 2π -periodic boundary condition (4.16). Hence \mathcal{X} is obtained via solving the following optimization problem

$$\begin{aligned} \min_{\mathcal{X}} J(\mathcal{X}) &\triangleq \mathbb{E}_{\hat{\boldsymbol{\theta}}} [F(\mathcal{X}, \hat{\boldsymbol{\theta}})] \\ &= \mathbb{E}_{\hat{\theta}_i} \left[\left(\mathcal{L}_\tau[\rho](\hat{\theta}_i) \right)^2 \right] + \sum_{\alpha=0}^2 \left(D^\alpha \rho(0; \mathcal{X}) - D^\alpha \rho(2\pi; \mathcal{X}) \right)^2 \\ &= \int_0^{2\pi} \left(\mathcal{L}_\tau[\rho](\hat{\theta}_i) \right)^2 \nu(\hat{\theta}_i) d\hat{\theta}_i + \sum_{\alpha=0}^2 \left(D^\alpha \rho(0; \mathcal{X}) - D^\alpha \rho(2\pi; \mathcal{X}) \right)^2, \end{aligned} \quad (4.23)$$

where $\nu(\hat{\theta}_i)$ is a probability density of $\hat{\theta}_i \in [0, 2\pi]$.

4.2.3 Stochastic gradient descent training algorithm

In order to solve (4.23) numerically, we use the stochastic gradient descent method shown in Algorithm 1.

Algorithm 1

```

Choose an initial guess  $\mathcal{X}_1$ 
for  $k = 1, 2, \dots$  do
    Generate  $m$  random points  $\hat{\boldsymbol{\theta}}_k = (\hat{\theta}_{k,i})_{i=1}^m$  from  $[0, 2\pi]$ ;
    Calculate the loss function at randomly sampled points  $F(\mathcal{X}_k, \hat{\boldsymbol{\theta}}_k)$ ;
    Compute a stochastic vector  $G(\mathcal{X}_k, \hat{\boldsymbol{\theta}}_k) = \nabla_{\mathcal{X}} F(\mathcal{X}_k, \hat{\boldsymbol{\theta}}_k)$ ;
    Set the new iterate as  $\mathcal{X}_{k+1} = \mathcal{X}_k - \alpha_n G(\mathcal{X}_k, \hat{\boldsymbol{\theta}}_k)$ ;
end for

```

Due to the non-convexity of $J(\mathcal{X})$, \mathcal{X}_k may stuck at a local minimum (not a global minimum). To guarantee a solution, we shall run the training process until the loss function is close to 0 (i.e., a global minimum).

4.3 Convergence of the neural network discretization

In this section, we shall prove that the numerical solution with the neural network discretization converges to the unknown boundary of system (4.4) as the number of hidden units tends to infinity, namely,

there exists $\rho \in \mathcal{C}^N$ such that $J(\rho(\theta; \mathcal{X})) \rightarrow 0$ as $N \rightarrow \infty$;

where

$$\mathcal{C}^N : \{\rho^N(\theta) : [0, 2\pi] \rightarrow \mathbb{R} \mid \rho^N(\theta) = \sum_{i=1}^N a_i \Psi(b_i \theta + c_i) + d\}. \quad (4.24)$$

The precise statement is included in Theorem 4.2.

4.3.1 Preliminary estimates

Denote

$$\begin{aligned} h(\mathbf{x}) &= \int_{\partial\Omega} \beta G_1(D[R]) dS_y, \\ g(\mathbf{x}) &= \int_{\partial\Omega} (\mu + \kappa_R(\mathbf{y})) Q(D[R])(\mathbf{y} - \mathbf{x}) \cdot \mathbf{n}_y dS_y, \\ w(\mathbf{x}) &= \int_{\partial\Omega} \frac{\kappa_R(\mathbf{y}) - \kappa_R(\mathbf{x})}{2\pi} \frac{\mathbf{y} - \mathbf{x}}{(D[R])^2} \cdot \mathbf{n}_y dS_y. \end{aligned}$$

Then the operator \mathcal{L} in (4.18) can be separated into three parts, namely,

$$\mathcal{L}[R](\mathbf{x}) = h(\mathbf{x}) - g(\mathbf{x}) + w(\mathbf{x}).$$

As mentioned before, since $G_1(\mathbf{x}, \mathbf{y}) = G_1(|\mathbf{x} - \mathbf{y}|) = \frac{i}{4} H_0^{(1)}(i|\mathbf{x} - \mathbf{y}|)$ is singular at $|\mathbf{x} - \mathbf{y}| = 0$, we further introduce,

$$\begin{aligned} h_\tau(\mathbf{x}) &= \int_{\partial\Omega} \beta G_1(D_\tau[R]) dS_y, \\ g_\tau(\mathbf{x}) &= \int_{\partial\Omega} (\mu + \kappa_R(\mathbf{y})) Q(D_\tau[R])(\mathbf{y} - \mathbf{x}) \cdot \mathbf{n}_y dS_y, \\ w_\tau(\mathbf{x}) &= \int_{\partial\Omega} \frac{\kappa_R(\mathbf{y}) - \kappa_R(\mathbf{x})}{2\pi} \frac{\mathbf{y} - \mathbf{x}}{(D_\tau[R])^2} \cdot \mathbf{n}_y dS_y. \end{aligned}$$

Correspondingly, \mathcal{L}_τ in (4.20) is also separated into three pieces:

$$\mathcal{L}_\tau[R](\mathbf{x}) = h_\tau(\mathbf{x}) - g_\tau(\mathbf{x}) + w_\tau(\mathbf{x}).$$

By *Lemmas 7.6 — 7.8* in [66], we have the following results:

Lemma 4.1. *Suppose that $\partial\Omega : r = R(\theta) \in C^3(-\infty, \infty)$ and 2π -periodic, then*

$$\|h - h_\tau\|_{L^\infty} \leq C\tau |\ln \tau|, \quad (4.25)$$

$$\|g - g_\tau\|_{L^\infty} \leq C\|\kappa_R\|_{L^\infty} \tau \leq C\tau, \quad (4.26)$$

$$\|w - w_\tau\|_{L^\infty} \leq C\|\kappa_R\|_{C^1}\tau \leq C\tau, \quad (4.27)$$

where the constant C is independent of τ .

Proof. The proof is really lengthy, here we only point out some key steps. Our definitions of $h(\mathbf{x})$ and $h_\tau(\mathbf{x})$ are equivalent to $h(\hat{s})$ and $h_\varepsilon(\hat{s})$ when $f(s) = \beta$ [66, (93)] (Note that functions in [66] are defined based on curve length s . Although they look different from our definitions, they are actually equivalent to our definitions of functions. The curve length parameters s and \hat{s} correspond to the parameters \mathbf{y} and \mathbf{x} here.) Hence (4.25) directly follows from *Lemma 7.6*. Similarly, $g(\mathbf{x})$ and $g_\tau(\mathbf{x})$ are equivalent to $g_2(\hat{s})$ and $g_{2\varepsilon}(\hat{s})$ when $f(s) = \mu + \kappa_R(\mathbf{y})$ [66, pg. 146]; $w(\mathbf{x})$ and $w_\tau(\mathbf{x})$ are equivalent to $-g_{11}(\hat{s})$ and $-g_{11\varepsilon}(\hat{s})$ when $f(s) = \kappa_R(\mathbf{y})$ and $f(\hat{s}) = \kappa_R(\mathbf{x})$ [66, (110), (111)]. By *Lemma 7.7 and 7.8*, we shall get estimates (4.26) and (4.27). Notice that we need $\|\kappa_R\|_{C^1}$ in (4.27), and κ_R involves at most second-order derivatives of $R(\theta)$, hence we require $\partial\Omega : r = R(\theta) \in C^3$. \square

Based on Lemma 4.1, we shall have

$$\|(\mathcal{L}_\tau - \mathcal{L})[R]\|_{L^\infty} \leq \|h - h_\tau\|_{L^\infty} + \|g - g_\tau\|_{L^\infty} + \|w - w_\tau\|_{L^\infty} \leq C\tau|\ln \tau| + C\tau,$$

which indicates that (4.20) is a good approximation of (4.18). Recall that it follows from (4.15) that $\mathcal{L}[R] \equiv 0$, then we immediately derive

$$\|\mathcal{L}_\tau[R]\|_{L^\infty} \leq C\tau|\ln \tau| + C\tau. \quad (4.3.27)$$

4.3.2 The neural network approximation

By *Theorem 3* of [70] we know that if the activation function $\Psi \in C^3(\mathbb{R})$ is nonconstant and bounded, then the space $\cup_{n=1}^\infty \mathcal{C}^n$ is uniformly 3-dense on compacta in $C^3(\mathbb{R})$. This means that for $R(\theta) \in C^3(-\infty, \infty)$ and every $0 < \delta < 1$, there is

$\rho(\theta; \mathcal{X}) \in \cup_{n=1}^{\infty} \mathcal{C}^n$ such that

$$\|\rho - R\|_{3,[0,2\pi]} \leq \delta, \quad (4.3.28)$$

where $\|f\|_{3,[0,2\pi]} := \max_{\alpha \leq 3} \sup_{x \in [0,2\pi]} |D^\alpha f(x)|$. Clearly, (4.3.29) implies

$$\|\rho - R\|_{L^\infty([0,2\pi])}, \|\rho' - R'\|_{L^\infty([0,2\pi])}, \|\rho'' - R''\|_{L^\infty([0,2\pi])}, \|\rho''' - R'''\|_{L^\infty([0,2\pi])} \leq \delta. \quad (4.3.29)$$

Based on (4.3.29), let's first bound $\|\mathcal{L}_\tau[\rho] - \mathcal{L}_\tau[R]\|_{L^\infty}$, which is a key estimate in proving the convergence theorem. Throughout the rest of this paper, C is used to represent a generic constant independent of τ and δ , which might change from a line to next.

Recall the formulas for $\mathcal{L}_\tau[R]$ and $D_\tau[R]$ in (4.20) and (4.19), respectively:

$$\begin{aligned} \mathcal{L}_\tau[R](\hat{\theta}) = \int_0^{2\pi} & \left[\beta G_1(D_\tau[R]) \sqrt{[R'(\theta)]^2 + R^2(\theta)} - \left((\mu + \kappa_R(\theta)) Q(D_\tau[R]) \right. \right. \\ & \left. \left. - \frac{\kappa_R(\theta) - \kappa_R(\hat{\theta})}{2\pi(D_\tau[R])^2} \right) \left(R^2(\theta) + R(\hat{\theta})R'(\theta) \sin(\hat{\theta} - \theta) - R(\hat{\theta})R(\theta) \cos(\hat{\theta} - \theta) \right) \right] d\theta, \end{aligned}$$

and

$$D_\tau[R] = \sqrt{R^2(\hat{\theta}) + R^2(\theta) - 2R(\hat{\theta})R(\theta) \cos(\hat{\theta} - \theta) + \tau^2}.$$

Correspondingly, $\mathcal{L}_\tau[\rho]$ takes the following form

$$\begin{aligned} \mathcal{L}_\tau[\rho](\hat{\theta}) = \int_0^{2\pi} & \left[\beta G_1(D_\tau[\rho]) \sqrt{[\rho'(\theta)]^2 + \rho^2(\theta)} - \left((\mu + \kappa_\rho(\theta)) Q(D_\tau[\rho]) \right. \right. \\ & \left. \left. - \frac{\kappa_\rho(\theta) - \kappa_\rho(\hat{\theta})}{2\pi(D_\tau[\rho])^2} \right) \left(\rho^2(\theta) + \rho(\hat{\theta})\rho'(\theta) \sin(\hat{\theta} - \theta) - \rho(\hat{\theta})\rho(\theta) \cos(\hat{\theta} - \theta) \right) \right] d\theta, \end{aligned} \quad (4.3.30)$$

where

$$D_\tau[\rho] = \sqrt{\rho^2(\hat{\theta}) + \rho^2(\theta) - 2\rho(\hat{\theta})\rho(\theta) \cos(\hat{\theta} - \theta) + \tau^2}. \quad (4.3.31)$$

Notice that we use κ_R and κ_ρ to differentiate the curvature on different curves. By

(4.17),

$$\kappa_R = \frac{R^2 + 2(R')^2 - RR''}{[R^2 + (R')^2]^{\frac{3}{2}}}, \quad \text{and} \quad \kappa_\rho = \frac{\rho^2 + 2(\rho')^2 - \rho\rho''}{[\rho^2 + (\rho')^2]^{\frac{3}{2}}}. \quad (4.3.32)$$

Subtracting $\mathcal{L}_\tau[\rho]$ from $\mathcal{L}_\tau[R]$, we derive, for each $\hat{\theta} \in [0, 2\pi]$,

$$\left| \mathcal{L}_\tau[\rho](\hat{\theta}) - \mathcal{L}_\tau[R](\hat{\theta}) \right| \leq \beta \int_0^{2\pi} |\text{I}| d\theta + \int_0^{2\pi} |\text{II}| d\theta + \int_0^{2\pi} |\text{III}| d\theta,$$

where

$$\begin{aligned} \text{I} &= G_1(D_\tau[\rho])\sqrt{[\rho'(\theta)]^2 + \rho^2(\theta)} - G_1(D_\tau[R])\sqrt{[R'(\theta)]^2 + R^2(\theta)}, \\ \text{II} &= Q(D_\tau[\rho])(\mu + \kappa_\rho(\theta))(\rho^2(\theta) + \rho(\hat{\theta})\rho'(\theta)\sin(\hat{\theta} - \theta) - \rho(\hat{\theta})\rho(\theta)\cos(\hat{\theta} - \theta)) \\ &\quad - Q(D_\tau[R])(\mu + \kappa_R(\theta))(R^2(\theta) + R(\hat{\theta})R'(\theta)\sin(\hat{\theta} - \theta) - R(\hat{\theta})R(\theta)\cos(\hat{\theta} - \theta)), \\ \text{III} &= \frac{\kappa_\rho(\theta) - \kappa_\rho(\hat{\theta})}{2\pi(D_\tau[\rho])^2}(\rho^2(\theta) + \rho(\hat{\theta})\rho'(\theta)\sin(\hat{\theta} - \theta) - \rho(\hat{\theta})\rho(\theta)\cos(\hat{\theta} - \theta)) \\ &\quad - \frac{\kappa_R(\theta) - \kappa_R(\hat{\theta})}{2\pi(D_\tau[R])^2}(R^2(\theta) + R(\hat{\theta})R'(\theta)\sin(\hat{\theta} - \theta) - R(\hat{\theta})R(\theta)\cos(\hat{\theta} - \theta)). \end{aligned}$$

In order to estimate $|\mathcal{L}_\tau[\rho](\hat{\theta}) - \mathcal{L}_\tau[R](\hat{\theta})|$, we need to estimate $|\text{I}|$, $|\text{II}|$, and $|\text{III}|$, respectively. For term I, we insert a term $G_1(D_\tau[\rho])\sqrt{[R'(\theta)]^2 + R^2(\theta)}$ and subtract the same term; after rearranging the terms in I, we obtain

$$\begin{aligned} |\text{I}| &\leq \left| G_1(D_\tau[\rho]) \right| \left| \sqrt{[\rho'(\theta)]^2 + \rho^2(\theta)} - \sqrt{[R'(\theta)]^2 + R^2(\theta)} \right| \\ &\quad + \left| G_1(D_\tau[\rho]) - G_1(D_\tau[R]) \right| \sqrt{[R'(\theta)]^2 + R^2(\theta)}. \end{aligned} \quad (4.3.33)$$

Using the inequality $|\sqrt{x} - \sqrt{y}| \leq \sqrt{|x - y|}$, and combining with estimates (4.3.29),

we have

$$\begin{aligned}
\left| \sqrt{[\rho'(\theta)]^2 + \rho^2(\theta)} - \sqrt{[R'(\theta)]^2 + R^2(\theta)} \right| &\leq \sqrt{\left| [\rho'(\theta)]^2 + \rho^2(\theta) - [R'(\theta)]^2 - R^2(\theta) \right|} \\
&\leq \sqrt{\left| [\rho'(\theta)]^2 - [R'(\theta)]^2 \right| + \left| \rho^2(\theta) - R^2(\theta) \right|} \\
&\leq C\delta^{\frac{1}{2}}.
\end{aligned} \tag{4.3.34}$$

In a similar manner, $|D_\tau[\rho] - D_\tau[R]|$ can also be estimated:

$$\begin{aligned}
&\left| D_\tau[\rho] - D_\tau[R] \right| \\
&\leq \sqrt{\left| \rho^2(\hat{\theta}) + \rho^2(\theta) - R^2(\hat{\theta}) - R^2(\theta) - 2(\rho(\hat{\theta})\rho(\theta) - R(\hat{\theta})R(\theta)) \cos(\hat{\theta} - \theta) \right|} \\
&\leq \sqrt{\left| \rho^2(\hat{\theta}) - R^2(\hat{\theta}) \right| + \left| \rho^2(\theta) - R^2(\theta) \right| + 2\left| \rho(\hat{\theta})\rho(\theta) - R(\hat{\theta})R(\theta) \right|} \\
&\leq C\delta^{\frac{1}{2}}.
\end{aligned} \tag{4.3.35}$$

In addition, since $R \in C^2$, we clearly have

$$\sqrt{[R'(\theta)]^2 + R^2(\theta)} \leq C. \tag{4.3.36}$$

Next we proceed to consider the terms involving G_1 . We compute

$$G_1(r) = \frac{i}{4}H_0^{(1)}(ir), \quad \text{and} \quad G_1'(r) = -\frac{1}{4}(H_0^{(1)})'(ir) = \frac{1}{4}H_1^{(1)}(ir);$$

and it is clear that both $G_1(r)$ and $G_1'(r)$ are singular at $r = 0$. Here we collect some

formulas for the Hankel function, and we focus on the approximation when $r \rightarrow 0$:

$$H_0^{(1)}(z) = J_0(z) + iY_0(z), \quad H_1^{(1)}(z) = J_1(z) + iY_1(z), \quad ([9.1.3] \text{ of } [1])$$

$$J_0(z) = \phi_1(-z^2), \quad \phi_1(0) = 1, \quad \phi_1 \in C^\infty, \quad ([9.1.12] \text{ of } [1])$$

$$Y_0(z) = \frac{2}{\pi} \left[\ln \left(\frac{1}{2} z \right) + \gamma \right] J_0(z) + \phi_2(z^2), \quad \phi_2 \in C^\infty, \quad ([9.1.13] \text{ of } [1])$$

$$J_1(z) = \frac{1}{2} z \phi_3(-z^2), \quad \phi_3(0) = 1, \quad \phi_3 \in C^\infty, \quad ([9.1.10] \text{ of } [1])$$

$$Y_1(z) = -\frac{2}{\pi z} + \frac{2}{\pi} \ln \left(\frac{1}{2} z \right) J_1(z) - \frac{z}{2\pi} \phi_4(-z^2), \quad \phi_4 \in C^\infty. \quad ([9.1.11] \text{ of } [1])$$

It follows that

$$\begin{aligned} G_1(r) &= \frac{i}{4} H_0^{(1)}(ir) = -\frac{1}{2\pi} \ln r \cdot \phi_1(r^2) + \phi_5(r^2), \quad \phi_5 \in C^\infty; \\ G_1'(r) &= \frac{1}{4} H_1^{(1)}(ir) = -\frac{1}{2\pi r} - \frac{1}{4\pi} r \ln r \cdot \phi_3(r^2) + r \phi_6(r^2), \quad \phi_6 \in C^\infty. \end{aligned}$$

Since $\tau > 0$, both $D_\tau[\rho]$ and $D_\tau[R]$ are greater than τ ; hence there exists a constant C which is independent of τ and δ such that

$$\begin{aligned} |G_1(D_\tau[\rho])| &\leq C |\ln \tau|, \\ |G_1(D_\tau[\rho]) - G_1(D_\tau[R])| &\leq \frac{C}{\tau} |D_\tau[\rho] - D_\tau[R]|. \end{aligned}$$

Substituting the above two inequalities, and estimates (4.3.34), (4.3.35) as well as (4.3.36) all into (4.3.33), we finally derive

$$|I| \leq C |\ln \tau| \delta^{\frac{1}{2}} + \frac{C}{\tau} \delta^{\frac{1}{2}}, \quad (4.3.37)$$

where the constant C is independent of τ and δ .

After we show the bound for I, we can estimate II and III in the same manner.

Recall that

$$Q(r) = \frac{1}{r} \left(G_1'(r) + \frac{1}{2\pi r} \right),$$

then

$$Q(r) = -\frac{1}{4\pi} \ln r \cdot \phi_3(r^2) + \phi_6(r^2), \quad Q'(r) = O(r^{-1}).$$

Therefore, similar as function G_1 , there exists a constant C not independent of τ and δ such that

$$\begin{aligned} |Q(D_\tau[\rho])| &\leq C |\ln \tau|, \\ |Q(D_\tau[\rho]) - Q(D_\tau[R])| &\leq \frac{C}{\tau} |D_\tau[\rho] - D_\tau[R]|. \end{aligned}$$

Next we turn our attention to the terms involving the curvature. Since $R, \rho \in C^3$, κ_R and κ_ρ are both bounded based on (4.3.32) (note that we are only interested in the solutions which are away from the origin, hence the denominator of the curvature is not close to 0). Moreover, subtracting κ_ρ from κ_R , recalling also (4.3.34) and (4.3.29), we have

$$\begin{aligned} |\kappa_\rho - \kappa_R| &\leq \left| \frac{\rho^2 + 2(\rho')^2 - \rho\rho''}{[\rho^2 + (\rho')^2]^{\frac{3}{2}}} - \frac{\rho^2 + 2(\rho')^2 - \rho\rho''}{[R^2 + (R')^2]^{\frac{3}{2}}} \right| \\ &\quad + \left| \frac{\rho^2 + 2(\rho')^2 - \rho\rho''}{[R^2 + (R')^2]^{\frac{3}{2}}} - \frac{R^2 + 2(R')^2 - RR''}{[R^2 + (R')^2]^{\frac{3}{2}}} \right| \\ &\leq C \left| (\sqrt{\rho^2 + (\rho')^2})^3 - (\sqrt{R^2 + (R')^2})^3 \right| + C\delta \\ &\leq C \left| \sqrt{\rho^2 + (\rho')^2} - \sqrt{R^2 + (R')^2} \right| + C\delta \\ &\leq C\delta^{\frac{1}{2}} + C\delta \leq C\delta^{\frac{1}{2}}. \end{aligned}$$

Therefore, we derive

$$\begin{aligned}
|\text{II}| &\leq \left| Q(D_\tau[\rho]) \right| \left| \mu + \kappa_\rho \right| \left| \rho^2(\theta) - R^2(\theta) + (\rho(\hat{\theta})\rho'(\theta) - R(\hat{\theta})R'(\theta)) \sin(\hat{\theta} - \theta) \right. \\
&\quad \left. - (\rho(\hat{\theta})\rho(\theta) - R(\hat{\theta})R(\theta)) \cos(\hat{\theta} - \theta) \right| \\
&\quad + \left| Q(D_\tau[\rho]) \right| \left| \kappa_\rho - \kappa_R \right| \left| R^2(\theta) + R(\hat{\theta})R'(\theta) \sin(\hat{\theta} - \theta) - R(\hat{\theta})R(\theta) \cos(\hat{\theta} - \theta) \right| \\
&\quad + \left| Q(D_\tau[\rho]) - Q(D_\tau[R]) \right| \left| \mu + \kappa_R \right| \left| R^2(\theta) + R(\hat{\theta})R'(\theta) \sin(\hat{\theta} - \theta) \right. \\
&\quad \left. - R(\hat{\theta})R(\theta) \cos(\hat{\theta} - \theta) \right| \\
&\leq C |\ln \tau| \delta + C |\ln \tau| \delta^{\frac{1}{2}} + \frac{C}{\tau} \delta^{\frac{1}{2}} \leq C |\ln \tau| \delta^{\frac{1}{2}} + \frac{C}{\tau} \delta^{\frac{1}{2}},
\end{aligned} \tag{4.3.38}$$

$$\begin{aligned}
|\text{III}| &\leq \left| \frac{\kappa_\rho(\theta) - \kappa_\rho(\hat{\theta})}{2\pi(D_\tau[\rho])^2} \right| \left| \rho^2(\theta) - R^2(\theta) + (\rho(\hat{\theta})\rho'(\theta) - R(\hat{\theta})R'(\theta)) \sin(\hat{\theta} - \theta) \right. \\
&\quad \left. - (\rho(\hat{\theta})\rho(\theta) - R(\hat{\theta})R(\theta)) \cos(\hat{\theta} - \theta) \right| \\
&\quad + \left| \frac{\kappa_\rho(\theta) - \kappa_\rho(\hat{\theta})}{2\pi(D_\tau[\rho])^2} - \frac{\kappa_\rho(\theta) - \kappa_\rho(\hat{\theta})}{2\pi(D_\tau[R])^2} \right| \left| R^2(\theta) + R(\hat{\theta})R'(\theta) \sin(\hat{\theta} - \theta) \right. \\
&\quad \left. - R(\hat{\theta})R(\theta) \cos(\hat{\theta} - \theta) \right| \\
&\quad + \left| \frac{\kappa_\rho(\theta) - \kappa_R(\theta) - \kappa_\rho(\hat{\theta}) + \kappa_R(\hat{\theta})}{2\pi(D_\tau[R])^2} \right| \left| R^2(\theta) + R(\hat{\theta})R'(\theta) \sin(\hat{\theta} - \theta) \right. \\
&\quad \left. - R(\hat{\theta})R(\theta) \cos(\hat{\theta} - \theta) \right| \\
&\leq \frac{C}{\tau^2} \delta + \frac{C}{\tau^3} \delta^{\frac{1}{2}} + \frac{C}{\tau^2} \delta^{\frac{1}{2}} \leq \frac{C}{\tau^3} \delta^{\frac{1}{2}}.
\end{aligned} \tag{4.3.39}$$

Now we are able to estimate $|\mathcal{L}_\tau[\rho](\hat{\theta}) - \mathcal{L}_\tau[R](\hat{\theta})|$. Recall that

$$|\mathcal{L}_\tau[\rho](\hat{\theta}) - \mathcal{L}_\tau[R](\hat{\theta})| \leq \beta \int_0^{2\pi} |\text{I}| d\theta + \int_0^{2\pi} |\text{II}| d\theta + \int_0^{2\pi} |\text{III}| d\theta;$$

together with (4.3.37), (4.3.38) and (4.3.39), it follows that, for each $\hat{\theta} \in [0, 2\pi]$,

$$\begin{aligned} |\mathcal{L}_\tau[\rho](\hat{\theta}) - \mathcal{L}_\tau[R](\hat{\theta})| &\leq 2\beta\pi \max |\text{I}| + 2\pi \max |\text{II}| + 2\pi \max |\text{III}| \\ &\leq 2\beta\pi \left(C|\ln \tau| \delta^{\frac{1}{2}} + \frac{C}{\tau} \delta^{\frac{1}{2}} \right) + 2\pi \left(C|\ln \tau| \delta^{\frac{1}{2}} + \frac{C}{\tau} \delta^{\frac{1}{2}} \right) + 2\pi \frac{C}{\tau^3} \delta^{\frac{1}{2}} \\ &\leq C|\ln \tau| \delta^{\frac{1}{2}} + \frac{C}{\tau^3} \delta^{\frac{1}{2}}, \end{aligned}$$

which is equivalent to

$$\|\mathcal{L}_\tau[\rho] - \mathcal{L}_\tau[R]\|_{L^\infty} \leq C|\ln \tau| \delta^{\frac{1}{2}} + \frac{C}{\tau^3} \delta^{\frac{1}{2}}. \quad (4.3.40)$$

4.3.3 Convergence theorem

Here is our convergence theorem:

Theorem 4.2. *Let $\mathcal{C}^N(\Psi)$ be given by (4.24) where Ψ is assumed to be in $C^3(\mathbb{R})$, bounded and non-constant. Then for every $0 < \delta < 1$, there exists $\rho(\theta; \mathcal{X}) \in \cup_{N=1}^\infty \mathcal{C}^N$ and a positive constant K such that*

$$J(\rho(\theta; \mathcal{X})) \leq K \delta^{\frac{1}{8}},$$

where the constant K does not depend upon δ .

In recent years, quantitative estimates are obtained on the order of approximation [80, 94]. Using these results, we can also quantify the approximation rate in Theorem 4.2. We combine Theorem 4.2 with *Theorem 3* in [94], recall also Sobolev embedding theorem, we then obtain the following theorem for the approximation rate if the activation function is periodic:

Theorem 4.3. *Given the smooth function $R(\theta)$, if the activation function $\Psi \in W^{4,\infty}$*

is a non-constant periodic function, we have

$$\inf_{\rho^N \in \mathcal{C}^N} \|\rho^N - R\|_{C^3([0, 2\pi])} \leq C(\Psi) N^{-\frac{1}{2}} \|R\|_{\mathcal{B}^4},$$

hence (recall that the convergence rate is $O(\delta^{1/8})$ in Theorem 4.1, and $O((N^{-1/2})^{1/8}) = O(N^{-1/16})$)

$$J(\rho(\theta; \mathcal{X})) \leq C(\Psi) N^{-\frac{1}{16}} \|R\|_{\mathcal{B}^4},$$

where $\|R\|_{\mathcal{B}^s} = \int_{\mathbb{R}} (1 + |\omega|)^s |\hat{R}(\omega)| d\omega$ denotes the Barron norm of function $R(\theta)$.

Remark 4.2. Given the nonlinearity and complexity of free boundary problems, there might be more than one local minima of the loss function, and SGD may get stuck at local optima. Theorem 4.2 indicates that in order to get a solution, the loss function should be close to 0 (i.e., a global minimum).

Proof of Theorem 4.2. We start from the definition of J in (4.23). Notice that R satisfies the 2π -periodic boundary condition, i.e., $R(0) = R(2\pi)$, $R'(0) = R'(2\pi)$, $R''(0) = R''(2\pi)$. Therefore, we have

$$\begin{aligned} J(\rho(\theta; \mathcal{X})) &= \int_0^{2\pi} (\mathcal{L}_\tau[\rho](\hat{\theta}_i))^2 \nu(\hat{\theta}_i) d\hat{\theta}_i + \sum_{\alpha=0}^2 \left(D^\alpha(\rho(0; \mathcal{X}) - \rho(2\pi; \mathcal{X})) \right)^2 \\ &= \int_0^{2\pi} (\mathcal{L}_\tau[\rho - R](\hat{\theta}_i) + \mathcal{L}_\tau[R](\hat{\theta}_i))^2 \nu(\hat{\theta}_i) d\hat{\theta}_i \\ &\quad + \sum_{\alpha=0}^2 \left(D^\alpha(\rho(0; \mathcal{X}) - R(0) - \rho(2\pi; \mathcal{X}) + R(2\pi)) \right)^2 \\ &\leq 2 \int_0^{2\pi} (\mathcal{L}_\tau[\rho - R](\hat{\theta}_i))^2 \nu(\hat{\theta}_i) d\hat{\theta}_i + 2 \int_0^{2\pi} (\mathcal{L}_\tau[R](\hat{\theta}_i))^2 \nu(\hat{\theta}_i) d\hat{\theta}_i \\ &\quad + 2 \sum_{\alpha=0}^2 \left((\rho(0; \mathcal{X}) - R(0)) \right)^2 + 2 \sum_{\alpha=0}^2 \left((\rho(2\pi; \mathcal{X}) - R(2\pi)) \right)^2 \\ &\leq 2 \|\mathcal{L}_\tau[\rho - R]\|_{L^\infty}^2 + 2 \|\mathcal{L}_\tau[R]\|_{L^\infty}^2 + 12 \|\rho - R\|_{2, [0, 2\pi]}^2. \end{aligned}$$

We combine it with estimates (4.3.27), (4.3.29) as well as (4.3.40), and use the fact

that $(a + b)^2 \leq 2(a^2 + b^2)$, to obtain

$$J(\rho(\theta; \mathcal{X})) \leq C \left(|\ln \tau|^2 \delta + \frac{\delta}{\tau^6} + |\ln \tau|^2 \tau^2 + \tau^2 + \delta^2 \right).$$

Take $\tau = \delta^{\frac{1}{8}}$, we have

$$J(\rho(\theta; \mathcal{X})) \leq C \left(|\ln \delta^{\frac{1}{8}}|^2 \delta + \delta^{\frac{1}{4}} + |\ln \delta^{\frac{1}{8}}|^2 \delta^{\frac{1}{4}} + \delta^{\frac{1}{4}} + \delta^2 \right) \leq C \left(|\ln \delta^{\frac{1}{8}}|^2 \delta^{\frac{1}{4}} + \delta^{\frac{1}{4}} \right).$$

It is easy to show, for $0 < x < 1$,

$$|\ln x|^2 x^2 < x;$$

hence when $0 < \delta < 1$,

$$|\ln \delta^{\frac{1}{8}}|^2 \delta^{\frac{1}{4}} \leq \delta^{\frac{1}{8}}.$$

By choosing $K = 2C$, we finally obtain

$$J(f) \leq C \left(\delta^{\frac{1}{8}} + \delta^{\frac{1}{4}} \right) \leq 2C \delta^{\frac{1}{8}} \leq K \delta^{\frac{1}{8}}$$

which completes the proof. □

4.4 Numerical Results

4.4.1 Verification of the bifurcation solutions

Near the bifurcation points $\mu = \mu_n(R_s)$, the shape of the symmetry-breaking free boundary is fully characterized by Theorem 4.1 (see also Remark 4.1). In this section we show that all these free boundary solutions can be fully recovered by the neural network discretization. In particular, we compute the numerical solution with

Algorithm 1 near the bifurcation points μ_n by (4.7) with $R_S = 1$, namely,

$$\mu_2 \approx 14.7496, \quad \mu_3 \approx 28.7234, \quad \mu_4 \approx 47.1794, \quad \mu_5 \approx 70.1169.$$

We choose μ in a small neighborhood of μ_n , i.e., $|\mu - \mu_n|$ is small; correspondingly, $\beta = (\mu+1)\frac{I_1(1)}{I_0(1)}$ is uniquely determined by (4.6). For the neural network discretization, we set the number of neurons $N = 20$, the number of Monte Carlo integration points $m = 4000$, $\tau = 10^{-3}$, the maximum number of iterations as 50, learning rate = 10^{-4} , and the activation function $\Psi(\theta) = \cos(\theta)$. The initial parameters are set to be: a_i is randomly chosen by $\mathbb{N}(0,1)$, $b_i = n$ (which corresponds to the n -mode bifurcation), $c_i = 0$, and $d = 1$; in this way, the Neural network representation $\rho(\theta, \mathcal{X}) = \sum_{i=1}^N a_i \Psi(b_i \theta + c_i) + d$ is close to the form of free boundary for the symmetry-breaking solution (4.8). Moreover, $\hat{\theta}_i$ are uniformly sampled from $[0, 2\pi]$, and are divided into 20 mini-batches, with each mini-batch containing 200 points. Therefore, all the parameters are updated 20 times in one epoch. The loss is shown in Figure 4.1 while the shapes of symmetry-breaking solutions on different bifurcation branches are shown in Figure 4.2 which is consistent with the theoretical results in Theorem 4.1 and Remark 4.1.

4.4.2 New non-radially symmetric solutions

In this section we generate some non-radially symmetric solutions that are not characterized by any theorems. Inspired by [83], we try to find some fingering patterns, hence we choose the activation function $\Psi(\theta) = 0.3/[(\cos(\theta))^2 + (0.3 \sin(\theta))^2]$, which generates fingering-like patterns. In particular, we take $\mu = 20$, $\beta = (\mu+1)\frac{I_1(1)}{I_0(1)}$, $N = 20$, $m = 10000$, $\tau = 10^{-3}$ and maximum number of iterations = 200. We divide 10000 random points $\hat{\theta}_i$ into 100 mini-batches, hence all the parameters are updated 100 times in one iteration.

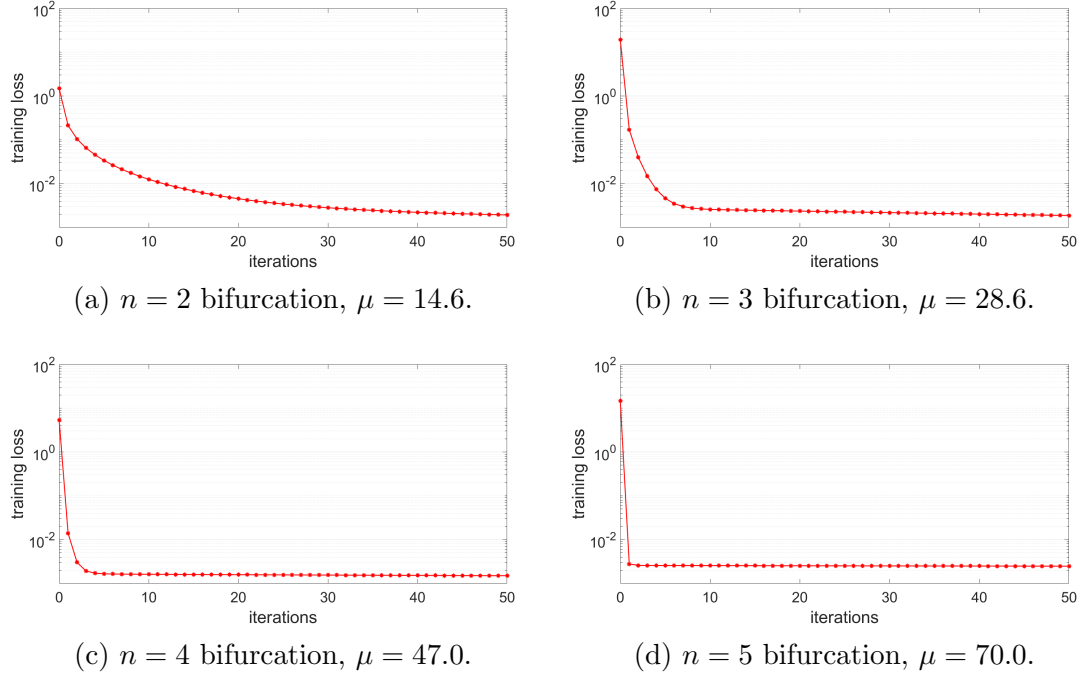


Figure 4.1. Training loss.

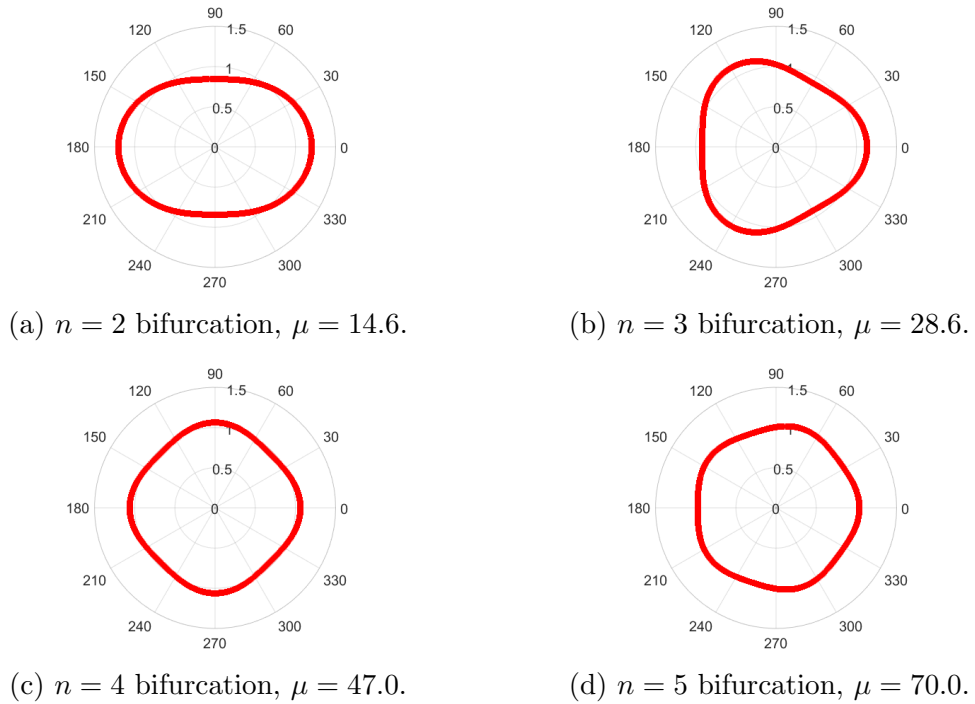
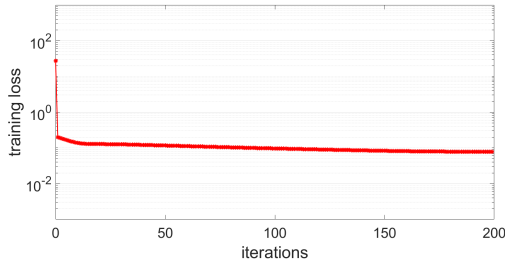


Figure 4.2. Contour plot of symmetry-breaking solutions in different bifurcation branches.

In Figure 4.3, we initially choose $b_i = 1$ and randomly choose other parameters. The learning rate is 10^{-3} at first and is decreased gradually to 10^{-6} . In Figure 4.4, we take $b_i = 2$, $c_i = 0$, random a_i , a random d , and a 10^{-5} learning rate. Compared with Figure 4.1, the loss in Figures 4.3 and 4.4 are larger. It is due to the numerical error introduced by calculating the curvature at the tip of each finger and the connecting points between two adjacent fingers.

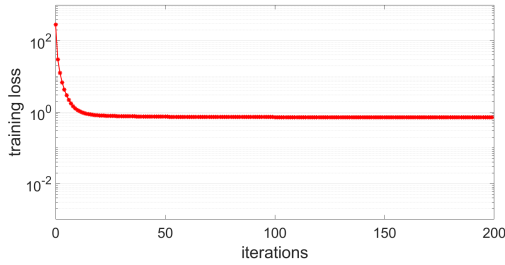


(a) Training loss.

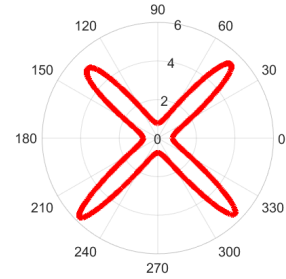


(b) Contour plot.

Figure 4.3. Non-radially symmetric solution with 2 fingers.



(a) Training loss.



(b) Contour plot.

Figure 4.4. Non-radially symmetric solution with 4 fingers.

4.5 Discussion

We have developed a novel numerical method based on the neural network discretization for solving a modified Hele-Shaw model of PDE free boundary problem. We established theoretically the existence of the numerical solution with this new discretization. Our simulations verify this new approach on known non-radially symmetric solutions. Moreover, using this new method, we also found some new non-radially symmetric solutions that were unknown based on the existing theories. With small changes, this new numerical method can be undoubtedly applied to solve more sophisticated free boundary problems such as obstacle problems, tumor growth models and the atherosclerotic plaque formation models. The research in this field will be continued in the near future.

APPENDIX A

PROPERTIES OF BESSEL FUNCTIONS

Here we collect some proprieties of the modified Bessel functions $I_n(\xi)$ for $n \geq 0$. Recall that the modified Bessel function $I_n(\xi)$ satisfies the differential equations

$$I_n''(\xi) + \frac{1}{\xi}I_n'(\xi) - \left(1 + \frac{n^2}{\xi^2}\right)I_n(\xi) = 0, \quad (\text{A.1})$$

and is given by

$$I_n(\xi) = \left(\frac{\xi}{2}\right)^n \sum_{k=0}^{\infty} \frac{1}{k!\Gamma(n+k+1)} \left(\frac{\xi}{2}\right)^{2k}, \quad (\text{A.2})$$

from which it is easy to derive

$$\frac{I_{n+1}(\xi)}{I_n(\xi)} < \frac{\xi}{2n}, \quad \text{for } \xi > 0, \ n \geq 1. \quad (\text{A.3})$$

Furthermore, by [32, 45, 52], $I_n(\xi)$ has the following properties:

$$I_n'(\xi) + \frac{n}{\xi}I_n(\xi) = I_{n-1}(\xi), \quad n \geq 1, \quad (\text{A.4})$$

$$I_n'(\xi) - \frac{n}{\xi}I_n(\xi) = I_{n+1}(\xi), \quad n \geq 0, \quad (\text{A.5})$$

$$\xi^{n+1}I_n(\xi) = \frac{d}{d\xi}(\xi^{n+1}I_{n+1}(\xi)), \quad n \geq 0, \quad (\text{A.6})$$

$$I_{n-1}(\xi) - I_{n+1}(\xi) = \frac{2n}{\xi}I_n(\xi), \quad n \geq 1, \quad (\text{A.7})$$

$$I_{n-1}(\xi)I_{n+1}(\xi) < I_n^2(\xi), \quad \xi > 0, \quad (\text{A.8})$$

$$I_{n-1}(\xi)I_{n+1}(\xi) > I_n^2(\xi) - \frac{2}{\xi}I_n(\xi)I_{n+1}(\xi), \quad \xi > 0, \quad (\text{A.9})$$

$$I_m(\xi)I_n(\xi) = \sum_{k=0}^{\infty} \frac{\Gamma(m+n+2k+1)(\xi/2)^{m+n+2k}}{k!\Gamma(m+k+1)\Gamma(n+k+1)\Gamma(m+n+k+1)}, \quad (\text{A.10})$$

$$\frac{I_n(\xi)}{\xi} \text{ is increasing in } \xi \text{ for } \xi > 0 \quad n \geq 1. \quad (\text{A.11})$$

These properties of $I_n(\xi)$ are needed in Sections 2 and 4.

APPENDIX B

CRANDALL-RABINOWITZ THEOREM

Theorem B.1. (Crandall-Rabinowitz theorem, [54]) *Let X, Y be real Banach spaces and $F(\cdot, \cdot)$ 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 μ in a neighborhood of μ_0 ,
- (2) $\text{Ker } F_x(0, \mu_0)$ 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 Γ_1 and Γ_2 which intersect only at the point $(0, \mu_0)$; Γ_1 is the curve $(0, \mu)$ and Γ_2 can be parameterized as follows:

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

APPENDIX C

SOME USEFUL LEMMAS

C.1 A comparison principle

For brevity, let us denote the operator L by $L = -\frac{d^2}{dr^2} - \frac{1}{r}\frac{d}{dr} + \frac{b}{r^2}$, where $b \geq 0$.

Lemma C.1. *For the operator L , maximum principle holds in a way that if we have*

$$\begin{cases} L[Q] = -Q''(r) - \frac{1}{r}Q'(r) + \frac{b}{r^2}Q(r) \geq 0 & \text{in } B_R, \\ Q(R) \geq 0, \quad |Q'| \text{ is bounded on } (0, R), \end{cases}$$

then $Q(r) \geq 0$ for $0 \leq r \leq R$.

Proof. We denote $Q^- = -\min\{0, Q\}$. Multiplying $L[Q]$ with Q^- and integrating with respect to r in B_R gives

$$\int_0^R -(rQ')'Q^- dr + b \int_0^R \frac{1}{r}QQ^- dr \geq 0,$$

which implies

$$-rQ'Q^- \Big|_0^R + \int_0^R rQ'(Q^-)' dr + b \int_0^R \frac{1}{r}QQ^- dr \geq 0.$$

Since $Q(R) \geq 0$, $Q^-(R) = 0$ by the definition of Q^- . Thus the first term in the above inequality disappears. We therefore have

$$\int_0^R r[(Q^-)']^2 dr + b \int_0^R \frac{1}{r}(Q^-)^2 dr \leq 0, \tag{C.1}$$

when $b \neq 0$, $\int_0^R \frac{1}{r} (Q^-)^2 dr = 0$ implies $Q^- \equiv 0$, which directly indicates the final result; when $b = 0$, the second term of $\int_0^R r [(Q^-)']^2 dr$ implies $(Q^-)' = 0$, then we infer that Q^- is a constant. Combining with the boundary condition $Q^-(R) = 0$, we have $Q^- \equiv 0$, which again directly indicates the final result. \square

C.2 A continuation lemma

The next lemma concerns the continuation of estimates. The proof is standard and we omit the details.

Lemma C.2. *Let $\{\vec{Q}_\delta^{(i)}\}_{i=1}^M$ be a finite collection of real vectors, and define the norm of the vector by $|\vec{Q}_\delta|_{\max} = \max_{1 \leq i \leq M} |Q_\delta^{(i)}|$. Suppose that $0 < C_1 < C_2$, and*

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

$$(ii) \quad \text{For any } 0 < \delta \leq 1, \text{ if } |\vec{Q}_\delta|_{\max} \leq C_2, \text{ then } |\vec{Q}_\delta|_{\max} \leq C_1;$$

$$(iii) \quad \vec{Q}_\delta \text{ is continuous in } \delta.$$

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

Remark C.1. *If the finite collection is replaced by an infinite collection, then (iii) will need to be replaced by “uniform continuity” in δ .*

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