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Stationary solutions of a free boundary problem modeling the growth of tumors with Gibbs–Thomson relation

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Abstract

In this paper we study a free boundary problem modeling tumor growth. The model consists of two elliptic equations describing nutrient diffusion and pressure distribution within tumors, respectively, and a first-order partial differential equation governing the free boundary, on which a Gibbs–Thomson relation is taken into account. We first show that the problem may have none, one or two radial stationary solutions depending on model parameters. Then by bifurcation analysis we show that there exist infinite many branches of non-radial stationary solutions bifurcating from given radial stationary solution. The result implies that cell-to-cell adhesiveness is the key parameter which plays a crucial role on tumor invasion.

MSC: 35B32; 35Q92; 35R35

Keywords: Free boundary problem; Tumor growth; Stationary solution; Bifurcation

1. Introduction

In this paper we study the following free boundary problem modeling tumor growth:

$$\Delta\sigma = \lambda\sigma \qquad \text{in } \Omega, \tag{1.1}$$

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$$\Delta p = -\mu(\sigma - \tilde{\sigma}) \qquad \text{in } \Omega, \tag{1.2}$$

$$\sigma = \bar{\sigma}(1 - \gamma\kappa) \qquad \text{on } \partial\Omega, \tag{1.3}$$

$$p = \bar{p} \qquad \text{on } \partial\Omega, \tag{1.4}$$

$$\partial_n p = 0 \qquad \text{on } \partial\Omega, \tag{1.5}$$

where $\sigma = \sigma(x)$ and $p = p(x)$ denote concentration of nutrient and internal pressure within tumor's region $\Omega \subset \mathbb{R}^3$, respectively. σ, p and Ω are unknown and have to be determined together. κ is the mean curvature and ∂_n is the outward normal derivative on free boundary $\partial\Omega$, respectively. λ, $\bar{\sigma}$, $\bar{p}$, $\tilde{\sigma}$, γ, μ are positive dimensionless constants, where λ is the nutrient consumption rate, $\bar{\sigma}$ and $\bar{p}$ represent constant external nutrient concentration and pressure, $\tilde{\sigma}$ is the threshold value of nutrient concentration at which tumor cell's birth and death meet the balance, γ is cell-to-cell adhesiveness, and μ is the proliferation rate of tumor cells.

The above problem is a stationary version of mathematical model for the growth of solid tumors established by Byrne and Chaplain [3]. The motion of cells within a solid tumor is regarded as an incompressible fluid flow in a porous medium. Equation (1.1) describes the diffusion and consumption of nutrient within tumor region; Equation (1.2) is formulated by mass conservation law div $\mathbf{v} = \mu(\sigma - \tilde{\sigma})$ and Darcy's law $\mathbf{v} = -\nabla p$, where $\mathbf{v}$ is the velocity of tumor cells; Equation (1.3) is due to a Gibbs–Thomson relation, which means the gap (experimentally observed) of nutrient concentration across tumor boundary is proportional to the local mean curvature (cf. [3,19]); Equation (1.4) means the pressure on tumor boundary is constant; The evolution of free boundary is governed by $V_n = -\partial_n p$ where V_n is the velocity of boundary in the direction of outward normal, so equation (1.5) means the solid tumor is in a dormant state.

Neglecting the gap of nutrient concentration across boundary, another natural physical boundary condition can be imposed as follows (cf. [11,18]):

$$\sigma = \bar{\sigma}, \qquad p = \gamma\kappa \qquad \text{on } \partial\Omega, \tag{1.6}$$

and by considering evolutionary condition of free boundary:

$$V_n = -\partial_n p \qquad \text{on } \partial\Omega, \tag{1.7}$$

we get a Hele-Shaw type tumor model (1.1)–(1.2), (1.6)–(1.7). In recent decades, mathematical analysis of this kind of tumor models has attracted a lot of attention and many illuminative results have been obtained. Friedman and Reitich [15] first proved that the Hele-Shaw type tumor model (1.1)–(1.2), (1.6)–(1.7) has a unique radial stationary solution for $0 < \tilde{\sigma}/\bar{\sigma} < 1$, and it is globally asymptotically stable under radially symmetric perturbations. By employing a power series method they also proved that in two-dimensional case there exist infinite many branches of symmetry-breaking stationary solutions bifurcating from the radial one in [16]. Fontelos and Friedman [10] generalized this result into three-dimensional case. Later, Borisovich and Friedman [1], Cui and Escher [7] simplified the proof by reformulating the problem as a bifurcation problem and using classical Crandall–Rabinowitz bifurcation theorem. Motivated by bifurcation result, Friedman and Hu [12], Cui and Escher [8] studied asymptotic stability of the radial stationary solution under non-radial perturbations. For extended studies of Hele-Shaw type tumor models, we refer readers to [6,11,14] and references therein.

Though the gap of nutrient concentration across boundary is small, it is significant to study the mechanism of its formation and influence on tumor growth. Byrne and Chaplain [3,4] hypothesized that energy is expended in maintaining the tumor's compactness by cell-to-cell adhesion on the boundary and the nutrient acts as a source of energy and satisfies the Gibbs–Thomson relation. For a special simplification by replacing equation (1.1) with $\Delta\sigma = \lambda$, which means the nutrient consumption is constant, they studied radial solution and its linear stability under asymmetric perturbations in [3], and Byrne did further a weakly nonlinear analysis and numerical verification in [2]. We also refer to [25] for a recent work of a similar multi-layer tumor problem.

In this paper, we study the existence of radial and non-radial stationary solutions of problem (1.1)–(1.5), and analyze the effect of Gibbs–Thomson relation on tumor growth by comparing with the Hele-Shaw type tumor model. Due to the non-local and coupled nonlinearity, it should be pointed out that many new difficulties arise and the analysis is complicated even in radial stationary case, we need to develop some new techniques. By employing a power series method and delicate analysis, we first prove that problem (1.1)–(1.5) may have none, one or two radial stationary solutions determined by the model parameters. Note that it is an interesting difference from the uniqueness of radial stationary solution of Hele-Shaw type tumor model. More precisely, our first main result is stated as follows:

Theorem 1.1. *There exists a positive constant $\theta_* \in (0, 1)$ which is given by (2.31) such that the following assertions hold:*

(i) For $0 < \tilde{\sigma}/\bar{\sigma} < \theta_*$, problem (1.1)–(1.5) has two radial stationary solutions.
(ii) For $\tilde{\sigma}/\bar{\sigma} = \theta_*$, problem (1.1)–(1.5) has a unique radial stationary solution.
(iii) For $\tilde{\sigma}/\bar{\sigma} > \theta_*$, problem (1.1)–(1.5) has none radial stationary solution.

Next we study the existence of non-radial stationary solutions in the neighborhood of radial stationary solution. We reduce problem (1.1)–(1.5) to a bifurcation problem and regarding γ as a bifurcation parameter. By studying the linearized problem and employing spherical harmonics and some profound properties of modified Bessel functions, we solve its nontrivial solutions and get a positive sequence of degenerate points of γ. Then based on the Crandall–Rabinowitz bifurcation theorem, we can find infinite many bifurcation points, and get non-radial bifurcation solutions.

Our second main result is stated as follows:

Theorem 1.2. *Let $0 < \tilde{\sigma}/\bar{\sigma} < \theta_*$. For a given radial stationary solution with radius $r = R_s$, there exist a positive integer $k^* \geq 2$ and a positive null sequence $\{\gamma_k\}_{k\geq k^*}$, such that there exists a family of bifurcation branches of solutions of problem (1.1)–(1.5) with free boundary*

$$r = R_s + \varepsilon Y_{k,0}(\omega) + O(\varepsilon^2) \quad \text{and} \quad \gamma = \gamma_k + O(\varepsilon) \quad (k \text{ even } \geq k^*), \tag{1.8}$$

where ε is a small real parameter, $Y_{k,0}(\omega)$ is the spherical harmonic of order $(k, 0)$.

Remark 1.3. It is interesting to compare results of problem (1.1)–(1.5) with the Hele-Shaw type tumor model (1.1)–(1.2), (1.6)–(1.7) well studied in [1,7,10]. For the Hele-Shaw type tumor model, the corresponding bifurcation point γ_k is a linear function on the proliferation rate μ (see (2.17) of [10]), so μ can be also taken as a bifurcation parameter and the result indicates that a lager value of μ may make the tumor more aggressive, see [1,7,10] and similar results in [13, 23,24]. While our result shows that γ_k is independent of μ (see (3.28)), so it cannot be taken as a bifurcation parameter and has no effect on tumor's instability. It is a remarkable phenomenon caused by the Gibbs–Thomson relation effecting on tumor growth.

The structure of the rest of this paper is arranged as follows. In the next section, we show the existence of radial stationary solutions. In section 3 we first linearize the problem at a given radial stationary solution and compute its eigenvalues. In Section 4 we prove Theorem 1.2 by bifurcation analysis. In the last section, we make a conclusion and give some interesting biological implications.

2. Radial stationary solutions

In this section we study radial stationary solutions of free boundary problem (1.1)–(1.5). For simplicity of notations, by a rescaling argument we always assume $\lambda \equiv 1$ later on.

We denote radial stationary solution by $(\sigma_s, p_s, \Omega_s)$ with radius $R_s > 0$, it means that

$$\Omega_s = \{x \in \mathbb{R}^3 : r = |x| < R_s\} \quad \text{and} \quad \sigma_s(x) = \sigma_s(r), \quad p_s(x) = p_s(r) \quad \text{for} \quad x \in \Omega_s.$$

It is easy to verify that in radial case, problem (1.1)–(1.5) equals to the following system

$$\begin{cases} \sigma_s''(r) + \dfrac{2}{r}\sigma_s'(r) = \sigma_s(r) & \text{for} \quad 0 < r < R_s, \\ p_s''(r) + \dfrac{2}{r}p_s'(r) = -\mu(\sigma_s(r) - \tilde{\sigma}) & \text{for} \quad 0 < r < R_s, \\ \sigma_s(R_s) = \bar{\sigma}(1 - \dfrac{\gamma}{R_s}), \\ p_s(R_s) = \bar{p}, \\ p_s'(R_s) = 0. \end{cases} \tag{2.1}$$

Clearly, for a fixed $R_s > 0$, the solution of problem $(2.1)_1$ and $(2.1)_3$ is given by

$$\sigma_s(r) = \bar{\sigma}(1 - \frac{\gamma}{R_s})\frac{R_s \sinh r}{r \sinh R_s}, \tag{2.2}$$

and the solution of problem $(2.1)_2$ and $(2.1)_4$ can be expressed as

$$p_s(r) = -\mu\bar{\sigma}(1 - \frac{\gamma}{R_s})\frac{R_s \sinh r}{r \sinh R_s} + \frac{1}{6}\mu\tilde{\sigma}r^2 + \bar{p} + \mu\bar{\sigma}(1 - \frac{\gamma}{R_s}) - \frac{1}{6}\mu\tilde{\sigma}R_s^2. \tag{2.3}$$

We compute

$$p_s'(R_s) = -\mu\bar{\sigma}(1 - \frac{\gamma}{R_s})(\coth R_s - \frac{1}{R_s}) + \frac{1}{3}\mu\tilde{\sigma}R_s. \tag{2.4}$$

Introduce two continuous functions $f(\eta)$ and $g(\eta)$ defined on $\mathbb{R}^+$:

$$g(\eta) = \frac{\eta \coth \eta - 1}{\eta^2} \qquad \text{and} \qquad f(\eta) = (1 - \frac{\gamma}{\eta})g(\eta). \tag{2.5}$$

Then we see that $p_s'(R_s) = 0$ is equivalent to the following equation

$$f(R_s) = \frac{1}{3}\frac{\tilde{\sigma}}{\bar{\sigma}}. \tag{2.6}$$

In conclusion, we have

Lemma 2.1. *The triple $(\sigma_s(r), p_s(r), R_s)$ with the form of (2.2) and (2.3) is a solution of problem (2.1) if and only if $R_s > 0$ is a solution of equation (2.6).*

Next we study the property of function $f(\eta)$ and show the existence of positive solutions of equation (2.6).

It is easy to verify that

$$\lim_{\eta\to 0^+} g(\eta) = \frac{1}{3}, \qquad \lim_{\eta\to +\infty} g(\eta) = 0 \qquad \text{and} \qquad g(\eta) > 0 \quad \text{for } \eta > 0, \tag{2.7}$$

so that

$$\lim_{\eta\to 0^+} f(\eta) = -\infty, \qquad \lim_{\eta\to +\infty} f(\eta) = 0 \qquad \text{and} \qquad f(\eta)\begin{cases} < 0, & \text{for } 0 < \eta < \gamma, \\ \geq 0, & \text{for } \eta \geq \gamma. \end{cases} \tag{2.8}$$

Since we seek for positive solutions of (2.6), we consider $\eta > \gamma$ later on.

By a direct computation,

$$\begin{aligned} f'(\eta) &= \frac{1}{\eta^2}\Big[\gamma g(\eta) + (\eta^2 - \gamma\eta) g'(\eta)\Big] \\ &= \frac{\gamma}{\eta^4}(\eta\coth\eta - 1) + \frac{\eta-\gamma}{\eta^4\sinh^2\eta}(2\sinh^2\eta - \eta\cosh\eta\sinh\eta - \eta^2) \\ &= \frac{1}{\eta^4}\Big[-\eta^2(\eta-\gamma)\coth^2\eta - \eta(\eta-2\gamma)\coth\eta + \eta^3 - \gamma\eta^2 + 2\eta - 3\gamma\Big]. \end{aligned} \tag{2.9}$$

Then if $\eta \geq 2\gamma + 2$, by using $\coth\eta > 1$, we have

$$\begin{aligned} f'(\eta) &< \frac{1}{\eta^4}\Big[-\eta^2(\eta-\gamma) - \eta(\eta-2\gamma) + \eta^3 - \gamma\eta^2 + 2\eta - 3\gamma\Big] \\ &= \frac{1}{\eta^4}\big[\eta(2+2\gamma-\eta) - 3\gamma\big] < 0. \end{aligned} \tag{2.10}$$

On the other hand, we rewrite (2.9) as

$$f'(\eta) = \frac{1}{\eta^4\sinh^2\eta} H(\eta), \tag{2.11}$$

where

$$\begin{aligned} H(\eta) = & \left(-\eta^3 - \eta^2 \sinh\eta\cosh\eta + 2\eta\sinh^2\eta\right) + \gamma\left(\eta^2 + 2\eta\sinh\eta\cosh\eta - 3\sinh^2\eta\right) \\ \equiv & \; H_1(\eta) + \gamma H_2(\eta). \end{aligned} \tag{2.12}$$

Recall the power series expansions

$$\sinh\eta = \sum_{k=0}^{\infty} \frac{1}{(2k+1)!}\eta^{2k+1}, \qquad \cosh\eta = \sum_{k=0}^{\infty} \frac{1}{(2k)!}\eta^{2k}, \tag{2.13}$$

and

$$\begin{aligned} \sinh\eta\cosh\eta &= \frac{1}{2}\sinh 2\eta = \sum_{k=0}^{\infty} \frac{1}{(2k+1)!}2^{2k}\eta^{2k+1}, \\ \sinh^2\eta &= \frac{1}{2}(\cosh 2\eta - 1) = \sum_{k=0}^{\infty} \frac{1}{(2k+2)!}2^{2k+1}\eta^{2k+2}. \end{aligned} \tag{2.14}$$

By substituting (2.14) into (2.12), we have

$$\begin{aligned} H_1(\eta) = & -\eta^3 - \eta^2 \sum_{k=0}^{\infty} \frac{1}{(2k+1)!}2^{2k}\eta^{2k+1} + 2\eta\sum_{k=0}^{\infty} \frac{1}{(2k+2)!}2^{2k+1}\eta^{2k+2} \\ = & \sum_{k=1}^{\infty} \frac{1}{(2k+2)!}2^{2k+1}(1-k)\eta^{2k+3}, \end{aligned} \tag{2.15}$$

$$\begin{aligned} H_2(\eta) = & \; \eta^2 + 2\eta \sum_{k=0}^{\infty} \frac{1}{(2k+1)!}2^{2k}\eta^{2k+1} - 3\sum_{k=0}^{\infty} \frac{1}{(2k+2)!}2^{2k+1}\eta^{2k+2} \\ = & \sum_{k=1}^{\infty} \frac{1}{(2k+2)!}2^{2k+1}(2k-1)\eta^{2k+2}, \end{aligned} \tag{2.16}$$

and

$$\begin{aligned} H(\eta) = & \; H_1(\eta) + \gamma H_2(\eta) \\ = & \sum_{k=1}^{\infty} \frac{1}{(2k+2)!}2^{2k+1}(1-k)\eta^{2k+3} + \gamma\sum_{k=1}^{\infty} \frac{1}{(2k+2)!}2^{2k+1}(2k-1)\eta^{2k+2} \\ = & \sum_{k=1}^{\infty} \frac{1}{(2k+2)!}2^{2k+1}\eta^{2k+2}\Big[(1-k)\eta + (2k-1)\gamma\Big]. \end{aligned} \tag{2.17}$$

Then for $0 < \eta \le 2\gamma$ and $k \ge 1$ we see that

$$(1-k)\eta + \gamma(2k-1) \ge (1-k)2\gamma + (2k-1)\gamma = \gamma > 0.$$

Hence we obtain

$$H(\eta) > 0 \qquad \text{for } 0 < \eta \le 2\gamma. \tag{2.18}$$

In summary, by (2.10)–(2.12) and (2.18), there holds the following result.

Lemma 2.2. *For any given $\gamma > 0$, we have*

$$f'(\eta) \begin{cases} > 0, & \textit{for } 0 < \eta \le 2\gamma, \\ < 0, & \textit{for } \eta \ge 2\gamma + 2. \end{cases}$$

Next we study the properties of $f'(\eta)$ on $(2\gamma, 2\gamma + 2)$.

We rewrite (2.12) as

$$\begin{aligned} H(\eta) =& -\eta^3 + \gamma\eta^2 - (\eta^2 - 2\gamma\eta)\sinh\eta\cosh\eta + (2\eta - 3\gamma)\sinh^2\eta \\ =& -\eta^3 + \gamma\eta^2 - (\eta^2 - 2\gamma\eta)\frac{\sinh 2\eta}{2} + (2\eta - 3\gamma)\frac{\cosh 2\eta - 1}{2}. \end{aligned} \tag{2.19}$$

A simple computation shows that

$$\begin{cases} H'(\eta) = -3\eta^2 + 2\gamma\eta - 1 + (-\eta^2 + 2\gamma\eta + 1)\cosh 2\eta + (\eta - 2\gamma)\sinh 2\eta, \\ H''(\eta) = -6\eta + 2\gamma - 2\gamma\cosh 2\eta + (-2\eta^2 + 4\gamma\eta + 3)\sinh 2\eta, \\ H'''(\eta) = -6 - 4\eta\sinh 2\eta + (-4\eta^2 + 8\gamma\eta + 6)\cosh 2\eta, \\ H^{(4)}(\eta) = (-16\eta + 8\gamma)\cosh 2\eta + (-8\eta^2 + 16\gamma\eta + 8)\sinh 2\eta, \\ H^{(5)}(\eta) = -16\eta(\eta - 2\gamma)\cosh 2\eta - 16(3\eta - 2\gamma)\sinh 2\eta. \end{cases} \tag{2.20}$$

One can easily verify that

$$H^{(5)}(\eta) < 0 \qquad \text{for } \eta \ge 2\gamma, \tag{2.21}$$

$$H^{(k)}(2\gamma + 2) < 0 \quad \text{for } k = 1, 2, 3, 4, \tag{2.22}$$

and

$$\begin{cases} H'(2\gamma) = -8\gamma^2 - 1 + \cosh 4\gamma > 0, \\ H''(2\gamma) = 3\sinh 4\gamma - 2\gamma\cosh 4\gamma - 10\gamma, \\ H'''(2\gamma) = 6\cosh 4\gamma - 8\gamma\sinh 4\gamma - 6, \\ H^{(4)}(2\gamma) = 8\sinh 4\gamma - 24\gamma\cosh 4\gamma. \end{cases} \tag{2.23}$$

By a basic analysis we can prove that

$$\text{Equation } H^{(k)}(2\gamma) = 0 \text{ has a unique positive root } \gamma_{(k)} > 0 \text{ for each } k = 2, 3, 4. \tag{2.24}$$

Moreover, the following assertions hold:

Lemma 2.3. *For any given $\gamma > 0$, we have:*
(i) If $H^{(4)}(2\gamma) \geq 0$, then $H'''(2\gamma) > 0$;
(ii) If $H'''(2\gamma) \geq 0$, then $H''(2\gamma) > 0$.

Proof. (i) Regard γ as a variable. By (2.23), we have

$$\frac{d}{d\gamma}\big[H'''(2\gamma)\big] = 16\sinh 4\gamma - 32\gamma\cosh 4\gamma > 16(\sinh 4\gamma - 3\gamma\cosh 4\gamma) = 2H^{(4)}(2\gamma).$$

For a given $\gamma > 0$, if $H^{(4)}(2\gamma) \geq 0$, we get $\frac{d}{d\gamma}[H'''(2\gamma)] > 0$. Note that

$$H^{(k)}(2\gamma)\Big|_{\gamma=0} = 0 \qquad \text{and} \qquad \lim_{\gamma\to+\infty} H^{(k)}(2\gamma) = -\infty \qquad \text{for } k = 2, 3, 4.$$

Then by (2.24), we immediately have $H'''(2\gamma) > 0$.

(ii) Since

$$\frac{d}{d\gamma}\big[H''(2\gamma)\big] = 10\cosh 4\gamma - 8\gamma\sinh 4\gamma - 10 > H'''(2\gamma),$$

the assertion (ii) follows similarly. □

With above preparations, we can prove the following result.

Lemma 2.4. *For any given $\gamma > 0$, $f'(\eta) = 0$ has a unique solution in* $[2\gamma, 2\gamma + 2]$.

Proof. Recall (2.11) we see $f'(\eta) = \frac{1}{\eta^4 \sinh^2 \eta} H(\eta)$, it suffices to show equation $H(\eta) = 0$ has a unique solution in $[2\gamma, 2\gamma + 2]$.

Case (i): $H^{(4)}(2\gamma) \geq 0$. By (2.21) and (2.22), we have

$$H^{(4)}(\eta) = 0 \text{ has a unique solution for } \eta \text{ in } [2\gamma, 2\gamma + 2]. \tag{2.25}$$

Note that Lemma 2.3 (i) implies that $H'''(2\gamma) > 0$. By a contradiction argument we claim that

$$H'''(\eta) = 0 \text{ has a unique solution for } \eta \text{ in } [2\gamma, 2\gamma + 2]. \tag{2.26}$$

In fact, if $H'''(\eta) = 0$ has two solutions in $[2\gamma, 2\gamma + 2]$, then by $H'''(2\gamma) > 0$ and $H'''(2\gamma + 2) < 0$, one can easily show that $H^{(4)}(\eta) = 0$ has at least two solutions in $[2\gamma, 2\gamma + 2]$, and it is a contradiction.

By (2.22), (2.23), Lemma 2.2 and Lemma 2.3 (ii), we have $H^{(k)}(2\gamma) > 0$ and $H^{(k)}(2\gamma + 2) < 0$ for $k = 0, 1, 2$. Then by a similar argument, we can get that

$$H(\eta) = 0 \text{ has a unique solution for } \eta \text{ in } [2\gamma, 2\gamma + 2]. \tag{2.27}$$

Case (ii): $H^{(4)}(2\gamma) < 0$. By (2.21) we immediately have

$$H^{(4)}(\eta) < 0 \qquad \text{for} \quad 2\gamma \leq \eta \leq 2\gamma + 2.$$

Then by a similar argument we see if $H'''(2\gamma) \geq 0$, the assertion is true. If $H'''(2\gamma) < 0$, then

$$H'''(\eta) < 0 \qquad \text{for} \quad 2\gamma \leq \eta \leq 2\gamma + 2.$$

By a similar discussion for $H''(2\gamma)$, and noting that $H'(2\gamma) > 0$ and $H(2\gamma) > 0$, we can finally get (2.27). The proof is complete. □

Now we give a proof of Theorem 1.1.

Proof of Theorem 1.1. For a given $\gamma > 0$, by Lemma 2.2 and Lemma 2.4, $f(\eta)$ has a unique extremum point $\eta_* \in (2\gamma, 2\gamma + 2)$ such that

$$f'(\eta) \begin{cases} > 0, & \text{for } 0 < \eta < \eta_*, \\ = 0, & \text{for } \eta = \eta_*, \\ < 0, & \text{for } \eta > \eta_*. \end{cases} \tag{2.28}$$

Note that

$$f(\eta_*) = \max_{2\gamma \leq \eta \leq 2\gamma+2} \left(1 - \frac{\gamma}{\eta}\right) \frac{\eta \coth \eta - 1}{\eta^2}, \tag{2.29}$$

and we have

$$f(\eta) < f(\eta_*) \qquad \text{for } \eta > 0, \ \ \eta \neq \eta_*. \tag{2.30}$$

Since $g'(\eta) < 0$ for $\eta > 0$ (cf. (2.7) of [15]), by (2.7) we have

$$0 < f(\eta_*) < \frac{1}{3}.$$

Denote that

$$\theta_* := 3f(\eta_*) = \max_{2\gamma \leq \eta \leq 2\gamma+2} 3\left(1 - \frac{\gamma}{\eta}\right) \frac{\eta \coth \eta - 1}{\eta^2}. \tag{2.31}$$

Clearly, $0 < \theta_* < 1$. By using (2.8) and (2.28), we immediately get that: (i) If $\tilde{\sigma}/\bar{\sigma} > \theta_*$, then equation (2.6) has no positive solution; (ii) If $\tilde{\sigma}/\bar{\sigma} = \theta_*$, then equation (2.6) has a unique positive solution $R_s = \eta_*$; (iii) If $0 < \tilde{\sigma}/\bar{\sigma} < \theta_*$, then equation (2.6) has two positive solutions R_s^1 and R_s^2 satisfying $\gamma < R_s^1 < \eta_* < R_s^2$.

Finally, by Lemma 2.1, we complete the proof. □

3. Linearization and eigenvalues

In this section we study linearization of problem (1.1)–(1.5) at radial stationary solution $(\sigma_s, p_s, \Omega_s)$ with radius R_s and compute its eigenvalues by employing spherical harmonics and modified Bessel functions.

Denote $r = |x|$ and $\omega = x/|x|$ for $x \in \mathbb{R}^3$. Let

$$\begin{cases} \sigma(x) = \sigma_s(r) + \varepsilon\, \phi(r,\omega), \\ p(x) = p_s(r) + \varepsilon\, \psi(r,\omega), \\ \Omega = \{r < R_s + \varepsilon\, \zeta(\omega)\}, \end{cases} \tag{3.1}$$

where ε is a small parameter, and ϕ, ψ and ζ are new unknown functions. Denote Δ_ω by the Laplace–Beltrami operator on the unit sphere $\mathbb{S}^2$, then

$$\Delta = \frac{\partial^2}{\partial r^2} + \frac{2}{r}\frac{\partial}{\partial r} + \frac{1}{r^2}\Delta_\omega.$$

On boundary $\partial\Omega = \{r = R_s + \varepsilon\zeta(\omega)\}$, the mean curvature κ can be expressed as (cf. Theorem 8.1 of [17])

$$\kappa = \frac{1}{R_s} - \frac{\varepsilon}{R_s^2}[\zeta(\omega) + \frac{1}{2}\Delta_\omega\zeta(\omega)] + o(\varepsilon).$$

Recall that for the simplicity of notations, we always let $\lambda \equiv 1$. Then by substituting (3.1) into (1.1)–(1.4), using (2.1) and collecting all ε-order terms, we easily obtain the linearized equations:

$$\frac{\partial^2\phi}{\partial r^2} + \frac{2}{r}\frac{\partial\phi}{\partial r} + \frac{1}{r^2}\Delta_\omega\phi = \phi, \tag{3.2}$$

$$\frac{\partial^2\psi}{\partial r^2} + \frac{2}{r}\frac{\partial\psi}{\partial r} + \frac{1}{r^2}\Delta_\omega\psi = -\mu\phi, \tag{3.3}$$

$$\phi(R_s,\omega) + \sigma_s'(R_s)\zeta(\omega) = \frac{\bar\sigma\gamma}{R_s^2}\Big[\zeta(\omega) + \frac{1}{2}\Delta_\omega\zeta(\omega)\Big], \tag{3.4}$$

$$\psi(R_s,\omega) = 0. \tag{3.5}$$

Finally, we compute

$$\begin{aligned} \partial_n p &= \Big[\nabla p \cdot \mathbf{n}\Big]_{r=R_s+\varepsilon\zeta} = \Big[\frac{\partial p}{\partial r}\omega + \frac{1}{r}\nabla_\omega p\Big]_{r=R_s+\varepsilon\zeta} \cdot \Big[\omega + O(\varepsilon)\Big] \\ &= \varepsilon\Big[\frac{\partial\psi}{\partial r}(R_s,\omega) + p_s''(R_s)\zeta(\omega)\Big] + o(\varepsilon). \end{aligned}$$

Here we used the relations $\omega \cdot \nabla_\omega = 0$ and $p_s'(R_s) = 0$. By (2.1) we also have

$$p_s''(R_s) = -\mu\big[\bar\sigma(1 - \frac{\gamma}{R_s}) - \tilde\sigma\big],$$

it follows that the linearization of (1.5) is given by

$$\frac{\partial\psi}{\partial r}(R_s,\omega) - \mu\big[\bar\sigma(1 - \frac{\gamma}{R_s}) - \tilde\sigma\big]\zeta(\omega) = 0. \tag{3.6}$$

Next we compute eigenvalues of the linearized problem (3.2)–(3.6). By the classical theory of elliptic partial differential equations, we see that the solutions ϕ and ψ of (3.2)–(3.6) belong to $C^\infty(\overline{\Omega}_s) \subseteq C^\infty([0, R_s], C^\infty(\mathbb{S}^2))$, and the solution ζ belongs to $C^\infty(\mathbb{S}^2)$. Thus we can write

$$\begin{cases} \phi(r,\omega) = \sum_{k=0}^{\infty}\sum_{l=-k}^{k} a_{kl}(r) Y_{k,l}(\omega), \\ \psi(r,\omega) = \sum_{k=0}^{\infty}\sum_{l=-k}^{k} b_{kl}(r) Y_{k,l}(\omega), \\ \zeta(\omega) = \sum_{k=0}^{\infty}\sum_{l=-k}^{k} c_{kl} Y_{k,l}(\omega), \end{cases} \tag{3.7}$$

where $Y_{k,l}(\omega)$ $(k \geq 0, -k \leq l \leq k)$ denotes the spherical harmonic of order (k,l), and $a_{kl}(r)$, $b_{kl}(r)$ and c_{kl} and are rapidly decreasing in k. It is well-known that

$$\Delta_\omega Y_{k,l}(\omega) = -(k^2+k) Y_{k,l}(\omega) \qquad \text{for } k \geq 0.$$

By substituting (3.7) into (3.2)–(3.6), and comparing coefficients of each $Y_{k,l}(\omega)$, we have

$$a''_{kl}(r) + \frac{2}{r} a'_{kl}(r) - \frac{k^2+k}{r^2} a_{kl}(r) = a_{kl}(r), \tag{3.8}$$

$$b''_{kl}(r) + \frac{2}{r} b'_{kl}(r) - \frac{k^2+k}{r^2} b_{kl}(r) = -\mu a_{kl}(r), \tag{3.9}$$

$$a_{kl}(R_s) + \sigma'_s(R_s)\, c_{kl} = \frac{\bar{\sigma}\gamma}{R_s^2}[1 - \frac{1}{2}(k^2+k)] c_{kl}, \tag{3.10}$$

$$b_{kl}(R_s) = 0, \tag{3.11}$$

$$b'_{kl}(R_s) - \mu[\bar{\sigma}(1 - \frac{\gamma}{R_s}) - \tilde{\sigma}] c_{kl} = 0. \tag{3.12}$$

To solve the above problem we recall the modified Bessel function (cf. [21])

$$I_m(r) = \sum_{k=0}^{\infty} \frac{(r/2)^{m+2k}}{k!\Gamma(m+k+1)} \qquad \text{for } m \geq 0, \tag{3.13}$$

which satisfies

$$\begin{cases} I''_m(r) + \frac{1}{r} I'_m(r) - (1 + \frac{m^2}{r^2})\, I_m(r) = 0 \qquad \text{for } r > 0, \\ I_m(r) \text{ bounded at } r \sim 0, \end{cases} \tag{3.14}$$

and there hold the following properties:

$$I_{1/2}(r)=\sqrt{\frac{2}{\pi r}}\sinh r, \tag{3.15}$$

$$I'_m(r)+\frac{m}{r}I_m(r)=I_{m-1}(r)\quad \text{for } m\geq 1, \tag{3.16}$$

$$I'_m(r)-\frac{m}{r}I_m(r)=I_{m+1}(r)\quad \text{for } m\geq 0, \tag{3.17}$$

$$I_m(r)=\sqrt{\frac{1}{2\pi r}}e^r\left[1-\frac{4m^2-1}{8r}+O(r^{-2})\right]\quad \text{as } r\to+\infty, \tag{3.18}$$

$$I_m(r)=\sqrt{\frac{1}{2\pi m}}(\frac{er}{2m})^m\left(1+O(\frac{1}{m})\right)\quad \text{as } m\to+\infty. \tag{3.19}$$

One can easily verify that (2.2) and (2.6) can be rewritten as

$$\sigma_s(r)=\bar{\sigma}(1-\frac{\gamma}{R_s})\frac{R_s^{1/2}I_{1/2}(r)}{r^{1/2}I_{1/2}(R_s)}, \tag{3.20}$$

$$\bar{\sigma}(1-\frac{\gamma}{R_s})\frac{I_{3/2}(R_s)}{R_sI_{1/2}(R_s)}=\frac{1}{3}\tilde{\sigma}. \tag{3.21}$$

Then we have

$$\sigma'_s(R_s)=\bar{\sigma}(1-\frac{\gamma}{R_s})\frac{I_{3/2}(R_s)}{I_{1/2}(R_s)}=\frac{1}{3}\tilde{\sigma}R_s. \tag{3.22}$$

By substituting (3.22) into (3.10), and using (3.14) we get the solution of problem (3.8) and (3.10) is given by

$$a_{kl}(r)=c_{kl}\Big[\frac{\bar{\sigma}\gamma}{R_s^2}(1-\frac{1}{2}(k^2+k))-\frac{1}{3}\tilde{\sigma}R_s\Big]\frac{R_s^{\frac{1}{2}}I_{k+\frac{1}{2}}(r)}{r^{\frac{1}{2}}I_{k+\frac{1}{2}}(R_s)}. \tag{3.23}$$

Similarly, by solving problem (3.9) and (3.11), we obtain

$$b_{kl}(r)=-\mu c_{kl}\Big[\frac{\bar{\sigma}\gamma}{R_s^2}(1-\frac{1}{2}(k^2+k))-\frac{1}{3}\tilde{\sigma}R_s\Big]\Big[\frac{R_s^{\frac{1}{2}}I_{k+\frac{1}{2}}(r)}{r^{\frac{1}{2}}I_{k+\frac{1}{2}}(R_s)}-\frac{r^k}{R_s^k}\Big]. \tag{3.24}$$

By (3.17) and (3.21) we compute

$$\begin{aligned}
&b'_{kl}(R_s)-\mu c_{kl}\Big[\bar{\sigma}(1-\frac{\gamma}{R_s})-\tilde{\sigma}\Big]\\
=\;&-\mu c_{kl}\Big\{\Big[\frac{\bar{\sigma}\gamma}{R_s^2}(1-\frac{1}{2}(k^2+k))-\frac{1}{3}\tilde{\sigma}R_s\Big]\frac{I_{k+\frac{3}{2}}(R_s)}{I_{k+\frac{1}{2}}(R_s)}+\bar{\sigma}(1-\frac{\gamma}{R_s})-\tilde{\sigma}\Big\}\\
=\;&\frac{\mu\bar{\sigma}}{R_s}c_{kl}\Big[\gamma(h_k+j_k)-j_kR_s\Big],
\end{aligned} \tag{3.25}$$

where

$$h_k = (\frac{k^2+k}{2} - 1)\frac{I_{k+\frac{3}{2}}(R_s)}{R_s I_{k+\frac{1}{2}}(R_s)}, \qquad j_k = 1 - \frac{I_{\frac{3}{2}}(R_s) I_{k+\frac{3}{2}}(R_s)}{I_{\frac{1}{2}}(R_s) I_{k+\frac{1}{2}}(R_s)} - \frac{3 I_{\frac{3}{2}}(R_s)}{R_s I_{\frac{1}{2}}(R_s)}. \tag{3.26}$$

By (4.46) of [22] we have

$$j_0 < 0, \qquad j_1 = 0 \qquad \text{and} \qquad j_k > 0 \quad \text{for } k \geq 2. \tag{3.27}$$

We introduce a sequence

$$\gamma_k = \frac{j_k}{h_k + j_k} R_s \qquad \text{for } k \geq 2. \tag{3.28}$$

Thus by (3.25) we see that equation (3.12) is equivalent to

$$(\gamma - \gamma_k) c_{kl} = 0 \qquad \text{for } k \geq 2. \tag{3.29}$$

We summarize:

Lemma 3.1. *If $\gamma = \gamma_k$ for some $k \geq 2$, then problem (3.8)–(3.12) has nontrivial solutions.*

Remark 3.2. If $k = 1$, we see that (3.12) holds for any $\gamma > 0$, and problem (3.8)–(3.12) has nontrivial solutions. It is due to the fact that problem (1.1)–(1.5) is translation invariant of tumor's region Ω.

Remark 3.3. If $k = 0$, recall that $f(\eta) = (1 - \frac{\gamma}{\eta})\frac{I_{3/2}(\eta)}{\eta I_{1/2}(\eta)}$, by using (3.16) and (3.17), a direct calculation shows that

$$f'(R_s) = -\frac{1}{R_s^2}\big[\gamma(h_0 + j_0) - j_0 R_s\big]. \tag{3.30}$$

By the proof of Theorem 1.1, we see in case $0 < \tilde{\sigma}/\bar{\sigma} < \theta_*$, there always holds $f'(R_s) \neq 0$, then by (3.25) and (3.30), we see that problem (3.8)–(3.12) has only trivial solution for any $\gamma > 0$.

Next we study the sequence $\{\gamma_k\}_{k \geq 2}$ and we have

Lemma 3.4. (i) *$\gamma_k > 0$ for $k \geq 2$ and $\lim\limits_{k \to +\infty} \gamma_k = 0$;*
(ii) *There exists $k^* \in \mathbb{N}$ such that γ_k is monotone decreasing and distinct for $k \geq k^*$.*

Proof. (i) By (3.26) and (3.27), we have

$$h_k > 0 \qquad \text{and} \qquad 0 < j_k < 1 \qquad \text{for } k \geq 2.$$

Then by the definition (3.28), we see that $\gamma_k > 0$ for each $k \geq 2$.

By using (3.19), we obtain

$$\frac{I_{k+\frac{3}{2}}(r)}{I_{k+\frac{1}{2}}(r)} = er\frac{(2k+1)^{k+1}}{(2k+3)^{k+2}}\Big(1+O\Big(\frac{1}{k}\Big)\Big) = \frac{r}{2k} + O\Big(\frac{1}{k^2}\Big) \qquad \text{as } k \to +\infty, \tag{3.31}$$

it implies that

$$h_k = (\frac{k^2+k}{2} - 1)\frac{I_{k+\frac{3}{2}}(R_s)}{R_s I_{k+\frac{1}{2}}(R_s)} = \frac{k}{4} + O(1) \qquad \text{as } k \to +\infty. \tag{3.32}$$

Since $0 < j_k < 1$, we have

$$0 < \gamma_k = \frac{j_k R_s}{h_k + j_k} < \frac{R_s}{h_k + 1}.$$

Thus we get $\lim\limits_{k\to+\infty} \gamma_k = 0$.

(*ii*) By (3.31) and (3.32),

$$\lim_{k\to+\infty} j_k = 1 - \frac{3I_{3/2}(R_s)}{R_s I_{1/2}(R_s)} \equiv \Lambda > 0,$$

and

$$\lim_{k\to+\infty} k\gamma_k = \lim_{k\to+\infty} j_k R_s \frac{k}{h_k + j_k} = \lim_{k\to+\infty} 4 j_k R_s = 4\Lambda R_s > 0, \tag{3.33}$$

we have

$$\gamma_{k+1} - \gamma_k = -\frac{4\Lambda R_s}{k^2} + O(\frac{1}{k^3}) \qquad \text{as } k \to +\infty. \tag{3.34}$$

Thus the assertions (*ii*) follows. The proof is complete. $\square$

4. Non-radial stationary solutions

In this section we take cell-to-cell adhesiveness γ as a bifurcation parameter and reduce the free boundary problem (1.1)–(1.5) to a bifurcation problem, then by using Crandall–Rabinowitz bifurcation theorem we study existence of non-radial stationary solutions.

Since a tumor region Ω nearby $\Omega_s = \{x \in \mathbb{R}^3, r < R_s\}$ can be written as

$$\Omega := \Omega_\rho = \{x \in \mathbb{R}^3 : r < R_s + \rho(\omega)\} \qquad \text{for some } \rho \in C(\mathbb{S}^2),$$

we rewrite the solution (σ, p, Ω) as (σ, p, ρ), and radial stationary solution $(\sigma_s, p_s, \Omega_s)$ as $(\sigma_s, p_s, 0)$.

We fix $\alpha \in (0, 1)$ and for given $0 < \delta < \min\{1/4, R_s/4\}$ sufficiently small, denote

$$\mathcal{O}_\delta = \{\rho \in C^{4+\alpha}(\mathbb{S}^2) : \|\rho\|_{C^{4+\alpha}(\mathbb{S}^2)} < \delta\}. \tag{4.1}$$

The mean curvature on $\partial\Omega = \{x \in \mathbb{R}^3 : r = R_s + \rho(\omega)\}$ is given by

$$\kappa(\rho) = \frac{1}{2}\left[\frac{2r - \Delta_\omega \rho}{r(r^2 + |\nabla_\omega \rho|^2)^{1/2}} + \frac{2r|\nabla_\omega \rho|^2 + \nabla_\omega |\nabla_\omega \rho|^2 \cdot \nabla_\omega \rho}{2r(r^2 + |\nabla_\omega \rho|^2)^{3/2}}\right]_{r=R_s+\rho(\omega)}. \tag{4.2}$$

It follows that

$$\kappa \in C^\infty(\mathcal{O}_\delta, C^{2+\alpha}(\mathbb{S}^2)). \tag{4.3}$$

For any given $\rho \in \mathcal{O}_\delta$ and $\gamma > 0$, by the standard theory of elliptic partial differential equations, there exists a unique solution $\sigma = U(\rho, \gamma) \in C^{2+\alpha}(\overline{\Omega})$ of problem (1.1) and (1.3), and then we get a unique solution $p = V(\rho, \gamma) \in C^{4+\alpha}(\overline{\Omega})$ of problem (1.2) and (1.4). Thus by substituting $V(\rho, \gamma)$ into (1.5) and denoting

$$F(\rho, \gamma) = \partial_n V(\rho, \gamma)\Big|_{r=R_s+\rho(\omega)}, \tag{4.4}$$

we obtain a bifurcation problem

$$F(\rho, \gamma) = 0. \tag{4.5}$$

Obviously, $F(\rho, \gamma) \in C^{3+\alpha}(\mathbb{S}^2)$ and

$$F(0, \gamma) \equiv 0 \qquad \text{for } \gamma > 0. \tag{4.6}$$

Moreover, we have

Lemma 4.1. *For any $\gamma > 0$, $F(\cdot, \gamma) \in C^\infty(\mathcal{O}_\delta, C^{3+\alpha}(\mathbb{S}^2))$.*

Proof. Take a function $\chi \in C^\infty(\mathbb{R})$ such that

$$0 \le \chi(t) \le 1, \qquad \chi(t) = \begin{cases} 1, & \text{for } |t| \le \delta, \\ 0, & \text{for } |t| \ge 3\delta, \end{cases} \qquad 0 \le |\chi'(t)| \le \frac{2}{3\delta}.$$

For given $\rho \in \mathcal{O}_\delta$, we introduce the so-called Hanzawa transformation

$$\Psi_\rho(x) = x + \chi(r - R_s)\rho(\omega)\omega \qquad \text{for } x \in \mathbb{R}^3. \tag{4.7}$$

Clearly, $\Psi_\rho(\Omega_s) = \Omega_\rho$ and $\Psi_\rho \in \mathrm{Diff}^{4+\alpha}(\mathbb{R}^3, \mathbb{R}^3) \cap \mathrm{Diff}^{4+\alpha}(\Omega_s, \Omega_\rho)$. We denote by Ψ_ρ^* and $(\Psi_\rho)_*$ the pullback and push-forward operators induced by Ψ_ρ, respectively, i.e.,

$$\Psi_\rho^* u = u \circ \Psi_\rho \quad \text{for } u \in C(\overline{\Omega}_\rho) \quad \text{and} \quad (\Psi_\rho)_* v = v \circ \Psi_\rho^{-1} \quad \text{for } v \in C(\overline{\Omega}_s).$$

The Laplace operator Δ on Ω_ρ can be transformed to Ω_s by

$$\mathcal{A}(\rho) = \Psi_\rho^* \circ \Delta \circ (\Psi_\rho)_* = \sum_{i,j,k=1}^{3} a_{ij}^\rho \partial_j (a_{ik}^\rho \partial_k), \tag{4.8}$$

where $a_{ij}^{\rho} = [D\Psi_\rho]_{ij}^{-1}$ for $i, j = 1, 2, 3$. It is easy to verify that $\mathcal{A}(\rho)$ is a uniformly elliptic operator and

$$\mathcal{A} \in C^\infty(\mathcal{O}_\delta, L(C^{2+\alpha}(\overline{\Omega}_s), C^\alpha(\overline{\Omega}_s))). \tag{4.9}$$

Moreover, by Theorem 4.3.4 of [20] we have

$$(\mathcal{A}(\rho), \Upsilon) \in \mathrm{Isom}(C^{2+\alpha}(\overline{\Omega}_s), C^\alpha(\overline{\Omega}_s) \times C^{2+\alpha}(\partial\Omega_s)), \tag{4.10}$$

where Υ denotes the trace operator on $\partial\Omega_s$.

Recall that we let $\lambda \equiv 1$. Denote $u = \Psi_\rho^* \sigma$ and $v = \Psi_\rho^* p$, then by using (4.7) and (4.8) we see that problem (1.1)–(1.4) is equivalent to the following

$$\begin{cases} \mathcal{A}(\rho)u = u & \text{in } \Omega_s, \\ \mathcal{A}(\rho)v = -\mu(u - \tilde{\sigma}) & \text{in } \Omega_s, \\ u = \bar{\sigma}(1 - \gamma\kappa(\rho)) & \text{on } \partial\Omega_s, \\ v = \bar{p} & \text{on } \partial\Omega_s. \end{cases} \tag{4.11}$$

By (4.3) and (4.10), for given $\rho \in \mathcal{O}_\delta$ and $\gamma > 0$, there exists a unique solution $(\mathcal{U}(\rho, \gamma), \mathcal{V}(\rho, \gamma)) \in C^{2+\alpha}(\overline{\Omega}_s) \times C^{4+\alpha}(\overline{\Omega}_s)$ of problem (4.11), and based on implicit function theorem in Banach spaces, we can furthermore prove (see Lemma 2.3 of [9] for details)

$$\mathcal{U}(\cdot, \gamma) \in C^\infty(\mathcal{O}_\delta, C^{2+\alpha}(\overline{\Omega}_s)) \quad \text{and} \quad \mathcal{V}(\cdot, \gamma) \in C^\infty(\mathcal{O}_\delta, C^{4+\alpha}(\overline{\Omega}_s)). \tag{4.12}$$

Note that $V(\rho, \gamma) = (\Psi_\rho)_* \mathcal{V}(\rho, \gamma)$ and $\nabla_x = \omega\partial_r + r^{-1}\nabla_\omega$, we have

$$\begin{aligned} \partial_n V(\rho, \gamma)\Big|_{r=R_s+\rho(\omega)} &= \Big[(\omega\partial_r V + r^{-1}\nabla_\omega V) \cdot \frac{r\omega - \nabla_\omega \rho}{\sqrt{r^2 + |\nabla_\omega \rho|^2}}\Big]_{r=R_s+\rho(\omega)} \\ &= \Big[\frac{r^2\partial_r V - \nabla_\omega V \cdot \nabla_\omega \rho}{r\sqrt{r^2 + |\nabla_\omega \rho|^2}}\Big]_{r=R_s+\rho(\omega)}. \end{aligned} \tag{4.13}$$

Then by (4.4) and (4.12), we immediately get the desired result. The proof is complete. □

We denote $D_\rho F(0, \gamma)$ by the Fréchet derivative of $F(\rho, \gamma)$ with respect to ρ at $\rho = 0$. Since bifurcation problem (4.5) is equivalent to free boundary problem (1.1)–(1.5), their corresponding linearizations at radial stationary solution are also equivalent, i.e., $D_\rho F(0, \gamma)\zeta = 0$ is equivalent to the linearized problem (3.2)–(3.6), and we have

$$D_\rho F(0, \gamma)\zeta = \frac{\partial \psi}{\partial r}(R_s, \omega) - \mu\big[\bar{\sigma}(1 - \frac{\gamma}{R_s}) - \tilde{\sigma}\big]\zeta(\omega), \tag{4.14}$$

where $\psi(r, \omega)$ is the solution of (3.2)–(3.5) for given $\zeta(\omega) \in C^\infty(\mathbb{S}^2)$.

Hence, by the deduction in Section 3 and (3.25)–(3.30) we have

Lemma 4.2. *For any $\zeta \in C^\infty(\mathbb{S}^2)$ with expansion $\zeta = \sum_{k=0}^{\infty}\sum_{l=-k}^{k} c_{kl} Y_{k,l}(\omega)$, there holds*

$$D_\rho F(0,\gamma)\zeta = \sum_{k=0}^{\infty}\sum_{l=-k}^{k} \lambda_k(\gamma) c_{kl} Y_{k,l}(\omega), \tag{4.15}$$

where

$$\lambda_0(\gamma) = -\mu\bar{\sigma} R_s f'(R_s), \qquad \lambda_1(\gamma) = 0, \tag{4.16}$$

and

$$\lambda_k(\gamma) = \frac{\mu\bar{\sigma}}{R_s}(h_k + j_k)(\gamma - \gamma_k) \qquad \textit{for } k \geq 2, \tag{4.17}$$

with h_k, j_k and γ_k given by (3.26) and (3.28).

Next we study bifurcation solutions and give a proof of our main result Theorem 1.2 based on Crandall–Rabinowitz theorem (cf. [5]).

To this end we introduce two Banach spaces

$$X = \text{the closure of the span}\{Y_{k,0}(\omega), k = 0, 2, 4, \cdots\} \text{ in } C^{4+\alpha}(\mathbb{S}^2),$$
$$Y = \text{the closure of the span}\{Y_{k,0}(\omega), k = 0, 2, 4, \cdots\} \text{ in } C^{3+\alpha}(\mathbb{S}^2).$$

Recall that in the spherical coordinates (θ, φ), $0 \leq \theta \leq \pi$, $0 \leq \varphi \leq 2\pi$, the spherical harmonics

$$Y_{k,l}(\theta,\varphi) = (-1)^l \sqrt{\frac{(2k+1)(k-l)!}{2(k+l)!}}\, P_k^l(\cos\theta) \frac{\mathrm{e}^{il\varphi}}{\sqrt{2\pi}},$$

where

$$P_k^l(z) = \frac{1}{2^k k!}(1-z^2)^{\frac{l}{2}} \frac{\mathrm{d}^{k+l}}{\mathrm{d}z^{k+l}}(z^2-1)^k.$$

It is easy to verify that for $k \geq 0$ even, $Y_{k,0}(\theta,\varphi)$ is independent of φ and satisfies $Y_{k,0}(\theta) = Y_{k,0}(\pi - \theta)$. Hence, for any function $\rho \in X$, ρ is independent of φ and $\rho(\theta) = \rho(\pi - \theta)$. Using this fact and Lemma 4.1, we can verify that (cf. [7,13])

$$F(\cdot,\gamma) \in C^\infty(\mathcal{O}_\delta \cap X, Y) \qquad \text{for} \quad \gamma > 0. \tag{4.18}$$

Next we denote the restriction of $F(\cdot,\gamma)$ on X by $F_X(\cdot,\gamma)$.

Theorem 4.3. *Assume $f'(R_s) \neq 0$. For $k \geq k^*$ and even, $(0, \gamma_k)$ is a bifurcation point of problem (4.5). More precisely, there exist a constant $\xi_k > 0$ and a smooth mapping $\varepsilon \to (\rho_\varepsilon, \gamma_\varepsilon)$ from $(-\xi_k, \xi_k)$ to $X \times \mathbb{R}^+$ of the form*

$$\rho_\varepsilon = \varepsilon Y_{k,0}(\omega) + O(\varepsilon^2) \qquad \textit{and} \qquad \gamma_\varepsilon = \gamma_k + O(\varepsilon) \qquad \textit{for } \varepsilon \in (-\xi_k, \xi_k), \tag{4.19}$$

such that $F(\rho_\varepsilon, \gamma_\varepsilon) = 0$.

Proof. From Lemma 4.2, we see that $D_\rho F_X(0,\gamma)Y_{0,0}(\omega) = \lambda_0(\gamma)Y_{0,0}(\omega) \neq 0$ for $f'(R_s) \neq 0$, and

$$D_\rho F_X(0,\gamma)Y_{k,0}(\omega) = \frac{\mu\bar{\sigma}}{R_s}(h_k + j_k)(\gamma - \gamma_k)Y_{k,0}(\omega) \qquad \text{for} \quad k \geq 2 \text{ even.}$$

By Lemma 3.4 (ii), γ_k is monotone decreasing and distinct for $k \geq k^*$, hence we have

$$\mathrm{Ker} D_\rho F_X(0,\gamma_k) = \mathrm{span}\{Y_{k,0}(\omega)\}, \tag{4.20}$$

$$\mathrm{Im} D_\rho F_X(0,\gamma_k) \text{ has codimension } 1 \tag{4.21}$$

and

$$D_\gamma D_\rho F_X(0,\gamma_k)Y_{k,0}(\omega) = \frac{\mu\bar{\sigma}}{R_s}(h_k + j_k)Y_{k,0}(\omega) \notin \mathrm{Im}\, D_\rho F_X(0,\gamma_k). \tag{4.22}$$

By (4.6) and (4.20)–(4.22) we see all conditions of the well-known Crandall–Rabinowitz theorem (see Theorem 1.7 in [5]) are satisfied, thus $(0,\gamma_k)$ is a bifurcation point of problem $F_X(\rho,\gamma) = 0$ and the proof is complete. □

Proof of Theorem 1.2. For $0 < \tilde{\sigma}/\bar{\sigma} < \theta_*$, by Remark 3.3 we see $f'(R_s) \neq 0$. Then for $k \geq k^*$ even, by Theorem 4.3 we see that $(0,\gamma_k)$ is a bifurcation point of problem (4.5). Since (4.5) is equivalent to problem (1.1)–(1.5), we immediately get the desired assertions. □

5. Conclusion

In this paper, we study a free boundary problem modeling dormant tumors with Gibbs–Thomson relation, which is based on the hypothesis that nutrient across tumor boundary is partially consumed by tumor cells for providing energy to maintain the tumor's compactness, and the consumption is assumed by $\gamma\bar{\sigma}\kappa$. As pointed out by T. Roose, S. Chapman and P. Maini [19], a number of interesting points are raised in this model and we find some new phenomena caused by Gibbs–Thomson relation.

(i) There exists a constant $\theta_* \in (0,1)$ (given by (2.31)) depending only on cell-to-cell adhesiveness γ, such that for $0 < \tilde{\sigma}/\bar{\sigma} < \theta_*$, the free boundary problem has two radial stationary solutions; and for $\theta_* < \tilde{\sigma}/\bar{\sigma} < 1$, there exists no radial stationary solution. It is an interesting difference from the well-studied Hele-Shaw type tumor model (1.1)–(1.2) and (1.6)–(1.7), which always has a unique radial stationary solution for $0 < \tilde{\sigma}/\bar{\sigma} < 1$.

(ii) By taking γ as a bifurcation parameter, and using bifurcation analysis we established the existence of non-radial stationary solutions with free boundary $r = R_s + \varepsilon Y_{k,0}(\omega) + O(\varepsilon^2)$ and $\gamma = \gamma_k + O(\varepsilon)$. Note that these bifurcation solutions shaped as protrusions, or 'fingers', are associated with the invasion of tumors into their surrounding stroma (cf. [13]). It implies that cell-to-cell adhesiveness γ plays a crucial role on tumor invasion. Our results also show that bifurcation point γ_k is independent of the proliferation rate μ, and μ cannot be taken as a bifurcation parameter; but in Hele-Shaw type model, the bifurcation parameter can be taken as μ/γ (cf. [7,10,13]). Thus γ is the key parameter in the model studied here and should be measured accurately in experiments.

We hope these results may be useful for tumor studies and treatment.

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