ON THE STABILITY OF STEADY STATES IN A GRANULOMA MODEL

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Abstract. We consider a free boundary problem for a system of two semilinear parabolic equations. The system represents a simple model of granuloma, a collection of immune cells and bacteria filling a 3-dimensional domain $\Omega(t)$ which varies in time. We prove the existence of stationary spherical solutions and study their linear asymptotic stability as time increases to infinity.

1. Introduction

Granuloma is a medical term for a collection of immune cells known as macrophages. Granulomas are formed when the immune system attempts to wall off bacteria or other foreign substances that is unable to eliminate. A typical example is the granulomas of tuberculosis. When a person inhales Micobacteria tuberculosis, macrophages in the lung surround the bacteria, engulf them and attempt to digest them. However, once inside macrophages the bacteria multiply so that instead of a macrophage killing the bacteria, the bacteria inside a macrophage may end up killing the host macrophage.

Recent review articles [5, 9] describe the involvement of other types of immune cells, e.g., T cells and dendritic cells, in the formation of granulomas associated with Micobacteria tuberculosis. A PDE model with several different populations of macrophages, defined by the number of bacteria within them, was introduced in [6]; an agent-based model was considered in [8], and a more recent hybrid model was developed in [7].

Approximately one third of the human population are infected by Micobacteria tuberculosis, yet only a few millions are clinically sick. The reason for this disparity is that under small amount of bacteria inhalation the granulomas formed by the macrophages are small and either remain stable or eventually shrink to zero.

In the present paper we develop a simple mathematical model of granuloma and consider, mathematically, the linearized stability/instability of small radially symmetric steady states.

The model involves just macrophages and bacteria, and was introduced earlier, in the radially symmetric case, in [1]. We first establish the existence of radially symmetric steady state granulomas with any radius R, $0 < R \leq R_*$, where R_* is given explicitly by one of the model's parameters. Next we proceed to study the linear asymptotic stability when R is sufficiently small. To do this we express the linearly perturbed non-radially symmetric solution in terms of spherical harmonics $Y_{n,m}(\theta, \varphi)$ ($n \geq 0$, $|m| \leq n$) and prove that the steady state is linearly unstable in mode $n = 0$ and is linearly stable for all modes $n \geq 2$. Perturbations of modes $n \geq 2$ do not change the intial volume of granuloma, while the perturbation of mode $n = 0$ either decreases or increases the volume of the granuloma. Thus, the steady granuloma is stable only under perturbation that leaves the initial volume fixed.

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In Section 2 we introduce the dynamical model, and in Sections 3 to 6 we establish the existence of steady radially symmetric solutions for granulomas with any radius $R \in (0, R_*]$.

In Sections 7 - 9 we consider the stability/instability of the linearized model about the radially symmetric stationary solution with initial condition expanded through spherical harmonics. Linear stability results of this type have been proved in [2] for a different PDE system modeling tumor growth.

Finally, in Section 10 we interpret our analytical results in the biological context of our model.

2. The mathematical model

The model variables are

- $M(x,t)$ = density of macrophages,
- $B(x,t)$ = density of bacteria

where x varies in a 3-d domain $\Omega(t)$ which evolves with time t. The model equations are

$$\begin{cases} \frac{\partial M}{\partial t} + \nabla\cdot(M\vec{v}) - \Delta M = -\mu_1 MB - \alpha M, \\ \frac{\partial B}{\partial t} + \nabla\cdot(B\vec{v}) - \Delta B = -\mu_2 MB + \lambda B. \end{cases} \tag{2.1}$$

Here $\vec{v}$ is the velocity by which both macrophages and bacteria are moving within the granuloma, μ_1 is the rate by which bacteria kill macrophages, μ_2 is the rate by which macrophages kill bacteria, λ is the growth rate of bacteria, and α is the natural death rate of macrophages; we take $\mu_1 > 0$, $\mu_2 > 0$, $\lambda > 0$ and $\alpha \geq 0$. Actually $\lambda = \lambda(B_{in}, M_{in})$ is a nonlinear function of the bacteria B_{in} residing in infected macrophages M_{in}. The bacterial population B_{in} grow in M_{in} and when the M_{in} die naturally or burst under the pressure of large bacteria burdens, there emerge new external bacteria B. For simplicity we overlook this complex process and take λ to be a positive constant. We implicitly assumed in the model (2.1) that all the bacteria reside within the macrophages so that they move with the same velocity and have the same dispersion coefficient 1.

We assume that necrotic cells and debris are continuously being removed and that the cellular density of macrophages and bacteria is constant in $\Omega(t)$, and take

$$M + B \equiv 1 \quad \text{in } \Omega(t). \tag{2.2}$$

Adding equations (2.1), (2.2) we obtain an equation for $\vec{v}$:

$$\nabla\cdot\vec{v} = \lambda - (\lambda+\mu+\alpha)M + \mu M^2 \tag{2.3}$$

where $\mu = \mu_1 + \mu_2$. In the sequal we shall replace the first equation in (2.1) by (2.3) and set $M = 1 - B$. Thus we shall consider the following equations:

$$\begin{cases} \frac{\partial B}{\partial t} - \Delta B + \nabla\cdot(B\vec{v}) = -\mu_2(1-B)B + \lambda B, \\ \nabla\cdot\vec{v} = -\mu(1-B)B - \alpha(1-B) + \lambda B. \end{cases} \tag{2.4}$$

We next assume that the granuloma lies in a tissue that has the texture of a porous medium. Then, by Darcy's law,

$$\vec{v} = -\nabla p$$

where p is the internal pressure associated with the mobile cells. Hence the system for B and $\vec{v}$ takes the following form:

$$\frac{\partial B}{\partial t} - \Delta B - \nabla p\cdot\nabla B = -\mu_2(1-B)B + \lambda B - f(B)B \quad \text{in } \Omega(t), \tag{2.5}$$

$$-\Delta p = f(B) \quad \text{in } \Omega(t), \tag{2.6}$$

where

$$f(\sigma) = -\alpha + (\lambda - \mu + \alpha)\sigma + \mu\sigma^2. \tag{2.7}$$

We assume that macrophages enter $\Omega(t)$ from the boundary $\Gamma(t)$ at rate β, that is,

$$\frac{\partial M}{\partial \nu} = \beta(1 - M) \quad \text{on } \Gamma(t),\ \beta > 0,$$

where ν is the outward normal, so that

$$\frac{\partial B}{\partial \nu} + \beta B = 0 \quad \text{on } \Gamma(t). \tag{2.8}$$

The granuloma is held together by adhesive forces between adjacent cells at the boundary, so that

$$p = \gamma\kappa \quad \text{on } \Gamma(t) \tag{2.9}$$

where γ is the adhesive force and κ is the mean curvature, with the convention that $\kappa > 0$ on a sphere. Finally we assume that the velocity of the free boundary $\Gamma(t)$ in the outward normal direction, V_ν, coincides with the component of the velocity of $\vec{v}$ in the normal direction, that is,

$$V_\nu = -\frac{\partial p}{\partial \nu} \quad \text{on } \Gamma(t). \tag{2.10}$$

We complement the system for (B, p, Γ) by prescribing initial conditions

$$\Omega|_{t=0} = \Omega_0, \quad B|_{t=0} = B_0(x), \quad 0 \le B_0(x) \le 1. \tag{2.11}$$

Using the method developed in [3] and the estimates of [4], one can prove the existence of a unique solution to the system (2.5)-(2.11) for a small time interval. In the case of radially symmetric data, global existence and uniqueness of radially symmetric solutions was proved in [1]. In the present paper we establish the existence of spherically symmetric stationary solutions with any radius $0 < R \le j_0/(\lambda^{1/2})$ where j_0 is the smallest zero of the zeroth-order Bessel function. We then consider the time-dependent system (2.5) - (2.11) linearized about a radially symmetric steady state with small enough radius R, and study its asymptotic stability when the initial data are perturbed by a series of spherical harmonics $Y_{n,m}(\theta, \varphi)$.

3. Spherically symmetric steady states

In this section we state three theorems regarding the existence of spherically symmetric stationary solutions. Setting

$$r = |x|, \quad B = B(r), \quad \vec{v} = \frac{x}{r}v(r)$$

and denoting the radius of free boundary by R, we have the following system:

$$\frac{1}{r^2}\frac{\partial}{\partial r}\left(r^2\frac{\partial B}{\partial r}\right) = \frac{1}{r^2}\frac{\partial}{\partial r}\left(r^2 B v\right) + B[(\mu_2 - \lambda) - \mu_2 B] \tag{3.1}$$

$$\frac{1}{r^2}\frac{\partial}{\partial r}\left(r^2 v\right) = f(B) \tag{3.2}$$

where the function $f(\sigma)$ was introduced in (2.7),

$$\frac{\partial}{\partial r}B(0) = v(0) = 0, \tag{3.3}$$

$$0 < B(r) \le 1 \quad \text{if } 0 < r \le R, \tag{3.4}$$

$$v(r) > 0 \quad \text{if } 0 < r \leq R, \tag{3.5}$$

and

$$v(R) = 0. \tag{3.6}$$

Actually instead of (3.5) we could assume, more generally, that $v(r) \neq 0$ for $0 < r < R$ but, as we shall see later on, the inequality $v(r) < 0$ for $0 < r < R$ is not biologically reasonable, and certainly cannot occur mathematically if $\mu_2 \leq \lambda$ (see Theorem 3).

We also need to impose the boundary condition

$$\frac{\partial}{\partial r} B(R) + \beta B(R) = 0.$$

However, the solution will be constructed by a shooting method with $\sigma = B(0)$, the bacterial density at the center of the granuloma, as the shooting parameter. Thus the values of $B(R)$ and $B_r(R)$ will be determined by σ, and so will β. Hence we shall prescribe

$$B(0) = \sigma \tag{3.7}$$

and then determine $\beta = \beta(\sigma)$ by

$$\beta = -\frac{\partial}{\partial r} B(R)/B(R). \tag{3.8}$$

The biological interpretation of (3.8) is that in order to have a steady state with radius R the influx of macrophages from the healthy tissue $\{r > R\}$ into the granuloma has to be at a specific value β, namely,

$$\frac{\partial}{\partial r} M = \beta(1 - M) \quad \text{at } r = R$$

where $\beta = \beta(\sigma)$ is determined by (3.8). We denote by σ_0 the positive root of $f(\sigma)$, i.e.,

$$\sigma_0 = \frac{1}{2\mu}\left[-(\lambda - \mu + \alpha) + \sqrt{(\lambda - \mu + \alpha)^2 + 4\alpha\mu}\right]. \tag{3.9}$$

Then

$$f(\sigma) = \begin{cases} > 0 & \text{if } \sigma > \sigma_0, \\ < 0 & \text{if } 0 < \sigma < \sigma_0. \end{cases} \tag{3.10}$$

Note that $0 \leq \sigma_0 < 1$. Note also that if $\mu > \lambda$ and $0 < \sigma < \frac{\mu-\lambda}{\mu}$ then

$$\frac{1}{\mu} f(\sigma) = \sigma\left(\sigma - \frac{\mu - \lambda}{\mu}\right) + \frac{\alpha}{\mu}(\sigma - 1) \leq \sigma\left(\sigma - \frac{\mu - \lambda}{\mu}\right) < 0, \tag{3.11}$$

so that $\sigma < \sigma_0$. It follows that

$$\sigma_0 \geq \max\left\{0, \frac{\mu - \lambda}{\mu}\right\}. \tag{3.12}$$

We denote by j_0 the smallest zero of the zeroth-order Bessel function $I_0(r)$, and set

$$R_* = \frac{j_0}{\lambda^{1/2}} \qquad (j_0 > 2.4048). \tag{3.13}$$

Theorem 1. *Assume either $\alpha > 0$, or $\alpha = 0$ and $\mu > \lambda$. Then there is a maximal interval $(\sigma_0, \sigma_1) \subset (\sigma_0, 1)$ such that for each $\sigma \in (\sigma_0, \sigma_1)$ there exists a unique solution of (3.1)-(3.7), and the range of the radii $R = R(\sigma)$ covers the interval $0 < R \leq R_*$; furthermore, the mapping $\sigma \to R(\sigma)$ is continuous, and for each solution there holds: $B_r(r) < 0$ for $0 < r \leq R$.*

Note that when $\alpha = 0$ the condition $\mu > \lambda$ is necessary for the existence of a solution. Indeed, multiplying (3.2) by r^2 and integrating in r, we obtain,

$$v(r) = \mu \int_0^r \frac{s^2}{r^2} B \left(B - \frac{\mu - \lambda}{\mu} \right) ds > 0 \quad \text{for all } r > 0$$

if $\mu \leq \lambda$, so that the free boundary condition (3.6) cannot be satisfied.

The next theorem asserts that the mapping $\sigma \mapsto R(\sigma)$ is 1-1 if $\sigma - \sigma_0$ is small enough.

Theorem 2. *The mapping $\sigma \mapsto R(\sigma)$ is strictly monotone increasing in the interval $\sigma_0 < \sigma < \sigma_0 + \epsilon_0$ for some small enough constant ϵ_0, and*

$$R(\sigma) = \left\{ \frac{10(\lambda + \mu + \alpha)}{[\mu_2 \sigma_0 - (\mu_2 - \lambda)](\alpha + \mu \sigma_0^2)} \right\}^{1/2} (\sigma - \sigma_0)^{1/2} + O\left((\sigma - \sigma_0)^{3/2} \right). \tag{3.14}$$

Notice that (3.12) implies that $\mu_2 \sigma_0 - (\mu_2 - \lambda) > 0$ (since $\mu = \mu_1 + \mu_2 > \mu_2$).

From (3.14) we deduce that the inverse function $\sigma(R)$ to $R = R(r)$ satisfies:

$$\sigma(R) = \sigma_0 + \frac{[\mu_2 \sigma_0 - (\mu_2 - \lambda)](\alpha + \mu \sigma_0^2)}{10(\lambda + \mu + \alpha)} R^2 + O(R^4).$$

Biologically one can expect that the density of macrophages will increase toward the boundary, i.e., $M_r > 0$ or $B_r < 0$. The next theorem says that this indeed holds if $\mu_2 \leq \lambda$, and then $v(r)$ must necessarily be positive:

Theorem 3. *If $\mu_2 \leq \lambda$ then any solution of (3.1)-(3.4) with $v(r) \neq 0$ for $0 < r < R$, $v(R) = 0$, must satisfy:*

$$B_r(r) < 0 \quad \text{if } 0 < r \leq R, \quad v(r) > 0 \quad \text{if } 0 < r < R$$

and $B(0) \in (\sigma_0, 1)$.

We shall first prove Theorem 2 (in the next section) and then prove Theorems 1 and 3 (in Section 5)

Remark 3.1. In the course of proving Theorems 1 and 2 it will be shown that any solution of (3.1)-(3.5) in $0 < r < r_0$ with $B(r) > 0$ for $0 < r < r_0$, satisfies the inequality $B_r(r) < 0$ for $0 < r < r_0$. Hence the condition $B(r) \leq 1$ in (3.4) is always satisfied in this case.

4. Proof of Theorem 2

We introduce the function

$$\begin{aligned} f_1(\sigma) &= [(\mu_2 - \lambda) - \mu_2 \sigma] + f(\sigma) \\ &= -(\lambda - \mu_2 + \alpha) + (\lambda - \mu - \mu_2 + \alpha)\sigma + \mu \sigma^2. \end{aligned} \tag{4.1}$$

It will be convenient to write (3.1) in the form

$$B_{rr} = -\frac{2}{r} B_r + v B_r + B[(\mu_2 - \lambda) - \mu_2 B] + B f(B) \tag{4.2}$$

and equation (3.2), after multiplying by r^2 and integrating in r, as

$$v_r = -\frac{2}{r} v + f(B). \tag{4.3}$$

Recalling that

$$B_r(0) = v(0) = 0 \quad \text{and } B(0) = \sigma, \tag{4.4}$$

we claim that

$$B_{rr}(0) = \frac{\sigma}{3} f_1(\sigma) < 0 \quad \text{if } \sigma_0 < \sigma < 1. \tag{4.5}$$

Indeed, the equality follows from (4.2) by taking $r \to 0$. To prove that $f_1(\sigma) < 0$ we observe that $f_1(\sigma)$ is a quadratic polynomial, $f_1(1) = 0$, $f_1'(1) = \lambda + \mu_1 + \alpha > 0$, and

$$f_1(\sigma_0) = (\mu_2 - \lambda) - \mu_2 \sigma_0 < 0$$

by (3.12). It follows that $f_1(\sigma) < 0$ if $\sigma_0 \le \sigma < 1$.

We next expand $B(r)$ and $v(r)$ into power series in r. It is easily seen that B contains only even powers of r and v contains only odd powers of r:

$$B(r) = \sum_{k=0}^{\infty} b_{2k} r^{2k}, \quad v(r) = \sum_{k=0}^{\infty} v_{2k+1} r^{2k+1},$$

where $b_0 = \sigma$. Substituting these series into (4.3) we get

$$\sum_{k=0}^{\infty} (2k+3) v_{2k+1} r^{2k} = -\alpha + (\lambda - \mu + \alpha) \sum_{k=0}^{\infty} b_{2k} r^{2k} + \mu \sum_{k=0}^{\infty} \left(\sum_{\ell=0}^{k} b_{2\ell} b_{2(k-\ell)} \right) r^{2k}.$$

Hence we can express v_{2k+1} in terms of $b_0, ..., b_{2k}$:

$$v_1 = \frac{1}{3} f(\sigma)$$

$$v_{2k+1} = \frac{1}{2k+3} \left[(\lambda - \mu + \alpha) b_{2k} + \mu \sum_{\ell=0}^{k} b_{2\ell} b_{2(k-\ell)} \right] \qquad (k \ge 1).$$

In particular

$$v_3 = \frac{b_2}{b_0} [\alpha + \mu b_0^2 + f(b_0)] = \frac{B_{rr}(0)}{10\sigma} [\alpha + \mu \sigma^2 + f(\sigma)].$$

Using (4.5) we get

$$v_3 = \frac{f_1(\sigma)}{30} [\alpha + \mu \sigma^2 + f(\sigma)] \quad \text{for } \sigma_0 < \sigma < 1, \tag{4.6}$$

and, in particular, for each $\sigma' \in (\sigma_0, 1)$, there exists $\delta_1 > 0$ such that

$$v_3 < -\delta_1 < 0 \quad \text{if } \sigma_0 \le \sigma \le \sigma'. \tag{4.7}$$

On the other hand, if $\sigma = \sigma_0 + \epsilon$, ϵ positive and small, then

$$v_1 = \frac{1}{3} f'(\sigma_0) \epsilon + O(\epsilon^2) = \frac{\lambda + \mu + \alpha}{3} \epsilon + O(\epsilon^2);$$

hence $v(r) > 0$ for r small enough.

In order to determine the smallest root of

$$v(r) = v_1 r + v_3 r^3 + O(r^5),$$

we set $\sigma = \sigma_0 + \epsilon$, consider v as a function of two variables, r and ϵ, and introduce a function

$$w(\bar{r}, \epsilon) = v(\bar{r}^{1/2}) / (\bar{r}^{1/2}).$$

Then

$$w(\bar{r}, \epsilon) = \frac{1}{3} f'(\sigma_0) \epsilon + v_3|_{\sigma=\sigma_0} \bar{r} + O(\epsilon^2 + \bar{r}^2)$$

and

$$w(0,0) = 0, \quad \frac{\partial w}{\partial \bar{r}}(0,0) < -\delta_1.$$

By the implicit function theorem it follows that the zero set of w near $(0,0)$ is given by a curve $(\bar{R}_\epsilon, \epsilon)$ where $\bar{R}_\epsilon$ is a smooth function of ϵ, and

$$\frac{d\bar{R}_\epsilon}{d\epsilon}\bigg|_{\epsilon=0} = -\frac{\partial\bar{w}/\partial\epsilon}{\partial\bar{w}/\partial\bar{r}}\bigg|_{\epsilon=0}.$$

Hence $\bar{R}_\epsilon$ is given by

$$\bar{R}_\epsilon = -\frac{f'(\sigma_0)/3}{v_3|_{\sigma=\sigma_0}}\epsilon + O(\epsilon^2) = -\frac{(\lambda+\mu+\alpha)/3}{f_1(\sigma_0)[\alpha+\mu\sigma_0^2+f(\sigma_0)]/30}\epsilon + O(\epsilon^2).$$

Noting that the radius $R(\sigma)$ corresponding to $\sigma = \sigma_0 + \epsilon$ is equal to $\bar{R}_\epsilon^{1/2}$, the assertion (3.14) follows.

5. Proof of Theorems 1, 3

Multiplying (3.1) by r^2 and integrating in r, we get

$$B_r = Bv + \int_0^r \frac{s^2}{r^2} B[(\mu_2 - \lambda) - \mu_2 B]\, ds. \tag{5.1}$$

In the same way we derive from (3.2) the equation

$$v(r) = \int_0^r \frac{s^2}{r^2} f(B(s))\, ds. \tag{5.2}$$

We need several lemmas.

Lemma 5.1. *If (B,v) is a solution of (3.1)-(3.4) with $0 < B(0) < 1$ and $v(r) \geq 0$ in some interval $(0,R]$, then $B_r(r) < 0$ in $(0,R]$.*

Proof. Since $v \geq 0$ and $B < 1$, we obtain from (5.1)

$$B_r(r) \leq v(r) + \int_0^r \frac{s^2}{r^2} B[(\mu_2-\lambda) - \mu_2 B]\, ds = -\mu_1 \int_0^r \frac{s^2}{r^2}(1-B)\left(B + \frac{\alpha}{\mu}\right) ds$$

by (5.2), and the definition of f, and the right-hand side is negative. □

Lemma 5.2. *If (B,v) is a solution of (3.1)-(3.4) and $\sigma_0 < B(0) < 1$,*

$$B(r) > 0 \quad \text{in } (0,R], \quad v(r) > 0 \quad \text{in } (0,R)$$

and $v(R) = 0$, then $v_r(R) < 0$.

Proof. As long as $B(s)$ remains strictly larger than σ_0 the function $f(B(s))$ is strictly monotone increasing in $B(s)$, while $B(s)$ is strictly monotone decreasing in $s \in (0,R)$ (Lemma 5.1). Assume for contradiction that $B(R) \geq \sigma_0$, then $B(s) \geq \sigma_0$ for all $s \in (0,R)$. But this contradicts the following consequence of (5.2):

$$\int_0^R s^2 f(B(s))\, ds = R^2 v(R) = 0.$$

It follows that $B(R) < \sigma_0$, which implies that $f(B(R)) < 0$. Then, by (4.3), $v_r(R) < 0$. □

Lemma 5.3. *If (B,v) is a solution of (3.1)-(3.4) such that $B(0) = \sigma$ with $\sigma > \sigma_0$ and*

$$B(r) \geq 0, \quad v(r) \geq 0 \quad \text{in } [0,R], \quad B(R) = 0,$$

then

$$R > \frac{j_0}{\lambda^{1/2}} \equiv R_*. \tag{5.3}$$

Proof. Multiplying (3.1) by $r^2 B$ and integrating in r, $0 < r < R$, we get, after some rearranging,

$$\int_0^R s^2 B_r^2\, ds - \int_0^R s^2 B_r B v\, ds = \mu_2 \int_0^R s^2 B^3\, ds - (\mu_2 - \lambda) \int_0^R s^2 B^2\, ds. \tag{5.4}$$

The integral $\int_0^R s^2 B_r B v\, ds$ turns out to be negative; indeed

$$\begin{aligned} -\int_0^R s^2 B_r B v\, ds = \quad & = -\int_0^R s^2 v\, d\left(B^2/2\right) \\ & = -\, s^2 v \frac{B^2}{2}\Big|_0^R + \frac{1}{2}\int_0^R s^2 B^2 \frac{1}{s^2}(s^2 v)_s\, ds \\ & = \frac{1}{2}\int_0^R s^2 B^2 \frac{1}{s^2}(s^2 v)_s\, ds \\ & = \frac{1}{2}\int_0^R s^2 B^2[-\alpha + (\lambda - \mu + \alpha)B + \mu B^2]\, ds \qquad \text{by (3.2)} \\ & > \frac{\sigma_0^2}{2}\int_0^R s^2[-\alpha + (\lambda - \mu + \alpha)B + \mu B^2]\, ds \\ & = \frac{\sigma_0^2}{2} R^2 v(R) \geq 0 \end{aligned} \tag{5.5}$$

the strict inequality holds since the terms in the bracket (which is $f(B)$), satisfies

$$f(B(s)) = \begin{cases} > 0 & \text{if } B(s) \in (\sigma_0, 1); \\ < 0 & \text{if } B(s) \in (0, \sigma_0); \end{cases}$$

whereas the last integral coincides with $R^2 v(R)$, by (5.2).

We also have

$$\mu_2 \int_0^R s^2 B^3 - (\mu_2 - \lambda) \int_0^R s^2 B^2 < \mu_2 \int_0^R s^2 B^2 - (\mu_2 - \lambda) \int_0^R s^2 B^2 = \lambda \int_0^R s^2 B^2.$$

Substituting these inequalities and (5.5) into (5.4) we get the estimate

$$\int_0^R s^2 B_r^2 \leq \lambda \int_0^R s^2 B^2. \tag{5.6}$$

We next note that if

$$A = \inf_{u(R)=0} \frac{\|\nabla u\|_{L^2(B_R)}}{\|u\|_{L^2(B_R)}}$$

where $B_R = \{r < R\}$, then the infimum is attained by the function $u = I_0\left(\frac{j_0}{R} r\right)$ and $A = j_0/R$. Hence

$$\int_0^R s^2 B^2 < \frac{R^2}{j_0^2} \int_0^R s^2 B_r^2.$$

Substituting this into (5.6), the assertion (5.3) follows. □

Proof of Theorem 1. For any $\sigma \in (\sigma_0, 1)$ we construct a solution (B, v) of (3.1)-(3.3), (3.7) for all $r > 0$ by existence and uniqueness of ODE. We say that $\sigma \in (\sigma_0, 1]$ belongs to the set $\mathcal{P}$ if there exists an $R > 0$ such that (3.4)-(3.6) hold. By Theorem 2, $\mathcal{P}$ contains a small interval $(\sigma_0, \sigma_0 + \epsilon_0)$. The set $\mathcal{P}$ is an open set. Indeed, if $\bar{\sigma} \in \mathcal{P}$ with the corresponding solution $(\bar{B}, \bar{v}, \bar{R})$, then

$$\bar{B}(r) > 0 \quad \text{in } [0, \bar{R}] \quad \bar{v}(r) > 0 \quad \text{in } (0, \bar{R}), \quad \bar{v}(\bar{R}) = 0$$

and, by Lemma 5.2, $\bar{v}_r(\bar{R}) < 0$. It follows that

$$\bar{v}(\bar{R} - \delta) > 0, \quad \bar{v}(\bar{R} + \delta) < 0, \quad \bar{B}(r) > 0 \quad \text{if } 0 < r \leq \bar{R} + \delta$$

for some small positive numbers δ. By continuity of solution (B, v) in the parameter σ it follows that if $|\sigma - \bar{\sigma}|$ is sufficiently small then the solution (B, v) with $B(0) = \sigma$ satisfies:

$$B(r) > 0 \quad \text{if } r \leq \bar{R} + \delta,$$

$$v(\bar{R} - \delta) > 0, \quad v(\bar{R} + \delta) < 0.$$

Hence $v(R) = 0$ for some $R = R(\sigma)$ in the interal $(\bar{R} - \delta, \bar{R} + \delta)$, and thus $\mathcal{P}$ is an open set. It follows that $\mathcal{P}$ consists of a union of open intervals. The above proof, and especially Lemma 5.2, also shows that the mapping $\sigma \to R(\sigma)$ is continuous.

We denote by (σ_0, σ_1) the largest interval contained in $\mathcal{P}$. Then either (i) $R(\sigma) \to \infty$ as $\sigma \to \sigma_1$, or (ii) $R(\sigma) \to R_1 < \infty$ for a subsequence $\sigma \to \sigma_1$. It suffices to show that $R_1 > R_*$ in Case (ii). The first case clearly occurs if $\sigma_1 = 1$ for then $B(r) \equiv 1$ and $v(r) = (\lambda v)/3$. Hence, in the second case, $\sigma_1 < 1$ and by the maximality of the interval (σ_0, σ_1) and the continuity argument above it follows that the solution corresponding to $B(0) = \sigma_1$ satisfies the conditions of Lemma 5.3, so that $R_1 > R_*$. Thus, in both cases, by the Intermediate Value Theorem, the continuous function $R(\sigma)$ takes all the values in $(0, R_1) \supset (0R_*]$ as σ varies in the interval (σ_0, σ_1). □

Proof of Theorem 3. We may assume that $0 < B(0) < 1$. Indeed if $B(0) = 1$ then by uniqueness of solutions of (3.1)-(3.3), $B(r) \equiv 1$ and $v(r) = \frac{\lambda r}{3}$ so that $v(R) \neq 0$. The assertion that $B_r < 0$ now follows by rewriting (5.1) in the form

$$B_r = -\mu_1 B \int_0^r \frac{s^2}{r^2}(1-B)\left(B + \frac{\alpha}{\mu_2}\right) ds + (1-B)\int_0^r \frac{s^2}{r^2} B[(\mu_2 - \lambda) - \mu_2 B]\, ds < 0$$

using the assumption that $\mu_2 \leq \lambda$.

Next, we note that if a solution of (3.1)-(3.4) satisfies $B_r < 0$, then $B(0)$ cannot belong to $[0, \sigma_0]$, for then $f(B(s)) < 0$ for all $0 < s < R$ and from (5.2) we would have $v(R) < 0$. Hence $B(0) \in (\sigma_0, 1)$. □

6. The linearized system

The rest of the paper is concerned with the linear asymptotic stability of the radially symmetric stationary solution satisfying (3.1) - (3.8) for small radius R. Let us first recall some of the estimates derived in Section 4, and add a few others for the steady state solution (B_S, p_S, v_S, R) with $B_S(0) = \sigma$, $\sigma - \sigma_0$ positive and small and $0 < r < R$:

$$\sigma - \sigma_0 = \frac{[\mu_2\sigma_0 - (\mu_2 - \lambda)](\alpha + \mu\sigma_0^2)}{10(\lambda + \mu + \alpha)} R^2 + O(R^4) := \sigma_1 R^2 + O(R^4), \tag{6.1}$$

$$B_S(r) = \sigma + \frac{\sigma}{3} f_1(\sigma) r^2 + O(r^4) = \sigma_0 + O(R^2), \tag{6.2}$$

$$\beta = -\frac{(B_S)_r(R)}{B_S(R)} = -\frac{\frac{2}{3}\sigma f_1(\sigma) R + O(R^3)}{\sigma + \frac{\sigma}{3} f_1(\sigma) R^2 + O(R^4)} = -\frac{2}{3} f_1(\sigma_0) R + O(R^3) := \lambda_\beta R + O(R^3), \tag{6.3}$$

$$\begin{aligned} \frac{\partial p_S}{\partial r}(r) = -v_S(r) &= -\frac{1}{3} f(\sigma) r - \frac{(B_S)_{rr}(0)}{10\sigma}[\alpha + \mu\sigma^2 + f(\sigma)] r^3 + O(r^5) \\ &= -\frac{1}{3} f'(\sigma_0)\sigma_1 R^2 r - \frac{f_1(\sigma_0)}{15}[\alpha + \mu\sigma_0^2] r^3 + O(R^5), \end{aligned} \tag{6.4}$$

$$\begin{aligned} \frac{\partial^2 p_S}{\partial r^2}(r) = -\frac{\partial v_S}{\partial r}(r) &= -\frac{1}{3} f(\sigma) - 3\frac{(B_S)_{rr}(0)}{10\sigma}[\alpha + \mu\sigma^2 + f(\sigma)] r^2 + O(r^4) \\ &= -\frac{1}{3} f'(\sigma_0)\sigma_1 R^2 - \frac{f_1(\sigma_0)}{5}(\alpha + \mu\sigma_0^2) r^2 + O(R^4). \end{aligned} \tag{6.5}$$

Since $0 = v_S(R) = v_1 R + v_3 R^3 + O(R^5)$, we have

$$v_3 R^2 = -v_1 + O(R^4) = -\frac{1}{3} f(\sigma) + O(R^4);$$

hence

$$\frac{\partial^2}{\partial r^2}p_S(R) = -\frac{\partial}{\partial r}v(R) = -v_1 - 3v_3R^2 + O(R^4) = \frac{2}{3}f(\sigma) + O(R^4) = \frac{2}{3}f'(\sigma_0)\sigma_1 R^2 + O(R^4). \tag{6.6}$$

To derive uniform stability estimate for all steady states with sufficiently small radius, it will be convenient to make a change of variables replacing the ball with radius R by the unit ball. Accordingly we set

$$\begin{gathered} t = R^2\bar{t}, \quad x = R\bar{x}, \\ B(x,t) = B_S(R\bar{r}) + \epsilon w(\bar{r},\theta,\varphi,\bar{t}), \\ p(x,t) = p_S(R\bar{r}) + \epsilon q(\bar{r},\theta,\varphi,\bar{t}), \\ \partial\Omega(t) : \bar{r} = 1 + \epsilon\rho(\theta,\varphi,\bar{t}) \end{gathered}$$

where $(B_S(r), p_S(r), R)$ is the steady state solution satisfying (3.1) - (3.8). Substituting these variables into the system (2.5) - (2.11) and dropping all the $O(\epsilon^2)$ terms, as well as the bar " $^-$ " from all the variables, we obtain, after multiplying by R^2, the following linearized system for $(w(r,\theta,\varphi,t), q(r,\theta,\varphi,t), \rho(\theta,\varphi,t))$:

$$w_t - \Delta w - (p_S)_r w_r - (B_S)_r q_r + R^2 g'(B_S(r))w = 0 \qquad \text{for } x \in B_1, t > 0, \tag{6.7}$$

$$\left(\frac{\partial}{\partial r}w + \beta R w\right)\Big|_{r=1} = -\left(\frac{\partial^2}{\partial r^2}B_S\big|_{r=1} + \beta R\frac{\partial}{\partial r}B_S\big|_{r=1}\right)\rho \qquad \text{for } t > 0, \tag{6.8}$$

$$-\Delta q = R^2 f'(B_S)w \qquad \text{for } x \in B_1, t > 0, \tag{6.9}$$

$$q\big|_{r=1} = \frac{-1}{R}(\rho + \frac{1}{2}\Delta_\omega \rho) \qquad \text{for } x \in \partial B_1, t > 0, \tag{6.10}$$

$$\frac{\partial \rho}{\partial t} = R^{-2}\left[\frac{\partial v_S}{\partial r}\bigg|_{r=1}\rho - \frac{\partial q}{\partial r}\bigg|_{r=1}\right] \qquad \text{for } t > 0, \tag{6.11}$$

with initial conditions

$$w\big|_{t=0} = w_0(r,\theta,\varphi), \quad \rho\big|_{t=0} = \rho_0(\theta,\varphi). \tag{6.12}$$

Here B_1 denotes the unit ball in $\mathbb{R}^3$, Δ_ω is the Laplace-Beltrami operator on ∂B_1,

$$B_S = B_S(Rr), \quad p_S = p_S(Rr), \quad v_S = v_S(Rr)$$

where $(B_S(r), p_S(r), v_S(r); R)$ is the steady state solution with radius R, and

$$g(B) = [(\mu_2 - \lambda) - \mu_2 B]B + Bf(B). \tag{6.13}$$

In the following two sections it will be shown that the system (6.7) - (6.12) has a unique solution. However the main focus is on the question whether the solution converges to zero as $t \to \infty$, which means asymptotic stability of the linearized problem. We shall expand the initial data in terms of spherical harmonics $Y_{n,m}(\theta,\varphi)$, and prove that the zero order modes are unstable whereas all modes of order $n \geq 2$ are stable. These results will be proved for R sufficiently small.

7. Zero modes are unstable

It will be convenient to introduce the following constants:

$$\begin{aligned} &\lambda_B = -\tfrac{2}{3}\sigma_0 f_1(\sigma_0), && \lambda_q = f'(\sigma_0), && \lambda_\beta = -\tfrac{2}{3}f_1(\sigma_0), \\ &\lambda_w = g'(\sigma_0), && \lambda_p = \tfrac{2}{3}f'(\sigma_0)\sigma_1. && \end{aligned}$$

(σ_0, σ_1 are defined in (3.9) and (6.1) respectively.) Note that, with the possible exception of λ_w, all other constants are positive. We first consider the stability of the zero mode, that is, the system (6.7) - (6.12) with

$$w\big|_{t=0} = w_0(r), \quad \rho\big|_{t=0} = \rho_0, \quad \text{where } w_0 \text{ is a given radial function and } \rho_0 \text{ is a constant.} \tag{7.1}$$

Then the corresponding solution of (6.7) - (6.12) is radially symmetric and its global existence can be established as in [2].

Theorem 4. *If R is sufficiently small then there exists a pair $(w(r), \rho)$ for which the corresponding solution has the form*

$$(e^{at}w(r), e^{at}q(r), e^{at}\rho)$$

with $a > 0$, namely,

$$a = \frac{R}{2}\left[-\lambda_p + \sqrt{\lambda_p^2 + 4\lambda_B\lambda_q} + O(R)\right].$$

Thus, the steady state solution is linearly asymptotically unstable with respect to zero modes.

Proof. We can take $\rho = R^{-2}$ and, after replacing q by $q - \frac{1}{R}\rho$, we obtain for w and the new q the following system:

$$-\Delta w - (p_S)_r w_r + [a + R^2 g'(B_S(r))]w = (B_S)_r q_r \qquad \text{in } B_1 \tag{7.2}$$

$$\frac{\partial}{\partial r}w + \beta R w = -R^{-2}\left(\frac{\partial^2}{\partial r^2}B_S\Big|_{r=1} + \beta R\frac{\partial}{\partial r}B_S\Big|_{r=1}\right) \qquad \text{on } \partial B_1, \tag{7.3}$$

$$-\Delta q = R^2 f'(B_S)w \qquad \text{in } B_1 \tag{7.4}$$

$$q\big|_{r=1} = 0 \tag{7.5}$$

where

$$a = R^{-2}\left(\frac{\partial v_S}{\partial r}\Big|_{r=1}\right) - \frac{\partial q}{\partial r}\Big|_{r=1}. \tag{7.6}$$

We introduce a set

$$\Gamma_R = \left\{z \in \mathbb{C} : \operatorname{Re} z \in (\epsilon_0 R, \epsilon_0^{-1}R), \quad |\operatorname{Im} z| < \epsilon_0^{-1}R\right\}$$

for small but fixed $\epsilon_0 > 0$ (hence $\epsilon_0^{-1}R \sim R$ will be sufficiently small) and take a to be in Γ_R; from the proof which follows it will be seen that ϵ_0 depends only on λ_p and $\lambda_B\lambda_q$. We wish first to solve for $(w, q) = (w(a), q(a))$ from (7.2) - (7.5), and then determine a from (7.6).

Lemma 7.1. *For any $a \in \gamma_R$ there exists a unique solution of* (7.2) - (7.5) *satisfying the following estimates:*

$$\|w\|_{W^{2,p}} \le \frac{C}{\epsilon_0 R}, \quad \|q\|_{W^{2,p}} \le \frac{CR}{\epsilon_0}. \tag{7.7}$$

Proof of Lemma 7.1. The existence can be proved by iteration: Let w_0 solve

$$\begin{cases} -\Delta w - (p_S)_r w_r + [a + R^2 g'(B_S(r))]w = 0, \\ \dfrac{\partial}{\partial r}w + \beta R w = -R^{-2}\left(\dfrac{\partial^2}{\partial r^2}B_S\Big|_{r=1} + \beta R\dfrac{\partial}{\partial r}B_S\Big|_{r=1}\right) = \lambda_B + O(R^2) \end{cases}$$

(note that $\beta R\frac{\partial}{\partial r}B_S\big|_{r=1} = O(R^2)$). Set

$$w_0 = u + iv, \quad W = |w_0|^2 = u^2 + v^2.$$

Then

$$-\frac{1}{2}\Delta W + [\operatorname{Re} a + R^2 g'(B_S(r))]W = (p_S)_r(uu_r + vv_r) - (|\nabla u|^2 + |\nabla v|^2).$$

Since

$$\mathrm{Re}\,\{a + R^2 g'(B_S(r))\} > \frac{1}{2}\epsilon_0 R$$

and $(p_S)_r = O(R^3)$, W satisfies the inequality

$$-\frac{1}{2}\Delta W + \left(\frac{1}{4}\epsilon_0 R\right) W < 0 \quad \text{in } B_1$$

and the boundary condition

$$\left(\frac{1}{2}\frac{\partial}{\partial r}W + \beta R W\right)\Big|_{r=1} = u\left(\frac{\partial}{\partial r}u + \beta R u\right)\Big|_{r=1} \le W[\lambda_B + O(R^2)].$$

We can then easily verify that $\frac{C}{\epsilon_0 R} e^{\epsilon_0 R r^2}$ is a supersolution for some constant C. Hence

$$\|w_0\|_{L^\infty} \le \frac{C}{\epsilon_0 R},$$

and by L^p estimates, we get the stronger bound

$$\|w_0\|_{W^{2,p}} \le \frac{C}{\epsilon_0 R}.$$

We next define successively, for $i = 0, 1, 2, \ldots$, sequences q_i, w_i where q_i is a solution of (7.4),(7.5) with $w = w_i$, and $w = w_{i+1}$ is the solution of (7.2) with $q = q_i$, satisfying the boundary condition

$$\frac{\partial}{\partial r}w + \beta r w = 0 \quad \text{on } \partial B_1.$$

We then have the estimates

$$\|q_i\|_{W^{2,p}} \le C R^2 \|w_i\|_{L^p}$$

and

$$\|w_{i+1}\|_{W^{2,p}} \le \frac{C}{R\epsilon_0}(\|(B_S)_r q_{i,r}\|_{L^p}) \le \frac{C}{R\epsilon_0}(R^2\|q_i\|_{W^{1,p}}) \le \frac{C}{R\epsilon_0}(R^4\|w_i\|_{L^p}) \le \frac{CR^3}{\epsilon_0}\|w_i\|_{L^p} \le \left(\frac{CR^3}{\epsilon_0}\right)^i \|w_0\|_{L^p}.$$

If R is chosen sufficiently small, then the functions $w = \sum w_k$ and $q = \sum q_k$ form the solution of (7.2) - (7.5) and the estimates in (7.7) hold. □

Lemma 7.2. *The following estimate holds in the C^1 norm:*

$$w(r) = \frac{I_{1/2}(r\sqrt{a + \lambda_w R^2})}{r^{1/2}} \frac{\lambda_B + O(R^2)}{\lambda_\beta R^2 I_{1/2}(\sqrt{a + \lambda_w R^2}) + \sqrt{a + R^2\lambda_w}\, I_{3/2}(\sqrt{a + R^2\lambda_w})} + O(R^2) \tag{7.8}$$

where $I_{j/2}(r)$ is the (modified) Bessel function of order $j/2$.

Proof of Lemma 7.2. We write (7.2) in the form

$$-\Delta w + (a + R^2\lambda_w)w = (p_S)_r w_r + R^2(g'(\sigma_0) - g'(B_S))w + (B_S)_r q_r.$$

By (6.4), $(p_S)_r = O(R^3)$, and by (6.1), (6.2),

$$g'(\sigma_0) - g'(B_S) = O(R^2), \quad (B_S)_r = O(R^2).$$

Recalling the estimate (7.7) and $\frac{\partial q}{\partial r} = O(R)$, we find that

$$-\Delta w + (a + R^2\lambda_w)w = O(R^2). \tag{7.9}$$

Next we note, by (6.2), (6.3), that the right-hand side of (7.3) is equal to

$$-R^{-2} \cdot R^2 \frac{2\sigma}{3} f_1(\sigma) + O(R^2) = \lambda_B + O(R^2),$$

and, by (6.3),

$$\beta R w = \lambda_\beta R^2 w + O(R^4) w = \lambda_\beta w + O(R^3).$$

Hence

$$\frac{\partial}{\partial r} w + \lambda_\beta R^2 w = \lambda_B + O(R^2). \tag{7.10}$$

Recalling the identity

$$\frac{d}{dr}\left(\frac{I_{1/2}(rz_0)}{r^{1/2}}\right) = \frac{z_0}{r^{1/2}} I_{3/2}(rz_0) \quad \text{for each } z_0 \in \mathbb{C},$$

we see that the solution of (7.9), (7.10) with $O(R^2)$ dropped is given by (7.8) with the $O(R^2)$ terms dropped out, and the assertion of the lemma then easily follows. □

Introducing the function

$$P_0(\xi) = \frac{I_{1/2}(\xi)}{\xi I_{3/2}(\xi)}$$

and setting $r = 1$ in (7.8), we get

$$w\big|_{r=1} = \frac{\lambda_B + O(R^2)}{\lambda_\beta R^2 + (a + R^2\lambda_w) P_0(\sqrt{a + R^2\lambda_w})} + O(R^2). \tag{7.11}$$

We next turn to the function q. Since by (6.1), (6.2) and (7.7),

$$R^2 f'(B_S) w - R^2 f'(\sigma_0) w = O(R^4) w = O(R^3),$$

the function q satisfies:

$$-\Delta q = R^2 \lambda_q w + O(R^3) \quad \text{in } B_1, \quad q\big|_{r=1} = 0. \tag{7.12}$$

Hence the function $\psi = q + \frac{\lambda_q R^2}{a + \lambda_w R^2} w$ then satisfies the equation

$$-\Delta\psi = O(R^3) + \frac{\lambda_q R^2}{a + \lambda_w R^2} O(R^2) = O(R^3) \quad \text{in } B_1,$$

and, by (7.11), the boundary condition

$$\psi\big|_{r=1} = \frac{\lambda_q R^2}{a + \lambda_w R^2} w\Big|_{r=1} = \frac{\lambda_q R^2}{a + \lambda_w R^2} \cdot \left(\frac{\lambda_B + O(R^2)}{\lambda_\beta R^2 + (a + \lambda_w R^2) P_0(\sqrt{a + \lambda_w R^2})} + O(R^2)\right).$$

We conclude that ψ is a constant up to $O(R^2)$, namely,

$$\psi(r) = \frac{\lambda_q \lambda_B R^2}{(a + \lambda_w R^2)[(\lambda_\beta R^2 + (a + \lambda_w R^2) P_0(\sqrt{a + \lambda_w R^2})]} + O(R^2).$$

Going back to the function $q = \psi - \frac{\lambda_q R^2}{a + \lambda_w R^2} w$, we have, by (7.10) and (7.11),

$$\begin{aligned}
\frac{\partial q}{\partial r}\Big|_{r=1} &= -\frac{\lambda_q R^2}{a + \lambda_w R^2} \frac{\partial w}{\partial r}\Big|_{r=1} + O(R^2) \\
&= -\frac{\lambda_q R^2}{a + \lambda_w R^2}\left[\lambda_B + O(R^2) - \lambda_\beta R^2 w\Big|_{r=1}\right] + O(R^2) \\
&= -\frac{\lambda_q R^2}{a + \lambda_w R^2}\left\{\lambda_B - \lambda_\beta R^2 \left[\frac{\lambda_B + O(R^2)}{\lambda_\beta R^2 + (a + \lambda_w R^2) P_0(\sqrt{a + \lambda_w R^2})} + O(R^2)\right]\right\} + O(R^2) \\
&= -\frac{\lambda_q R^2}{a + \lambda_w R^2} \lambda_B \left[1 - \frac{\lambda_\beta R^2}{\lambda_\beta R^2 + (a + \lambda_w R^2) P_0(\sqrt{a + \lambda_w R^2})}\right] + O(R^2) \\
&= -\frac{\lambda_q R^2}{a + \lambda_w R^2} \lambda_B \left[\frac{(a + \lambda_w R^2) P_0(\sqrt{a + \lambda_w R^2})}{\lambda_\beta R^2 + (a + \lambda_w R^2) P_0(\sqrt{a + \lambda_w R^2})}\right] + O(R^2).
\end{aligned}$$

Hence,

$$\frac{\partial q}{\partial r}\Big|_{r=1} = -\frac{\lambda_B \lambda_q R^2 P_0(\sqrt{a+\lambda_w R^2})}{\lambda_\beta R^2 + (a+\lambda_w R^2) P_0(\sqrt{a+\lambda_w R^2})} + O(R^2).$$

From (6.6) and the definition of λ_p we also have

$$R^{-2}\frac{\partial v_S}{\partial r}\big|_{r=1} = R^{-2}\left(-\frac{2}{3}f'(\sigma_0)\sigma_1 R^3 + O(R^4)\right) = -\lambda_p R + O(R^2),$$

and equation (7.6) for a then becomes

$$a = R^{-2}\left.\frac{\partial v_S}{\partial r}\right|_{r=1} - \left.\frac{\partial q}{\partial r}\right|_{r=1} = -\lambda_p R + \frac{\lambda_B \lambda_q R^2 P_0(\sqrt{a+\lambda_w R^2})}{\lambda_\beta R^2 + (a+\lambda_w R^2) P_0(\sqrt{a+\lambda_w R^2})} + O(R^2).$$

We set $a = R\tilde{a}$, so that $\epsilon_0 < \operatorname{Re}\tilde{a} < \epsilon_0^{-1}$ and $|\operatorname{Im}\tilde{a}| < \epsilon_0^{-1}$. Then, after canceling R, we obtain the following equation for $\tilde{a}$:

$$\tilde{a} = -\lambda_p + \frac{\lambda_B \lambda_q P_0(\sqrt{R\tilde{a}+\lambda_w R^2})}{\lambda_\beta R + (\tilde{a}+\lambda_w R) P_0(\sqrt{R\tilde{a}+\lambda_w R^2})} + O(R). \tag{7.13}$$

Consider this equation for $R = 0$ and use the fact that $P_0(0) > 0$. Then

$$\tilde{a} + \lambda_p - \frac{\lambda_B \lambda_q}{\tilde{a}} = 0.$$

It follows that

$$\tilde{a} = \frac{1}{2}\left\{-\lambda_p \pm \sqrt{\lambda_p^2 + 4\lambda_B\lambda_q}\right\} + O(R).$$

Hence the solutions of (7.13) for R small are

$$a = \frac{R}{2}\left\{-\lambda_p \pm \sqrt{\lambda_p^2 + 4\lambda_B\lambda_q}\right\} + O(R^2).$$

Since $\lambda_B\lambda_q > 0$, one of the roots is positive, and from the above analysis we see that ϵ_0 can be chosen from the beginning to depend only on the parameters λ_p and $\lambda_B\lambda_q$. This completes the proof of Theorem 4. $\square$

8. Stability of higher modes

In this section we consider the system (6.7) - (6.12) with higher modes in the initial conditions $w(r,\theta,\varphi)$, $\rho(\theta,\varphi)$ and construct the solution in the form

$$w = \sum_{n,m} w_{n,m}(r,t) Y_{n,m}(\theta,\varphi), \quad q = \sum_{n,m} q_{n,m}(r,t) Y_{n,m}(\theta,\varphi),$$

$$\rho = \sum_{n,m} \rho_{n,m}(t) Y_{n,m}(\theta,\varphi),$$

where $Y_{n,m}$ are the spherical harmonic of mode (n,m), $m = 0, \pm 1, \ldots, \pm n$, and we shall take $n \geq 2$; the case $n = 1$ will be discussed in Remark 8.1 at the end of the section.

Suppressing the subscripts n, m, each triplet $(w_{n,m}, q_{n,m}, \rho_{n,m})$ satisfies the following system:

$$w_t - \Delta w - (p_S)_r w_r + \left[\frac{n(n+1)}{r^2} + R^2 b_w\right] w = (B_S)_r q_r \qquad \text{for } x \in B_1, t > 0, \tag{8.1}$$

$$\left(\frac{\partial}{\partial r} w + \beta R w\right)\Big|_{r=1} = -\left(\frac{\partial^2}{\partial r^2} B_S\big|_{r=1} + \beta R \frac{\partial}{\partial r} B_S\big|_{r=1}\right) R^{-2}\rho := b_B \rho \qquad \text{for } t > 0, \tag{8.2}$$

$$-\Delta q + \frac{n(n+1)}{r^2} q = R^2 f'(B_S) w \qquad \text{for } x \in B_1, t > 0, \tag{8.3}$$

$$q\big|_{r=1} = \frac{1}{R^3}\left(\frac{n(n+1)}{2} - 1\right)\rho \qquad \text{for } t > 0, \tag{8.4}$$

$$\frac{\partial \rho}{\partial t} = R^{-2} \frac{\partial v}{\partial r}\Big|_{r=1} \rho - \frac{\partial q}{\partial r}\Big|_{r=1} := -R b_p \rho - \frac{\partial q}{\partial r}\Big|_{r=1} \qquad \text{for } t > 0, \tag{8.5}$$

$$w(r,0) = w_{0,n,m}(r) \quad \rho\big|_{t=0} = \rho_{0,n,m} \tag{8.6}$$

where we have also replaced ρ by $R^{-2}\rho$ (which does not affect the linear stability/instability), and

$$b_w = \lambda_w + O(R), \quad b_B = \lambda_B + O(R), \quad b_p = \lambda_p + O(R)$$

are positive constants plus an $O(R)$ term. We will make use of the following estimate.

Lemma 8.1. *Consider, for any positive number $n \geq 1$, the elliptic problem*

$$\begin{cases} -\Delta w + \dfrac{n(n+1)}{r^2} w = b(r) \quad \text{in } B_1, \quad \text{and} \quad w\big|_{r=1} = 0. \end{cases} \tag{8.7}$$

If $b \in L^\infty(B_1)$, then this problem has a unique solution w in $H^2(B_1) \cap C^1(\bar{B}_1)$; furthermore, for all $p > 3$,

$$\|w\|_{C^1(\bar{B}_1)} \leq C_0 \|b\|_{L^p(B_1)}, \tag{8.8}$$

where $C_0 = C_0(p)$ is a constant independent of n.

The proof is given in Section 9.

We now state the main result of this section.

Theorem 5. *There exists a constant C_0 such that, for all R sufficiently small, and $\delta = (2R^2)^{-1}$, the solution (w, q, ρ) of (8.1) - (8.6) satisfies:*

$$\|(w,q,\rho)(\cdot,t)\|_{L^\infty} \leq C_0 n^3 e^{-\delta n^2 t} \left(\|w_{0,n,m}\|_{L^\infty} + \|\rho_{0,n,m}\|_{L^\infty}\right) \quad \textit{for all } n \geq 2, |m| \leq n. \tag{8.9}$$

Proof. Fix n, m and choose R small such that

$$\frac{2}{R^2} + R^2 (\inf_{[0,1]} g') > 0$$

and, with $\delta = \frac{1}{2R^2}$,

$$2n^2\delta < \frac{n(n+1)}{R^2} + R^2 g'(B_S(r)) \quad \text{for all } n \geq 2 \text{ and } 0 < r < 1). \tag{8.10}$$

Let $\tilde{w} = e^{\delta n^2 t} w$, $\tilde{q} = e^{\delta n^2 t}$ and $\tilde{\rho} = e^{\delta n^2 t}\rho$. Then it suffices to show that $\tilde{w}$ and $\tilde{q}$ are bounded uniformly in t. The equations for $\tilde{w}$ and $\tilde{q}$ and $\tilde{\rho}$ are

$$\tilde{w}_t - \Delta\tilde{w} - (p_S)_r\tilde{w}_r + \left[-\delta n^2 + \frac{n(n+1)}{r^2} + R^2 b_w\right]\tilde{w} = (B_S)_r\tilde{q}_r \qquad \text{in } B_1, \tag{8.11}$$

$$\left(\frac{\partial}{\partial r}\tilde{w} + \beta R\tilde{w}\right)\Big|_{r=1} = -\left(\frac{\partial^2}{\partial r^2}B_S\big|_{r=1} + \beta R\frac{\partial}{\partial r}B_S\big|_{r=1}\right)R^{-2}\tilde{\rho} = b_B\rho, \tag{8.12}$$

$$-\Delta\tilde{q} + \frac{n(n+1)}{r^2}\tilde{q} = R^2 f'(B_S)\tilde{w} \qquad \text{in } B_1, \tag{8.13}$$

$$\tilde{q}\big|_{r=1} = \frac{1}{R^3}\left(\frac{n(n+1)}{2} - 1\right)\tilde{\rho}, \tag{8.14}$$

$$\frac{\partial\tilde{\rho}}{\partial t} = \left(\delta n^2 + R^{-2}\frac{\partial v_S}{\partial r}\big|_{r=1}\right)\tilde{\rho} - \frac{\partial\tilde{q}}{\partial r}\Big|_{r=1} = \left(\delta n^2 - Rb_p\big|_{r=1}\right)\tilde{\rho} - \frac{\partial\tilde{q}}{\partial r}\Big|_{r=1}, \tag{8.15}$$

$$\tilde{w}(r,0) = w_{0,n,m}(r), \quad \tilde{\rho}(0) = \rho_{0,n,m} \in \mathbb{R}. \tag{8.16}$$

Note that b_w, b_B and b_p are uniformly bounded. We decompose $\tilde{w} = \tilde{w}_1 + \tilde{w}_2$ and $\tilde{q} = \tilde{q}_1 + \tilde{q}_2$, where $(\tilde{w}_1, \tilde{q}_1)$ satisfies the system

$$(\tilde{w}_1)_t - \Delta\tilde{w}_1 - (p_S)_r(\tilde{w}_1)_r + \left[-\delta n^2 + \frac{n(n+1)}{r^2} + R^2 g'(B_S(r))\right]\tilde{w}_1 = (B_S)_r(\tilde{q}_1)_r \qquad \text{in } B_1, \tag{8.17}$$

$$\left(\frac{\partial}{\partial r}\tilde{w}_1 + \beta R\tilde{w}_1\right)\Big|_{r=1} = -\left(\frac{\partial^2}{\partial r^2}B_S\big|_{r=1} + \beta R\frac{\partial}{\partial r}B_S\big|_{r=1}\right)R^{-2}\tilde{\rho} = b_B\tilde{\rho}, \tag{8.18}$$

$$-\Delta\tilde{q}_1 + \frac{n(n+1)}{r^2}\tilde{q}_1 = R^2 f'(B_S)\tilde{w}_1 \qquad \text{in } B_1, \tag{8.19}$$

$$\tilde{q}_1\Big|_{r=1} = \frac{1}{R^3}\left(\frac{n(n+1)}{2} - 1\right)\tilde{\rho}, \tag{8.20}$$

$$\tilde{w}_1(r,0) = 0, \tag{8.21}$$

and $(\tilde{w}_2, \tilde{q}_2)$ satisfies the system

$$(\tilde{w}_2)_t - \Delta\tilde{w}_2 - (p_S)_r(\tilde{w}_2)_r + \left[-\delta n^2 + \frac{n(n+1)}{r^2} + R^2 b_w\right]\tilde{w}_2 = (B_S)_r(\tilde{q}_2)_r \qquad \text{in } B_1, \tag{8.22}$$

$$\left(\frac{\partial}{\partial r}\tilde{w}_2 + \beta R\tilde{w}_2\right)\Big|_{r=1} = 0, \tag{8.23}$$

$$-\Delta\tilde{q}_2 + \frac{n(n+1)}{r^2}\tilde{q}_2 = R^2 f'(B_S)\tilde{w}_2 \qquad \text{in } B_1, \tag{8.24}$$

$$\tilde{q}_2\Big|_{r=1} = 0, \tag{8.25}$$

$$\tilde{w}_2(r,0) = w_{0,n,m}(r). \tag{8.26}$$

Lemma 8.2. *There exist constants C, R_1, δ_1 independent of n, $n \geq 2$ such that for all $R \in (0, R_1)$,*

$$\sup_{B_1\times[0,\infty)}|\tilde{w}_2| \leq C\sup_{B_1}|w_{0,n,m}| \quad \textit{and} \quad |\tilde{q}_2|_{C^1(\bar{B}_1\times[0,\infty)}\leq CR^2\sup_{B_1}|w_{0,n,m}|.$$

Proof of Lemma 8.2. To see that $\tilde{w}_2$ and $\tilde{q}_2$ are bounded, we note that the coefficient of the zeroth order term of (8.1) satisfies $\left[-\delta n^2 + \frac{n(n+1)}{r^2} + R^2 g'(B_S(r))\right] > \frac{\delta n^2}{R^2} > 0$. Therefore we can apply the maximum principle to (8.22) - (8.23) and obtain the estimate

$$\sup_{B_1\times[0,T]}|\tilde{w}_2| \leq \sup_{B_1}|w_{0,n,m}| + \frac{\|(B_S)_r(\tilde{q}_2)_r\|_\infty}{\delta n^2/R^2} \leq \sup_{B_1}|w_{0,n,m}| + \frac{CR^3}{\delta n^2}\sup_{B_1\times[0,T]}|(\tilde{q}_2)_r|. \tag{8.27}$$

Next, by Lemma 8.1,

$$\sup_{B_1} |(\tilde{q}_2)_r(\cdot,t)| \le CR^2 \sup_{B_1} |\tilde{w}_2(\cdot,t)| \tag{8.28}$$

with C independent of n. Combining (8.27) and (8.28), we have

$$\sup_{B_1\times[0,T]} |\tilde{w}_2| \le \sup_{B_1} |w_{0,n,m}| + \frac{CR^3\|(\tilde{q}_2)_r\|_\infty}{\delta n^2} \le \sup_{B_1} |w_{0,n,m}| + \frac{CR^5}{\delta n^2} \sup_{B_1\times[0,T]} |\tilde{w}_2|$$

and boundedness assertion for $\tilde{w}_2$ follows if we choose $R \in (0, R_1)$ where $\frac{CR_1^5}{\delta n^2} < \frac{1}{2}$. The asserted estimate for $\tilde{q}_2$ follows by applying Lemma 8.1 to (8.24) - (8.25) and using the estimate on $\tilde{w}_2$. □

To estimate $(\tilde{w}_1, \tilde{q}_1)$, we decompose $\tilde{q}_1 = \tilde{q}_{1,1} + \tilde{q}_{1,2}$ such that

$$-\Delta\tilde{q}_{1,1} + \frac{n(n+1)}{r^2}\tilde{q}_{1,1} = 0 \quad \text{in } B_1, \quad \text{and} \quad \tilde{q}_{1,1} = \frac{1}{R^3}\left(\frac{n(n+1)}{2} - 1\right)\tilde{\rho} \quad \text{on } \partial B_1, \tag{8.29}$$

$$-\Delta\tilde{q}_{1,2} + \frac{n(n+1)}{r^2}\tilde{q}_{1,2} = R^2 f'(B_S)\tilde{w}_1 \quad \text{in } B_1, \quad \text{and} \quad \tilde{q}_{1,2} = 0 \quad \text{on } \partial B_1. \tag{8.30}$$

Then

$$\tilde{q}_{1,1}(r,t) = \frac{r^n}{R^3}\left(\frac{n(n+1)}{2} - 1\right)\tilde{\rho}(t). \tag{8.31}$$

Moreover, by Lemma 8.1,

$$\|\tilde{q}_{1,2}(\cdot,t)\|_{C^1(\bar{B}_1)} \le C_0 R^2 \|\tilde{w}_1(\cdot,t)\|_{L^\infty(B_1)} \tag{8.32}$$

and by the maximum principle (recalling (8.10)),

$$\begin{aligned}
\|\tilde{w}_1\|_{L^\infty(\bar{B}_1\times[0,T])} &\le \frac{CR^2}{\delta n^2}\|(\tilde{q}_1)_r\|_\infty \\
&= \frac{2R^4}{2^2}\left(\|(\tilde{q}_{1,1})_r\|_\infty + \|(\tilde{q}_{1,2})_r\|_\infty\right) \\
&\le \frac{2R^4}{2^2}\left[\frac{nr^{n-1}}{R^3}\left(\frac{n(n+1)}{2} - 1\right)\max_{[0,T]}|\tilde{\rho}| + \|\tilde{q}_{1,2}\|_{C^1(\bar{B}_1)}\right] \quad \text{(by (8.31))} \\
&\le CR^4\left[\frac{n^3}{R^3}\max_{[0,T]}|\tilde{\rho}|\right] + \frac{C_0R^6}{2}\|\tilde{w}_1\|_{L^\infty(\bar{B}_1\times[0,T])} \quad \text{(by (8.32))}.
\end{aligned} \tag{8.33}$$

Hence, if R is sufficiently small independently of $n \ge 2$, then

$$\|\tilde{w}_1\|_{C^1(\bar{B}_1\times[0,T])} \le CRn^3 \max_{[0,T]}|\tilde{\rho}|, \tag{8.34}$$

and by (6.3),

$$\|\tilde{q}_{1,2}(\cdot,t)\|_{C^1(\bar{B}_1)} \le C_0R^2\|\tilde{w}_1(\cdot,t)\|_{L^\infty(B_1)} \le CR^3n^3 \max_{[0,T]}|\tilde{\rho}|. \tag{8.35}$$

Therefore, (8.15) becomes for $0 < t \le T$, T arbitrary,

$$\begin{aligned}
\frac{\partial\tilde{\rho}}{\partial t} &= \left(\delta n^2 - Rb_\rho\big|_{r=1}\right)\tilde{\rho} - \frac{\partial\tilde{q}}{\partial r}\Big|_{r=1} \\
&= \left(\delta n^2 - Rb_\rho\big|_{r=1}\right)\tilde{\rho} - \frac{\partial\tilde{q}_{1,1}}{\partial r}\Big|_{r=1} - \frac{\partial\tilde{q}_{1,2}}{\partial r}\Big|_{r=1} - \frac{\partial\tilde{q}_2}{\partial r}\Big|_{r=1} \\
&= \left\{\delta n^2 - Rb_\rho\big|_{r=1} - \frac{n}{R^3}\left(\frac{n(n+1)}{2} - 1\right)\right\}\tilde{\rho} + O(R^3n^3)\max_{[0,T]}|\tilde{\rho}| + O(R^2\sup_{B_1}|w_{0,n,m}|).
\end{aligned}$$

Hence, choosing R small such that for all $n \geq 2$,

$$\delta n^2 - Rb_\rho - \frac{n}{R^3}\left(\frac{n(n+1)}{2} - 1\right) < \min\left\{-\frac{n^3}{10R^3}, -\left|O(R^3n^3)\right|\right\} \leq -\frac{n^3}{20R^3}, \tag{8.36}$$

we deduce that

$$\max_{[0,\infty)} |\tilde{\rho}| \leq |\rho_{0,n,m}| + \frac{CR^5}{n^3}.$$

This in turn yields, by (8.31), (8.34) and (8.35), the bound

$$\frac{1}{Rn^3} \sup_{B_1\times[0,\infty)} |\tilde{w}_1| + \frac{R^3}{n^2} \sup_{B_1\times[0,\infty)} |\tilde{q}_{1,1}| + \frac{1}{R^3n^3} \sup_{B_1\times[0,\infty)} |\tilde{q}_{1,2}| \leq C \max_{[0,\infty)} |\tilde{\rho}|.$$

Combining this with the bounds on $\tilde{w}_2$ and $\tilde{q}_2$ obtained in Lemma 8.2, the proof of Theorem 5 is complete. □

We now take any initial values

$$w\big|_{t=0} = \sum_{\substack{n,\,m\\ n\geq 2}} w_{0,n,m}(r)Y_{n,m}(\theta,\varphi), \quad \rho\big|_{t=0} \sum_{\substack{n,\,m\\ n\geq 2}} \rho_{0,n,m}Y_{n,m}(\theta,\varphi) \tag{8.37}$$

such that

$$A := \sum_{n,m} n^3 \left(\|w_{0,n,m}\|_{L^\infty(B_1)} + \|\rho_{0,n,m}\|_{L^\infty(\partial B_1)}\right) < \infty. \tag{8.38}$$

Then, from Theorem 5 we immediately obtain the more general result:

Theorem 6. *If R is sufficiently small then the system* (6.7) - (6.12) *with initial data given by* (8.37), (8.38) *has a unique solution with converges to zero as $t \to \infty$, and*

$$\|w(\cdot,t), q(\cdot,t)\|_{L^\infty(B_1)} + \|\rho(\cdot,t)\|_{L^\infty(\partial B_1)} \leq Ce^{-\frac{2}{R^2}t} \tag{8.39}$$

where C is a constant depending only on A.

Remark 8.1. *Consider finally initial data of the form*

$$w\big|_{r=0} = \sum_{m=-1}^{1} w_{0,1,m}(r)Y_{n,m}(\theta,\varphi), \quad \rho\big|_{t=0} = \sum_{m=-1}^{1} \rho_{0,1,m}Y_{1,m}(\theta,\varphi).$$

In this case the proof of Theorem 5 does not extend directly. In fact, due to the nature of our free-boundary problem, the linear system (6.7) - (6.12) *is invariant with respect to translation of initial data. Therefore, we may expect to establish asymptotic stability only after an appropriate translation of the center of the ball by a small vector, as in* [2].

9. Proof of Lemma 8.1

The existence of a solution to (8.7) in $H^2(B_1)$ for any $b \in L^2(B_1)$ follows from Lemma 3.2 in [2]. The proof goes as follows: Let B_δ denote the ball $\{|x| < \delta\}$ and consider the sequence w_δ of solutions of (8.7) in $B_1 \setminus B_\delta$ with the zero boundary condition on $\partial(B_1 \setminus B_\delta)$. Then, a uniform (in δ) H^2-estimate is established, which shows that a subsequence w_{δ_k} converges weakly in H^1 to the unique solution w of (8.7), and the uniform H^2 estimate on the w_δ implies that $w \in H^2$.

It remains to derive the L^∞ estimate of w_r.

Written in radial coordinates, (8.7) becomes

$$-\frac{1}{r^2}(r^2w_r)_r + \frac{n(n+1)}{r^2}w = b(r) \quad \text{for } r \in (0,1] \quad \text{and} \quad w(1) = 0. \tag{9.1}$$

Set $w(r) = r^n z(r)$, then $w_r = nr^{n-1}z + r^n z_r$, and

$$(r^2 w_r)_r = n(n+1)r^n z + 2r^{n+1}(n+1)z_r + r^{n+2}z_{rr}.$$

By (9.1) we can then write

$$r^2 b = -(r^2 w_r)_r + n(n+1)w = -2r^{n+1}(n+1)z_r - r^{n+2}z_{rr} = -(r^{2(n+1)}z_r)_r r^{-n},$$

so that

$$-(r^{2(n+1)}z_r)_r = r^{n+2}b. \tag{9.2}$$

By elliptic estimates, $|w| + |w_r|$ and hence $|r^{2(n+1)}z_r|$ is uniformly bounded away from $r = 0$, therefore we may integrate (9.2) from r to 1 to obtain

$$r^{2(n+1)}z_r = C + \int_r^1 s^{n+2}b(s)\,ds = C_1 + \int_0^r s^{n+2}b(s)\,ds = C_1 + O(r^{n+2+\frac{p-3}{p}}) \tag{9.3}$$

where we have used the estimate

$$\left|\int_0^r s^{n+2}b(s)\,ds\right| = \int_0^r s^{2/p}|b| \cdot s^{n+2-2/p}\,ds \le \left(\int_0^1 s^2|b|^p\,ds\right)^{1/p}\left(\int_0^r s^{\frac{p}{p-1}\left(n+2-\frac{2}{p}\right)}\,ds\right)^{\frac{p-1}{p}}.$$

From (9.3) we deduce that $z_r = C_1 r^{-2(n+1)} + O(r^{-n+\frac{p-3}{p}})$ and hence, by integration from r to 1,

$$z = C_0 - \frac{C_1}{2n+1}r^{-2n-1} + O(r^{-n+1+\frac{p-3}{p}}), \tag{9.4}$$

so that

$$w = C_0 r^n - \frac{C_1}{2n+1}r^{-n-1} + O(r^{1+\frac{p-3}{p}}).$$

Since $w \in H^2$, we must have $C_1 = 0$. By (9.3), (9.4) (with $C_1 = 0$) we then get

$$w_r = nr^{n-1}z + r^n z_r = nC_0 r^{n-1} + O(r^{\frac{p-3}{p}}).$$

A review of the proof shows that the right-hand side is actually bounded by

$$C(nr^{n-1} + r^{(p-3)/p})\|b\|_{L^p(B_1)},$$

where C is a constant depending on $p > 3$, but independent of b, and $n \ge 1$. The proof of (8.8) follows.

Remark 9.1. The proof of Lemma 8.1 does not extend to the case $n < 1$. A counter-example is the function $w = r^n - r^2$ $(0 < n < 1)$, which satisfies

$$\begin{cases} -\frac{1}{r^2}(r^2 w_r)_r + \frac{n(n+1)}{r^2}w = -n(n+1) + 6, \\ w|_{r=1} = 0, \end{cases}$$

while $|w_r|$ is unbounded.

10. Discussion

In this paper we have proved the existence of radially symmetric steady state granulomas and analyzed their linear stability when their radii are sufficiently small. Precisely, steady granulomas of radii $0 < R \le R_*$ are shown to exist, where $R_* = j_0/\lambda^{\frac{1}{2}}$ with j_0 being the smallest zero of the zeroth-order Bessel function and λ being the proliferation rate of bacteria. Furthermore, the solution is linearly asymptotically stable with respect to any perturbation of mode $n \ge 2$, but linearly unstable under any perturbation of mode 0.

A perturbation of mode 0 changes the volume (i.e. the radius R) of the steady granuloma, and the instability that we proved is actually suggested by the underlying biology of the model. For this we recal that the macrophages recruitment rate β (i.e. $\frac{\partial M}{\partial \nu} = \beta(1-M)$ on the boundary) is related to the radius R of steady granuloma by the relation $\beta = -\frac{\partial B}{\partial r}(R)/B(R)$. It can be seen from our previous analysis that the radius R is a monotone increasing function of the macrophages recruitment rate β for all small values of β and R. Thus $R = \Phi(\beta)$ where Φ is an increasing function of β. We may then view a perturbation of R as a perturbation of β. Suppose we perturb β by increasing it to $\beta + \Delta\beta$. Then the recruitment rate of macrophages increases which helps combat the bacterial population, so we expect the granuloma to shrink. Assuming that the steady state is asymptotically stable, the perturbed system must then converge to a steady state with radius R'. Moreover, R' should be strictly smaller than R. But it violates the relation $R' = \Phi(\beta+\Delta\beta)$, as Φ is an increasing function. Hence 0-mode perturbation cannot be asymptotically stable. We conjecture that by increasing β to $\beta + \Delta\beta$, the radius $R(t)$ of the granuloma will actually converge to 0.

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