A Stefan problem for a protocell model

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Abstract

The paper considers a simple model of radially symmetric cell which undergoes growth due to a continuous supply of nutrient, and disintegration as a result from the various tasks the cell performs. The boundary of the cell is a "free boundary", unknown in advance, which evolves by responding to both the growth and disintegration processes. If the nutrient concentration (at infinity) exceeds a certain critical number, then two stationary solutions exist. It is established, by rigorous mathematical proofs, that the stationary solution with the smaller radius is unstable, whereas the stationary solution with the larger radius is stable.

Keywords. protocell, parabolic system, free boundary problem.

1 The model

In this paper we consider a physico-chemical model of a self-maintaining protocell which undergoes process of growth and dissolution that mimics (but greatly simplifies) biological cells. The model was initiated and studied in [4] [5]. The protocell can be visualized as having a porous structure maintained by building materials with concentration C; the structure is sustained only as long as C exceeds a critical concentration C^*. Metabolism is maintained by nutrient material with concentration σ which is distributed in the entire space with $\sigma = \tau$ at ∞ ($\tau > 0$). C and σ satisfy a coupled system of reaction diffusion equations:

$$c\frac{\partial C}{\partial t} - \Delta C = -\sigma, \quad \Delta\sigma + \sigma = 0 \quad \text{in the cell,}$$

$$\Delta\sigma = 0 \quad \text{outside the cell,}$$

where c is a positive constant. The constant c is the quotient of the time scale of diffusion to the time scale of cell doubling. In cases of interest, such as in tumor growth [1], [2], c is a very small constant.

On the boundary of the protocell $C = C^*$. The various tasks that the cell continuously performs take their toll on the cell: they cause it to shrink. This is modelled by disintegration at the boundary at a rate β, $\beta > 0$. On the other hand the flux of building material at the boundary causes the cell to grow. The total result of these two effects is

$$V_n = -\frac{\partial C}{\partial n} - \beta$$

where n is the exterior normal, and V_n is the velocity of the boundary points in the direction n.

We shall consider here only the case of a spherical cell (in 3-dimensions). Setting

$$r = \sqrt{x_1^2 + x_2^2 + x_3^2}, \quad u = C^* - C$$

and denoting the boundary of the cell by $r = s(t)$, we then have the following system for $u = u(r,t), \sigma = \sigma(r,t)$ and $r = s(t)$:

$$\Big(\frac{\partial^2}{\partial r^2} + \frac{2}{r}\frac{\partial}{\partial r}\Big)\sigma = \sigma\chi_{\{r<s(t)\}}(r,t) \quad \text{in } \mathbb{R}^3, \tag{1.1}$$

$$\sigma \to \tau \quad \text{as } |x| \to \infty, \tag{1.2}$$

and

$$cu_t - \Big(\frac{\partial^2}{\partial r^2} + \frac{2}{r}\frac{\partial}{\partial r}\Big)u = \sigma \quad \text{if } r < s(t),\ t > 0, \tag{1.3}$$

$$u = 0 \quad \text{on } r = s(t),\ t > 0, \tag{1.4}$$

$$u = u_0(r) \quad \text{for } t = 0, \tag{1.5}$$

and finally, the free boundary condition

$$s'(t) = -u_r(s(t),t) - \beta. \tag{1.6}$$

As shown in [4], if τ/β is less than a critical number μ^* then no steady state solutions exist, whereas if τ/β is larger than μ^* then there exist two steady state solution, with free boundary radii R_0^- and R_0^+, $R_0^- < R_0^+$. Numerical results and some heuristic arguments are given in [4] to show that the solution with R_0^- is unstable whereas the solution with R_0^+ is stable. The purpose of this paper is to give rigorous mathematical proofs of these results.

In §§2, 3 we establish various estimates and prove existence and uniqueness of the solution to (1.1)–(1.6). In §4 we prove that the stationary solution corresponding to R_0^- is unstable. In §5 we prove that the stationary solution corresponding to R_0^+ is stable if c is suitably small.

2 A priori bounds on the solution

The function

$$g(r) = \frac{r^2}{r - \tanh r} \quad (0 < r < \infty) \tag{2.1}$$

will play a fundamental role in what follows. One can easily verify that $r - \tanh r > 0$, so that $g(r) > 0$; furthermore, $g(r) \to \infty$ if $r \to 0$ or $r \to \infty$ and there is a unique $r = R^*$ where $g(r)$ attains its minimum μ^*, i.e.,

$$\min_{0<r<\infty} g(r) = g(R^*) = \mu^*. \tag{2.2}$$

One can compute that

$$R^* \approx 1.6061486, \quad \text{and} \quad \mu^* \approx 3.7739398.$$

The steady state solutions with free boundary $r = R_0$ are given by

$$u(r) = \frac{\tau}{\cosh R_0}\Big(\frac{\sinh R_0}{R_0} - \frac{\sinh r}{r}\Big) \quad \text{for } r < R_0, \tag{2.3}$$

where R_0 satisfies

$$\frac{\tau}{\beta} = \frac{R_0^2}{R_0 - \tanh R_0} = g(R_0). \tag{2.4}$$

If $\tau/\beta < \mu^*$ then there are no steady state solutions, whereas if $\tau/\beta > \mu^*$ then there are two solutions, $u_{R_0^+}$ and $u_{R_0^-}$, corresponding to $R_0 = R_0^+$ and $R_0 = R_0^-$, where $R_0^- < R^* < R_0^+$. As τ/β increases from μ^* to ∞, R_0^- decreases from R^* to 0 and R_0^+ increases from R^* to $+\infty$.

For a given $s(t)$, equation (1.1) with the boundary condition (1.2) can be solved explicitly ([4] (8), (9)):

$$\sigma(r,t) = \begin{cases} \tau\Big(1 - \dfrac{s(t) - \tanh s(t)}{r}\Big) & \text{for } r \geqslant s(t), \\ \tau\ \dfrac{1}{\cosh s(t)}\ \dfrac{\sinh r}{r} & \text{for } r < s(t). \end{cases} \tag{2.5}$$

Substituting (2.5) into (1.3), we get an equation for u involving the free boundary:

$$cu_t - \Big(\frac{\partial^2}{\partial r^2} + \frac{2}{r}\frac{\partial}{\partial r}\Big)u = \tau\ \frac{1}{\cosh s(t)}\ \frac{\sinh r}{r} \quad \text{if } r < s(t),\ t > 0. \tag{2.6}$$

Further,

$$u = 0 \quad \text{on } r = s(t),\ t > 0, \tag{2.7}$$

$$s'(t) = -u_r(s(t),t) - \beta \quad \text{if } t > 0, \tag{2.8}$$

and

$$u = u_0(r) \quad \text{for } t = 0. \tag{2.9}$$

Lemma 2.1 *If a solution of (2.6)–(2.9) exists for the time interval $[0,T]$, then*

$$\begin{aligned} \frac{4\pi}{3}s^3(t) = \frac{4\pi}{3}s^3(0) &+ c\int_{\{r<s(0)\}} u_0(r)dV - c\int_{\{r<s(t)\}} u(r,t)dV \\ &+ 4\pi\tau\int_0^t \Big[\frac{1}{g(s(\xi))} - \frac{\beta}{\tau}\Big]s^2(\xi)d\xi \end{aligned} \tag{2.10}$$

for $0 < t \leqslant T$.

Proof. By integration of (2.6) we get

$$\begin{aligned} & c\int_{\{r<s(t)\}} u(r,t)dV - c\int_{\{r<s(0)\}} u_0(r)dV \\ &= c\int_0^t \int_{\{r<s(\xi)\}} u_t(r,\xi)dVd\xi \\ &= \int_0^t \int_{\{r=s(\xi)\}} \frac{\partial u}{\partial r}dS + \tau\int_0^t \int_0^{s(\xi)} \frac{1}{\cosh s(t)}\frac{\sinh r}{r}4\pi r^2 drd\xi \\ &= 4\pi\int_0^t \Big\{s^2(\xi)[-s'(\xi) - \beta] + \tau[s(\xi) - \tanh s(\xi)]\Big\}d\xi \\ &= \frac{4\pi}{3}[s^3(0) - s^3(t)] + 4\pi\int_0^t \{\tau[s(\xi) - \tanh s(\xi)] - \beta s^2(\xi)\}d\xi, \end{aligned}$$

from which the lemma follows. □

We shall henceforce assume that

$$0 \leqslant u_0(r) \leqslant C_0(s(0) - r) \quad \text{for } 0 \leqslant r < s(0), \tag{2.11}$$

where C_0 is a positive constant.

Theorem 2.2 *If a solution $(u(r,t), s(t))$ of (2.6)–(2.9) exists for all $0 < t < T$ $(T \leqslant \infty)$, then*

$$s(t) < R \quad \forall 0 < t < T \tag{2.12}$$

where R is a constant independent of T.

Proof. We distinguish two cases:

Case (i): $\tau/\beta \leqslant \mu^*$. Since $u_0(r) \geqslant 0$, we have, by the maximum principle, $u(r,t) > 0$ for $0 \leqslant r < s(t)$. From (2.10) and the definition of μ^* we obtain

$$\frac{4\pi}{3}s^3(t) \leqslant \frac{4\pi}{3}s^3(0) + c\int_{\{r<s(0)\}} u_0(r)dV - 4\pi\beta\int_0^t \Big(1 - \frac{1}{\mu^*}\frac{\tau}{\beta}\Big)s^2(\xi)d\xi. \tag{2.13}$$

It follows that

$$s(t) \leqslant \Big(s^3(0) + 3c\int_0^{s(0)} u_0(r)r^2dr\Big)^{1/3}. \tag{2.14}$$

Case (ii): $\tau/\beta > \mu^*$. In this case, the equation (2.3) has exactly two solutions R_0^- and R_0^+.

Setting

$$C_1 = \max(R_0^+, s(0)), \tag{2.15}$$

we can choose (using (2.11)) a constant R such that

$$C_1^3 + \frac{\tau}{2}cC_1^3R \leqslant R^3, \qquad \text{and } 0 \leqslant u_0(r) \leqslant \frac{\tau}{2}(R-r),\ 0 < r < s(0). \tag{2.16}$$

We shall prove that (2.12) holds for this choice of R. Indeed, if this is not true, then there is a first $t^* > 0$ such that $s(t^*) = R$. Since $s(t) < R$ for $0 < t < t^*$, we have, by comparison (using the maximum principle),

$$0 \leqslant u(r,t) \leqslant \frac{\tau}{2}(R-r), \quad 0 < r < s(t),\ 0 < t \leqslant t^*. \tag{2.17}$$

Take $t_1 \in [0, t^*)$ such that

$$s(t_1) = C_1, \quad C_1 < s(t) < R \quad \text{for } t_1 < t < t^*.$$

Then $\Big\{\frac{\tau}{\beta}[s(\xi) - \tanh s(\xi)] - s^2(\xi)\Big\} \leqslant 0$ for $t_1 < t < t^*$ and (2.10) yields

$$\begin{aligned} s^3(t) &< s^3(t_1) + 3c\int_0^{s(t_1)} u(r,t_1)r^2dr + 3\beta\int_{t_1}^t \Big\{\frac{\tau}{\beta}[s(\xi) - \tanh s(\xi)] - s^2(\xi)\Big\}d\xi \\ &\leqslant C_1^3 + \frac{\tau}{2}cC_1^3R \leqslant R^3 \quad \text{for } t_1 < t \leqslant t^*. \end{aligned}$$

Thus $s(t^*) < R$, which is a contradiction. □

From the uniform boundedness of $s(t)$ we can infer (by comparison) the uniform boundedness of $u(r,t)$:

$$0 \leqslant u(r,t) \leqslant C(R-r) \quad \text{where } R > \sup_{0\leqslant t\leqslant T} s(t). \tag{2.18}$$

The next lemma gives a sharper estimate on $u(r,t)$ for r near $s(t)$, as well as a useful estimate for $s'(t)$.

Lemma 2.3 *Let R, C_1 be positive constant for which*

$$\begin{aligned} &R > \sup_{0\leqslant t\leqslant T} s(t), \\ &0 \leqslant u_0(r) \leqslant C_1 \tanh(c\beta s(0)) \left\{1 - e^{-c\beta(s(0)-r)}\right\} \quad \textit{for } 0 \leqslant r < s(0). \end{aligned} \tag{2.19}$$

Then there is a constant K depending only on C_1, R, τ, c and β such that

$$0 \leqslant u(r,t) \leqslant K \tanh(c\beta s(t)) \left\{1 - e^{-c\beta(s(t)-r)}\right\} \quad \textit{for } 0 < t \leqslant T, \tag{2.20}$$

and

$$-\beta < s'(t) < -\beta + cK \tanh(c\beta s(t)) \quad \textit{for } 0 < t \leqslant T. \tag{2.21}$$

Proof. By the maximum principle, $u(r,t) > 0$ if $r < s(t)$ and $u_r(s(t),t) < 0$; hence

$$s'(t) > -\beta \quad \text{for } t > 0. \tag{2.22}$$

Let

$$w(r,t) = K \tanh(c\beta s(t)) \left\{1 - e^{-c\beta(s(t)-r)}\right\},$$

where we choose K large enough so that

$$w(r,0) \geqslant u_0(r). \tag{2.23}$$

Clearly,

$$\begin{aligned} & cw_t - \Big(\frac{\partial^2}{\partial r^2} + \frac{2}{r}\frac{\partial}{\partial r}\Big) w \\ &= Kc\beta \tanh(c\beta s(t)) e^{-c\beta(s(t)-r)} \Big\{ cs'(t) + c\beta + \frac{2}{r} + \frac{c\left[e^{c\beta(s(t)-r)} - 1\right] s'(t)}{\sinh(c\beta s(t)) \cosh(c\beta s(t))} \Big\} \\ &\geqslant Kc\beta \tanh(c\beta s(t)) e^{-c\beta(s(t)-r)} \Big\{ \frac{2}{r} - \frac{2c\beta}{\cosh(c\beta s(t))} \Big\} \\ &\geqslant (2-\sqrt{2}) Kc\beta \tanh(c\beta s(t)) e^{-c\beta(s(t)-r)} \frac{1}{r}; \end{aligned}$$

in deriving the above inequalities, we made use of (2.22) and of the inequalities:

$$\begin{aligned} &e^{\xi} - 1 \leqslant 2\sinh\xi \quad \text{for } \xi \geqslant 0, \\ &\cosh(\xi) \geqslant 1 + \frac{\xi^2}{2} \geqslant \sqrt{2}\xi. \end{aligned}$$

We claim that for a suitable choice of the constant K,

$$(2-\sqrt{2})Kc\beta\tanh(c\beta s(t))e^{-c\beta(s(t)-r)}\frac{1}{r}\geqslant\tau\frac{1}{\cosh(s(t))}\frac{\sinh r}{r}\qquad\text{for } 0<r<s(t);\tag{2.24}$$

the proof of this inequality will be given later. If (2.24) holds then, by the maximum principle,

$$u(r,t)\leqslant w(r,t);\tag{2.25}$$

(note that $w_r\Big|_{r=0}<0, u_r\Big|_{r=0}=0$ so $w-u$ cannot take minimum at $r=0$). It follows that

$$u_r(s(t),t)\geqslant w_r(s(t),t)=-Kc\beta\tanh(c\beta s(t)),\tag{2.26}$$

and so

$$s'(t)\leqslant-\beta+Kc\beta\tanh(c\beta s(t)).$$

To finish the proof of the lemma, it remains to verify (2.24). Observe that (2.24) is equivalent to

$$(2-\sqrt{2})K\tanh(c\beta s(t))\geqslant\frac{\tau}{c\beta}\,\frac{e^{c\beta s(t)}}{\cosh s(t)}e^{-c\beta r}\sinh r\qquad\text{for } 0<r<s(t).\tag{2.27}$$

The function $e^{-c\beta r}\sinh r$ is monotonically increasing in the following cases:

Case (i): $c\beta\leqslant 1$;

Case (ii): $c\beta>1$, $r\leqslant s(t)\leqslant\frac{1}{2}\log\frac{c\beta+1}{c\beta-1}$ for all $0\leqslant t\leqslant T$.

In these two cases, it suffices to prove (2.27) for $r=s(t)$, so that, (2.27) holds if K is such that

$$(2-\sqrt{2})K\geqslant\frac{\tau}{c\beta}\sup_{0<\xi<\infty}\frac{\tanh(\xi)}{\tanh(c\beta\xi)}\equiv\frac{\tau}{c\beta}\max\Big(1,\frac{1}{c\beta}\Big).\tag{2.28}$$

Finally, if $c\beta>1$ and $\max\limits_{0\leqslant t\leqslant T}s(t)>\frac{1}{2}\log\frac{c\beta+1}{c\beta-1}$, we rewrite (2.24) in the form

$$(2-\sqrt{2})K\tanh(c\beta s(t))e^{-(c\beta-1)(s(t)-r)}\geqslant\frac{\tau}{c\beta}\,\frac{e^{s(t)}}{\cosh s(t)}e^{-r}\sinh r\qquad\text{for } 0<r<s(t)\tag{2.29}$$

and observe that the function $e^{-r}\sinh r$ is monotonically increasing. It therefore suffices to prove (2.29) just for $r=s(t)$ on the right-hand side. But, since $s(t)<R$, this is a consequence of

$$(2-\sqrt{2})Ke^{-(c\beta-1)R}\geqslant\frac{\tau}{c\beta}\sup_{0<\xi<\infty}\frac{\tanh(\xi)}{\tanh(c\beta\xi)}\equiv\frac{\tau}{c\beta},\tag{2.30}$$

which holds if K is chosen sufficiently large. □

3 Existence and uniqueness

In this section we assume, in addition to (2.11), that

$$u_0'(r) \text{ is continuous if } 0 \leqslant r \leqslant s(0). \tag{3.1}$$

Theorem 3.1 *Let (2.11) and (3.1) hold. Then*

(i) There exists a unique solution $(u(r,t), s(t))$ of (2.6), (2.9) with $s'(t)$ continuous for a time interval $0 \leqslant t < \delta_0$;

(ii) If a solution $(u(r,t), s(t))$ exists for $0 \leqslant t < T$ and $\liminf_{t \to T-0} s(t) > 0$, then the solution can be continued to $0 \leqslant t \leqslant T + \delta$ for some $\delta > 0$.

The proof, by a fixed point theorem for a contraction mapping, is similar to the corresponding proof for the Stefan problem [3, Chap. 8], and is therefore omitted.

Theorem 3.2 *If*

$$\frac{\tau}{\beta} < \mu^*,$$

then there exists a finite t^* such that the solution exists for $0 \leqslant t < t^*$ and $s(t) \to 0$ for $t \to t^*$, i.e., the cell shrinks to zero at time t^*.

Proof. From (2.13) we get

$$s^3(t) + \delta \int_0^t s^2(\xi) d\xi \leqslant \widetilde{C}_1$$

for some positive constants $\widetilde{C}_1$ and δ.

By Theorem 3.1, the solution can be continued as long as $s(t)$ remains uniformly positive. If the assertion of the theorem is not true, then the solution exists (and $s(t)$ is positive) for all $0 < t < \infty$. Let K be as in Lemma 2.3 and take s_0 such that $K \tanh(\beta s_0) < \beta/2$. Since $\int_0^t s^2(\xi) d\xi$ is uniformly bounded, there exists a $\widetilde{t} > 0$ such that $s(\widetilde{t}) < s_0$. By Lemma 2.3 and a continuation argument, we then have $s'(t) \leqslant -\beta/2$ for all $t > \widetilde{t}$. This is a contradiction to the assumption that $s(t) > 0$ for all $t > 0$. □

In view of theorems 2.2 and 3.1, a solution $(u(r,t), s(t))$ exists for all $0 \leqslant t < \infty$ if and only if, for any $T > 0$, there is $s > 0$ such that

$$\inf_{0 \leqslant t < T} s(t) \geqslant s > 0.$$

Furthermore, by Lemma 2.3, the constant s can be chosen to be independent of T if a global solution exists.

Next we establish a lower bound for $s(t)$ in the case $\tau/\beta > \mu^*$.

Let C_1, C_2 and D_1, D_2 be positive constants such that

$$C_1 \geqslant R_0^+, \quad C_1^3 + \frac{\tau}{2} c C_1^3 C_2 = C_2^3, \tag{3.2}$$

$$D_2 \geqslant R_0^-, \quad D_1 = D_2 \Big(\frac{\tau}{2} c C_2 + 1 \Big)^{1/3}. \tag{3.3}$$

Theorem 3.3 *Assume that*

$$D_1 < R_0^+. \tag{3.4}$$

If $s(0), u_0(r)$ *satisfy*

$$D_1 \leqslant s(0) \leqslant C_1, \tag{3.5}$$

$$0 \leqslant u_0(r) \leqslant \frac{\tau}{2}(C_2 - r) \quad \textit{for } 0 < r < s(0), \tag{3.6}$$

then there exists a global solution $(u(r,t), s(t))$ *of (2.6)–(2.9) with*

$$s(t) > D_2 \quad \textit{for all } t > 0. \tag{3.7}$$

Proof. In view of (3.2), we can apply case (ii) of Theorem 2.2 to conclude that $s(t) \leqslant C_2$ and then, by the maximum principle,

$$0 \leqslant u(r,t) \leqslant \frac{\tau}{2}(C_2 - r). \tag{3.8}$$

It follows that if

$$R_0^- < s(t) < R_0^+ \quad \text{for } t_1 < t < t_2,$$
$$s(t_1) = \min[s(0), R_0^+], \quad s(t_2) = D_2,$$

then

$$3\int_0^{s(t_2)} u(r,t_2) r^2 dr - 3\int_0^{s(t_1)} u(r,t_1) r^2 dr \leqslant \frac{\tau}{2} C_2 D_2^3 = \frac{1}{c}(D_1^3 - D_2^3) \tag{3.9}$$

where the inequality follows from (3.8).

To prove the theorem it suffices to show that (3.7) holds as long as the solution exists. If this is not true then there is a smallest $t = t_2$ such that $s(t_2) = D_2$. By (3.4), (3.5) there exists a t_1 such that $t_1 < t_2$, $s(t_1) = \min[s(0), R_0^+]$ and $s(t_2) < s(t) < s(t_1)$ for $t_1 < t < t_2$. As in case (ii) of Theorem 2.2,

$$s^3(t_1) - D_2^3 < 3c\int_0^{D_2} u(r,t_2) r^2 dr - 3c\int_0^{s(t_1)} u(r,t_1) r^2 dr$$

and since $D_1^3 \leqslant \min[s^3(0), (R_0^+)^3]$, this is a contradiction to (3.9). □

Remark 3.1. If c is suitably small, then (3.4) is satisfied. In this case we have, by (3.7), (3.8),

$$D_2 < s(t) < C_2 \quad \text{for all } t > 0.$$

In particular, if

$$R_0^- + 2\delta < s(0) < C_1 \qquad (\delta > 0) \tag{3.10}$$

and c is sufficiently small, depending on δ and C_1, then

$$R_0^- + \delta < s(t) < C_1 + \delta, \quad \text{for all } t > 0. \tag{3.11}$$

4 R_0^- is unstable

From Lemma 2.3 we infer that if $s(0)$ is very small, then $s'(t)$ remains uniformly negative as long as the solution exists. In this section we shall prove, under more general assumptions on $s(0)$, that $s(t)$ is monotone decreasing, and, in particular, deduce that the stationary solution corresponding to R_0^- is unstable.

Theorem 4.1 *Suppose that*

$$u_r(r,0) \geqslant -\frac{\tau}{\cosh s(0)}\frac{r\cosh r-\sinh r}{r^2}-\frac{\tau}{s(0)}\Big[\frac{\beta}{\tau}-\frac{1}{g(s(0))}\Big]r, \tag{4.1}$$

$$u_r(s(0),0) > -\beta, \tag{4.2}$$

and

$$s(0) \leqslant R_0^-. \tag{4.3}$$

Then $s'(t) < 0$ as long as $s(t)$ remains positive, and $s(t)$ shrinks to zero in finite time.

Proof. From (4.2) we deduce that $s'(0) < 0$ and, by continuity, $s'(t) < 0$ for small $t > 0$. If $s'(t)$ does not remain negative while $s(t)$ is positive, then there exists a first t^* such that $s(t^*) > 0,\ s'(t^*) = 0$. Since $s'(t) < 0$ for $0 \leqslant t < t^*$, we have

$$\begin{aligned} &u_r(s(t),t) > -\beta \quad \text{for } 0 \leqslant t < t^*,\\ &0 < s(t) < s(0) \leqslant R_0^- \quad \text{for } 0 \leqslant t < t^*. \end{aligned}$$

We introduce the auxiliary function

$$w = u_r(r,t)+\frac{\tau}{\cosh s(t)}\frac{r\cosh r-\sinh r}{r^2}+\frac{\tau}{s(t)}\Big[\frac{\beta}{\tau}-\frac{1}{g(s(t))}\Big]r,$$

where $g(r)$ is defined in (2.1).

Since $g'(r) < 0$ for $0 < r \leqslant R_0^-$, $g(R_0^-) = \tau/\beta$ and $0 < s(t) \leqslant R_0^-$, we have

$$\Big[\frac{\beta}{\tau}-\frac{1}{g(s(t))}\Big] > 0 \quad \text{for } 0 < t < t^*. \tag{4.4}$$

Using the relation $(r\cosh r-\sinh r)/r^2 = (\partial/\partial r)(\sinh r/r)$ we easily deduce that

$$\begin{aligned} &-\Delta\Big(\frac{r\cosh r-\sinh r}{r^2}\Big)+\frac{2}{r^2}\Big(\frac{r\cosh r-\sinh r}{r^2}\Big)\\ &\quad = -\frac{\partial}{\partial r}\Delta\frac{\sinh r}{r} = -\frac{\partial}{\partial r}\frac{\sinh r}{r} = -\frac{r\cosh r-\sinh r}{r^2}, \end{aligned}$$

Combining this relation with (4.4) and the inequality $s'(t) < 0$, we find that

$$cw_t - w_{rr} - \frac{2}{r}w_r + \frac{2}{r^2}w > 0 \quad \text{for } 0 < t < t^*.$$

Clearly, $w(s(t),t) > 0$ for $0 < t < t^*$, and, by (4.1), $w(r,0) \geqslant 0$. It follows, by the maximum principle, that $w(r,t) > 0$ for $0 < t < t^*$. Since $s'(t^*) = 0$, we also have (from the definition of w and g) that $w(s(t^*),t^*) = 0$ and, therefore, by the maximum principle,

$$w_r(s(t^*),t^*) < 0.$$

i.e.,

$$u_{rr}(s(t^*),t^*) \leqslant -\frac{\tau}{s(t^*)}\Big[\frac{\beta}{\tau} - \frac{3}{s(t^*)} + \frac{3\tanh s(t^*)}{s^2(t^*)} + \tanh s(t^*)\Big].$$

On the other hand from $s'(t^*) = 0$ we deduce that $u_t(s(t^*),t^*) = 0$, so that

$$\begin{aligned} 0 \;=\; cu_t(s(t^*),t^*) \;&=\; u_{rr}(s(t^*),t^*) + \frac{2}{s(t^*)}u_r(s(t^*),t^*) + \frac{\tau}{\cosh s(t^*)}\,\frac{\sinh s(t^*)}{s(t^*)} \\ &\leqslant\; -\frac{\tau}{s(t^*)}\Big[\frac{3\beta}{\tau} - \frac{3}{s(t^*)} + \frac{3\tanh s(t^*)}{s^2(t^*)}\Big] \\ &=\; -\frac{3\tau}{s(t^*)}\Big[\frac{\beta}{\tau} - \frac{1}{g(s(t^*))}\Big] \;<\; 0 \quad \text{by (4.4)}, \end{aligned}$$

which is a contradiction. Having now proved that $s'(t) < 0$ as long as $s(t)$ remains positive, we shall next show that $s(t)$ converges to zero in finite time. Indeed, otherwise the limit $s_0 = \lim_{t\to\infty} s(t)$ lies in the interval $(0, R_0^-)$. By a standard theorem on parabolic equations [3, Chap. 6] $(u(r,t), s(t))$ converges to a stationary solution and, consequently, s_0 must coincide with either R_0^- or R_0^+, which is a contradiction. □

If, in Theorem 4.1, we take $s(0) = R_0^-$, then we get:

Corollary 4.2 *Suppose*

$$u_r(r,0) \geqslant -\frac{\tau}{\cosh R_0^-}\,\frac{r\cosh r - \sinh r}{r^2} \qquad \textit{for } 0 < r < R_0^-, \tag{4.5}$$

$$s(0) = R_0^-, \qquad u_r(R_0^-,0) > -\beta. \tag{4.6}$$

Then $s'(t) < 0$ as long as $s(t)$ remains positive, and $s(t)$ shrinks to zero in finite time.

Since there are arbitrarily small perturbations of the stationary solution

$$\frac{\tau}{\cosh R_0^-}\Big(\frac{\sinh R_0^-}{R_0^-} - \frac{\sinh r}{r}\Big)$$

which satisfy (4.5), (4.6), we conclude:

Corollary 4.3 *The stationary solution (4.5) is unstable.*

One can even choose small perturbations of the stationary solution with $s(0) > R_0^-$ (but $s(0) - R_0^-$ small) for which $s(t)$ shrinks to zero in finite time.

The method of proof of Theorem 4.1 can be extended to establish monotonic decrease of $s(t)$ under different assumptions on the data. We give here one example.

Theorem 4.4 *Suppose*

$$u_r(r,0) \geqslant -\beta\frac{r}{s(0)}, \qquad u_r(s(0),0) > -\beta, \tag{4.7}$$

$$\tau \leqslant \frac{3\beta}{\tanh s(0)}. \tag{4.8}$$

Then $s'(t) < 0$ as long as $s(t)$ remains positive.

The proof is essentially the same as the proof of Theorem 4.1, with w replaced by $u_r(r,t)+\beta r/s(t)$.

We note that Theorem 4.4 is not contained in Theorem 4.1 since, in general, $-\beta r/s(0)$ is not larger than the right-hand side of (4.1).

5 R_0^+ is stable

In this section we prove that the stationary solution corresponding to R_0^+ is stable provided the coefficient c is sufficiently small. As we note that in the Introduction in actual biological cells of interest, c may indeed be very small. In the case $c = 0$, the solution $(\varphi(r,t), R(t))$ of (2.6)–(2.9) can be computed explicitly [4]:

$$\varphi(r,t) = \frac{\tau}{\cosh R(t)}\Big(\frac{\sinh R(t)}{R(t)} - \frac{\sinh r}{r}\Big) \quad \text{for } r < R(t)$$

where the free boundary $R(t)$ satisfies:

$$\frac{dR}{dt} = \tau\frac{R - \tanh R}{R^2} - \beta = \tau\Big[\frac{1}{g(R)} - \frac{\beta}{\tau}\Big] \equiv \tau\Big(h(R) - \frac{\beta}{\tau}\Big). \tag{5.1}$$

Note that

$$h(R) > \frac{\beta}{\tau} \quad \text{and} \quad \dot R > 0 \quad \text{for } R_0^- < R < R_0^+,$$
$$h(R) < \frac{\beta}{\tau} \quad \text{and} \quad \dot R < 0 \quad \text{for } R > R_0^+,$$

and $h'(R_0^+) < 0$. Hence, by standard ODE analysis it follows that, if $R(0) > R_0^-$, then

$$|R(t) - R_0^+| \leqslant Ce^{-\alpha t} \quad \forall t > 0, \tag{5.2}$$

where C, α are positive constants.

In this section we want to extend this result to the case where c is positive and small.

Theorem 5.1 *Let $s(0) > R_0^-$. If c is sufficiently small then the solution the solution $(u(r,t), s(t))$ of (2.6)–(2.9) exists for all $t > 0$,*

$$\lim_{t\to\infty} s(t) = R_0^+, \tag{5.3}$$

and the convergence is exponentially fast.

This establishes a global asymptotic stability of the stationary solution corresponding to R_0^+.

From Remark 3.1 we already know that the solution exists for all $t > 0$ and that (3.11) holds, i.e.,

$$R_0^- < \underline{S} \leqslant s(t) \leqslant \overline{S} < \infty \quad \text{for all } t > 0. \tag{5.4}$$

Lemma 5.2 *Define*

$$\underline{R} = \liminf_{t\to\infty} s(t), \quad \overline{R} = \limsup_{t\to\infty} s(t).$$

If c is sufficiently, then $\overline{R} = \underline{R} = R_0^+$.

Proof. By (5.4)

$$R_0^- < \underline{R} \leqslant \overline{R} \leqslant \overline{S}.$$

We claim that

$$R_0^- < \underline{R} \leqslant R_0^+ \leqslant \overline{R} \leqslant \overline{S}. \tag{5.5}$$

In fact, if $\underline{R} > R_0^+$, then $g(s(\xi)) > \tau/\beta + \varepsilon$ for some small $\varepsilon > 0$ and all sufficiently large ξ. Therefore,

$$\int_0^\infty \Big[\frac{1}{g(s(\xi))} - \frac{\beta}{\tau}\Big] s^2(\xi) d\xi = -\infty,$$

which is a contradiction to Lemma 2.1. This proves that $\underline{R} \leqslant R_0^+$. Similarly, $R_0^- \leqslant \overline{R}$.

Next, we claim that

$$\liminf_{t\to\infty} u(r,t) \geqslant \frac{\tau}{\cosh \overline{R}}\Big(\frac{\sinh \underline{R}}{\underline{R}} - \frac{\sinh r}{r}\Big) \quad \text{uniformly for } r < s(t), \tag{5.6}$$

$$\limsup_{t\to\infty} u(r,t) \leqslant \frac{\tau}{\cosh \underline{R}}\Big(\frac{\sinh \overline{R}}{\overline{R}} - \frac{\sinh r}{r}\Big) \quad \text{uniformly for } r < s(t). \tag{5.7}$$

To prove (5.6), let $\varphi(r,t)$ be the solution of the following problem

$$\begin{aligned} &c\varphi_t - \Delta\varphi = \frac{\tau}{\cosh(\overline{R}+\varepsilon)}\frac{\sinh r}{r} \quad \text{for } r < \underline{R} - \varepsilon,\ t > T,\\ &\varphi(\underline{R}-\varepsilon, t) = 0 \quad \text{for } t > T,\\ &\varphi(r, T) = 0 \quad \text{for } r < \underline{R} - \varepsilon, \end{aligned}$$

where $\varepsilon > 0$ is small. If we take $T = T(\varepsilon)$ to be large enough, then

$$\underline{R} - \varepsilon \leqslant s(t) \leqslant \overline{R} + \varepsilon \quad \text{for } t > T,$$

and, by maximum principle, $u(r,t) \geqslant \varphi(r,t)$ for $t > T$. Hence

$$\liminf_{t\to\infty} u(r,t) \geqslant \lim_{t\to\infty} \varphi(r,t) = \frac{\tau}{\cosh(\overline{R}+\varepsilon)}\Big(\frac{\sinh(\underline{R}-\varepsilon)}{\underline{R}-\varepsilon} - \frac{\sinh r}{r}\Big).$$

Letting $\varepsilon \to 0+$, we obtain the inequality (5.6). The inequality (5.7) can be established in a similar way.

Next, we estimate $\overline{R} - R_0^+$ in case $\overline{R} > R_0^+$. Choose a sequence $t_j \to \infty$ such that $s(t_j) \to \overline{R}$ and take $\widetilde{t}_j < t_j$ such that

$$R_0^+ + \frac{1}{j} = s(\widetilde{t}_j) < s(t) \quad \text{for } \widetilde{t}_j < t < t_j;$$

since $\liminf_{t\to\infty} s(t) \leqslant R_0^+ < \overline{R}$, such a choice of $\widetilde{t}_j$ is possible. Then $g(s(\xi)) > \tau/\beta$ for $\widetilde{t}_j < \xi < t_j$ and Lemma 2.1 implies that

$$s^3(t_j) - s^3(\widetilde{t}_j) \leqslant 3c\int_0^{s(\widetilde{t}_j)} u(r,\widetilde{t}_j)r^2dr - 3c\int_0^{s(t_j)} u(r,t_j)r^2dr.$$

Using (5.6), (5.7) in the last inequality, and letting $j \to \infty$, we obtain

$$\begin{aligned}
\overline{R}^3 - (R_0^+)^3 &\leqslant 3c\int_0^{R_0^+} \frac{\tau}{\cosh \underline{R}}\Big(\frac{\sinh \overline{R}}{\overline{R}} - \frac{\sinh r}{r}\Big)r^2dr \\
&\quad -3c\int_0^{\underline{R}} \frac{\tau}{\cosh \overline{R}}\Big(\frac{\sinh \underline{R}}{\underline{R}} - \frac{\sinh r}{r}\Big)r^2dr \\
&\leqslant 3c\tau\int_0^{R_0^+} \Big(\frac{1}{\cosh \underline{R}}\frac{\sinh \overline{R}}{\overline{R}} - \frac{1}{\cosh \overline{R}}\frac{\sinh \underline{R}}{\underline{R}}\Big)r^2dr \\
&\quad +3c\tau\int_0^{R_0^+} \Big(\frac{1}{\cosh \overline{R}} - \frac{1}{\cosh \underline{R}}\Big)r\sinh r dr.
\end{aligned}$$

Since the last integrand is $\leqslant 0$, we obtain

$$\begin{aligned}
\overline{R}^3 - (R_0^+)^3 &\leqslant c\tau\Big(\frac{1}{\cosh \underline{R}}\frac{\sinh \overline{R}}{\overline{R}} - \frac{1}{\cosh \overline{R}}\frac{\sinh \underline{R}}{\underline{R}}\Big)(R_0^+)^3 \\
&= \frac{c\tau}{\cosh \underline{R}\cosh \overline{R}}[k(\overline{R}) - k(\underline{R})](R_0^+)^3,
\end{aligned} \tag{5.8}$$

where $k(r) = \sinh r \cosh r/r$; note that $k'(r) > 0$. Similarly, we have (with $s(\tau_j) \to \underline{R}$, $s(\widetilde{\tau}_j) = R_0^+ - 1/j, s(t) < R_0^+ - 1/j$ if $\widetilde{\tau}_j < t < \tau_j$)

$$\underline{R}^3 - (R_0^+)^3 \geqslant -\frac{c\tau}{\cosh \underline{R}\cosh \overline{R}}[k(\overline{R}) - k(\underline{R})](R_0^+)^3, \tag{5.9}$$

provided $\underline{R} < R_0^+$. Notice that if $\overline{R} = R_0^+$ (or $\underline{R} = R_0^+$) then (5.8) (or (5.9)) is trivially satisfied. Combining (5.8) with (5.9) we get

$$\overline{R} - \underline{R} \leqslant \frac{c\tau}{A}(\overline{R} - \underline{R}), \tag{5.10}$$

where

$$A = \frac{(\overline{R}^2 + \overline{R}\underline{R} + \underline{R}^2)\cosh \underline{R}\cosh \overline{R}}{2(R_0^+)^3 k'(\overline{R})} \geqslant A_0,$$

and A_0 is a positive constant depending only on $\underline{S}$, $\overline{S}$ and R_0^+. If $c\tau/A_0 < 1$, then $\overline{R} - \underline{R} = 0$ and the lemma is proved. □

Having proved (5.2), we shall next prove local stability of R_0^+ with exponential convergence of $s(t)$. Introduce the functions

$$\varphi(r,t) = \frac{\tau}{\cosh s(t)}\Big(\frac{\sinh s(t)}{s(t)} - \frac{\sinh r}{r}\Big), \tag{5.11}$$

and $v = u - \varphi$. A direct computation shows that

$$cv_t - \Big(\frac{\partial^2}{\partial r^2} + \frac{2}{r}\frac{\partial}{\partial r}\Big)v = -c\varphi_t \quad \text{for } 0 \leqslant r < s(t), \tag{5.12}$$

$$v(s(t),t) = 0, \tag{5.13}$$

$$s'(t) = -v_r(s(t),t) - \beta + \tau\frac{s(t) - \tanh s(t)}{s^2(t)}. \tag{5.14}$$

Lemma 5.3 *Suppose that $c\tau < 3/2$. Then there exists an $\varepsilon > 0$ such that if*

$$|s(0) - R_0^+| < \varepsilon^2, \quad |s'(0)| < \varepsilon,$$

and

$$\Big|u_0(r) - \frac{\tau}{\cosh s(0)}\Big(\frac{\sinh s(0)}{s(0)} - \frac{\sinh r}{r}\Big)\Big| < \frac{\tau}{7}\varepsilon\Big(s(0) - \frac{r^2}{s(0)}\Big),$$

then a global solution $(u(r,t), s(t))$ exists and $s(t)$ converges to the steady state (corresponding to R_0^+) exponentially fast.

The proof requires the fact that $g'(R_0^+) > 0$ (g is defined in (2.1)), and thus does not apply to R_0^- (since $g'(R_0^-) < 0$).

Proof. Clearly,

$$\begin{aligned}
|\varphi_t| &= \tau|s'(t)|\Big|\frac{s(t) - \tanh s(t)}{s^2(t)} - \frac{\sinh s(t)}{\cosh^2 s(t)}\Big(\frac{\sinh s(t)}{s(t)} - \frac{\sinh r}{r}\Big)\Big| \\
&\leqslant \tau|s'(t)|\max\Big[\frac{s(t) - \tanh s(t)}{s^2(t)}, \frac{\sinh s(t)}{\cosh^2 s(t)}\Big(\frac{\sinh s(t)}{s(t)} - \frac{\sinh r}{r}\Big)\Big] \\
&\leqslant \tau|s'(t)|\max\Big[\frac{s(t) - \tanh s(t)}{s^2(t)}, \frac{\sinh^2 s(t)}{s(t)\cosh^2 s(t)}\Big] \\
&\leqslant \tau|s'(t)|\frac{1}{s(t)}.
\end{aligned} \tag{5.15}$$

We claim that

$$|s'(t)| < \varepsilon e^{-\varepsilon t} \quad \text{for } 0 < t < \infty. \tag{5.16}$$

By assumption (5.16) is satisfied for $t = 0$. If the assertion (5.16) is not true, then there is a first t^* such that $|s'(t^*)| = \varepsilon e^{-\varepsilon t^*}$. Introduce the function

$$w(r,t) = \frac{c\tau\varepsilon}{6 - C^*\varepsilon}e^{-\varepsilon t}\Big(s(t) - \frac{r^2}{s(t)}\Big) \quad \text{for } 0 \leqslant t \leqslant t^*,$$

where $C^* > s^2(t) + 2c$ for all $0 < t < \infty$. Then

$$\begin{aligned}
cw_t - \Delta w &= \frac{c\tau\varepsilon}{6 - C^*\varepsilon}\,\frac{1}{s(t)}\Big[6 + c\Big(1 + \frac{r^2}{s^2(t)}\Big)s'(t) - \varepsilon(s^2(t) - r^2)\Big]e^{-\varepsilon t} \\
&\geqslant \frac{c\tau\varepsilon}{6 - C^*\varepsilon}\,\frac{1}{s(t)}(6 - C^*\varepsilon)e^{-\varepsilon t} \\
&\geqslant \frac{c\tau\varepsilon}{s(t)}e^{-\varepsilon t},
\end{aligned}$$

and, by assumption, $w(r,0) > |v(r,0)|$. Recalling (5.15) and (5.12), (5.13), we can use the maximum principle to compare $\pm v$ with w and conclude that

$$|v(r,t)| \leqslant w(r,t).$$

Since $v(s(t),t) = w(s(t),t)$, we then also have

$$|v_r(s(t),t)| \leqslant \frac{2c\tau\varepsilon}{6 - C^*\varepsilon} e^{-\varepsilon t}.$$

Thus

$$\Big| s'(t) + \beta - \tau \frac{s(t) - \tanh s(t)}{s^2(t)} \Big| \leqslant \frac{2c\tau\varepsilon}{6 - C^*\varepsilon} e^{-\varepsilon t}. \tag{5.17}$$

Let

$$h(r) = \frac{1}{g(r)}, \qquad f(t) = \tau \frac{h(R_0^+) - h(s(t))}{s(t) - R_0^+},$$

where $g(r)$ is defined by (2.1). Then we can rewrite (5.17) in the form

$$\Big| (s(t) - R_0^+)' + f(t)(s(t) - R_0^+) \Big| \leqslant \frac{2c\tau\varepsilon}{6 - C^*\varepsilon} e^{-\varepsilon t}. \tag{5.18}$$

It follows that

$$|s(t) - R_0^+| \leqslant |s(0) - R_0^+| \exp\Big(- \int_0^t f(\xi) d\xi \Big) + \frac{2c\tau\varepsilon}{6 - C^*\varepsilon} \int_0^t \exp\Big(- \varepsilon\eta - \int_\eta^t f(\xi) d\xi \Big) d\eta.$$

Notice that for $s(t)$ near R_0^+, $h(R_0^+) - h(s(t))/(s(t) - R_0^+) \sim -h'(R_0^+) \equiv \delta > 0$. Thus, for $s(t)$ near R_0^+, $\tau(\delta + C^*\varepsilon) \geqslant f(t) \geqslant \tau(\delta - C^*\varepsilon)$. Consequently,

$$|s(t) - R_0^+| \leqslant \frac{\varepsilon^2}{\tau(\delta - C^*\varepsilon)} e^{-\tau(\delta - C^*\varepsilon)t} + \frac{2c\tau\varepsilon}{6 - C^*\varepsilon} \, \frac{1}{\tau(\delta - C^*\varepsilon) - \varepsilon} e^{-\varepsilon t}. \tag{5.19}$$

Using this in (5.18) we obtain

$$\begin{aligned} |s'(t)| &\leqslant \frac{2c\tau\varepsilon}{6 - C^*\varepsilon} e^{-\varepsilon t} + |f(t)||s(t) - R_0^+| \\ &\leqslant \frac{2c\tau\varepsilon}{6 - C^*\varepsilon} e^{-\varepsilon t} \\ &\qquad + \tau(\delta + C^*\varepsilon) \Big(\frac{\varepsilon^2}{\tau(\delta - C^*\varepsilon)} e^{-\tau(\delta - C^*\varepsilon)t} + \frac{2c\tau\varepsilon}{6 - C^*\varepsilon} \, \frac{1}{\tau(\delta - C^*\varepsilon) - \varepsilon} e^{-\varepsilon t} \Big) \\ &< \varepsilon e^{-\varepsilon t} \quad \text{for } 0 < t \leqslant t^*, \end{aligned}$$

provided

$$\frac{2c\tau}{6 - C^*\varepsilon} + \Big[\frac{\tau(\delta + C^*\varepsilon)\varepsilon}{\tau(\delta - C^*\varepsilon)} + \frac{2c\tau}{6 - C^*\varepsilon} \, \frac{\tau(\delta + C^*\varepsilon)}{\tau(\delta - C^*\varepsilon) - \varepsilon} \Big] < 1,$$

which is satisfied if $c\tau < 3/2$ and ε is sufficiently small, and this is a contradiction to the assumption that $|s'(t^*)|$ is equal to $e^{-\varepsilon t^*}$. Finally, from (5.19), we deduce that $s(t)$ converges to R_0^+ exponentially fast. □

Proof of Theorem 5.1. From Lemma 5.2 and (5.6), (5.7) we see that the assumptions of Lemma 5.3 are satisfied at some sufficiently large time $t = T$. It follows that

$$\begin{aligned} |s(t) - R_0^+| &\leqslant Ce^{-\alpha t}, \\ |s'(t)| &\leqslant Ce^{-\alpha t} \end{aligned}$$

for all large enough t, where C, α are positive constants, and this completes the proof of Theorem 5.1. □

Remark 5.1. The above proof shows that if (3.6) and (3.10) hold then the assertion of Theorem 5.1 holds for any $0 < c < c^*$ where c^* depends only on δ, C_1 and C_2, in addition to τ and β.

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