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环柱状血管化肿瘤生长模型的自由边界问题

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摘要: 该文研究环柱状血管化肿瘤生长模型的自由边界问题. 假设肿瘤环绕血管外侧生长,考虑其垂直截面的生长规律. 肿瘤区域的内侧边界是固定的,外侧边界是自由边界. 证明了: (i) 该问题存在稳态解; (ii) 若血管化函数 $\alpha(t)$ 保持一致有界,则自由边界 $R(t)$ 保持一致有界; (iii) 若 $\lim\limits_{t\to\infty}\alpha(t)=0$,则自由边界将收缩至内边界,即肿瘤消失.

关键词: 环柱状肿瘤; 自由边界; 稳态解; 径向对称解

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0　引言

肿瘤是危害人类生命的重要疾病之一. 在过去的 30 年中,越来越多的偏微分方程自由边界问题被用来描述肿瘤的生长[1-9],迄今已获得许多深刻的结果. 本文研究沿着血管外壁环绕生长的肿瘤模型,假设肿瘤沿着血管长度方向的性质各向相同,则只需考虑其垂直于血管长度方向的横截面内肿瘤生长的规律. 此时肿瘤的区域 $\Omega(t)$ 为 $\mathbf{R}^2$ 中有界的环形区域,其边界由内边界 Γ_1 和外边界 Γ_2 组成,内边界固定,外边界为自由边界,且营养物从固定的内边界输入. 与球状肿瘤类似[2,7,10-11],环柱状肿瘤内的营养物质浓度 $\hat{u}$ 满足反应扩散方程:

$$c\partial\hat{u}/\partial t=\Delta_r\hat{u}+\Gamma(u_B-\hat{u})-\lambda_0\hat{u},a<r<R(t),\quad(1)$$

其中 $\Delta_r=\partial^2/\partial r^2+\partial/(r\partial r)$,$c$ 为肿瘤细胞的分裂速率与营养物质的扩散速率的比值(正常数,通常很小),$\Gamma(u_B-\hat{u})$ 表示内部血管网提供的营养,Γ 为营养物质的转化率,u_B 为血管内的营养物质浓度,λ_0 为细胞消耗养分的速率. 在肿瘤的演化过程中,由于肿瘤细胞的增殖和死亡,肿瘤区域随时间变化,a 为肿瘤区域内半径,$R(t)$ 为肿瘤区域外半径.

利用无维化变换[2,4,10],方程(1)可改写为

$$c\partial u/\partial t=\Delta_r u-\lambda u,a<r<R(t),$$

其中 $\lambda>0$. 在内边界 Γ_1 上满足如下边界条件:

$$\partial u/\partial r+\alpha(t)(u-\bar{u})=0,r=a,$$

其中 $\alpha(t)$ 为正值函数,与血管化程度有关,血管化越多,则 $\alpha(t)$ 越大. 假设肿瘤在外边界不与外边界组织有营养交换,即在外边界 Γ_2 处满足

$$\partial u/\partial r=0,r=R(t).$$

假定肿瘤细胞生长函数[12]为 $s(u-\tilde{u})$,其中 s 为一正常数,由质量守恒定律可知

$$\mathrm{d}R(t)/\mathrm{d}t=\frac{s}{R(t)}\int_a^{R(t)}r(u(r,t)-\tilde{u})\,\mathrm{d}r.$$

由最大值原理得,若 $0\leqslant u(r,0)\leqslant\bar{u}$,则 $0\leqslant u(r,t)\leqslant\bar{u}$; 因此,若 $\tilde{u}>\bar{u}$,当 $t\to\infty$ 时,$R(t)\to0$,则肿瘤将会消亡,所以总假设 $\tilde{u}<\bar{u}$.

利用伸缩变换,可将上述问题改写为如下形式:

$$\partial u/\partial t=\Delta_r u-u,a<r<R(t),\quad(2)$$

$$\partial u/\partial r+\alpha(t)(u-\bar{u})=0,r=a,\quad(3)$$

$$\partial u/\partial r=0,r=R(t),\quad(4)$$

$$\frac{\mathrm{d}R(t)}{\mathrm{d}t}=\frac{\mu}{R(t)}\int_a^{R(t)}r(u(r,t)-\tilde{u})\,\mathrm{d}r,\tilde{u}\in(0,\bar{u}),\quad(5)$$

$$u(r,0)=u_0(r),\quad(6)$$

其中 $u_0(r)\in C^2(a,R(0))$ 且 $0\leqslant u_0(r)\leqslant\bar{u}$.

A. Friedman 等[12]研究了球对称血管化肿瘤的自由边界问题. 他们首先讨论了在 $\alpha(t)$ 为常数时稳态解的存在唯一性; 然后给出了 $\alpha(t)$ 与 $R(t)$ 的有界性关系; 最后,讨论了当侵袭参数 μ 足够小时稳态

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解的全局渐近稳定性.

Zhou Fujun 等[13-14] 研究了一个环柱状血管化肿瘤生长模型的自由边界问题,其中内侧边界条件考虑第 1 边值条件: $u = \bar{u}$. 他们讨论了解的局部适定性问题,给出了径向对称稳态解的存在性,并证明了径向对称稳态解是渐近稳定的.

受以上研究的启发,本文将研究环柱状血管化肿瘤生长的自由边界问题(2) ~ (6). 主要研究其稳态解的存在性及自由边界的渐近行为.

1　稳态解

在这一节中,将研究问题(2) ~ (6) 在 $\alpha(t) \equiv \alpha$ 的情形下,其径向对称稳态解的存在性. 下面给出该稳态问题的形式,

$$\partial^2 u/\partial r^2 + \partial u/(r\partial r) - u = 0, a < r < R, \quad (7)$$

$$\partial u/\partial r = \alpha(u - \bar{u}), r = a, \quad (8)$$

$$\partial u/\partial r = 0, r = R, \quad (9)$$

$$\frac{\mathrm{d}R}{\mathrm{d}t} = \frac{\mu}{R}\int_a^R r(u - \tilde{u})\,\mathrm{d}r, \tilde{u} \in (0, \bar{u}). \quad (10)$$

为证明上述问题存在解,引入修正的 Bessel 函数[15] $K_n(x)$ 和 $I_n(x)$,它们满足 $x^2y'' + xy' - (x^2 + n^2)y = 0$,及

$I_{n+1}(x) = I_{n-1}(x) - 2nI_n(x)/x, K_{n+1}(x) = K_{n-1}(x) + 2nK_n(x)/x, n \geqslant 1$;

$I_n'(x) = (I_{n-1}(x) + I_{n+1}(x))/2, K_n'(x) = (K_{n-1}(x) + K_{n+1}(x))/2, n \geqslant 1$;

$I_n'(x) = I_{n-1}(x) - nI_n(x)/x, K_n'(x) = -K_{n-1}(x) - nK_n(x)/x, n \geqslant 1$;

$I_n'(x) = nI_n(x)/x + I_{n+1}(x), K_n'(x) = nK_n(x)/x - K_{n+1}(x), n \geqslant 0$.

此外,$I_n'(x) > 0, K_n'(x) < 0$.

定理 1　若 $\bar{u} - \tilde{u} > 0$,则问题(7) ~ (10) 至少存在 1 个解.

证　由 $I_0(r)$ 与 $K_0(r)$ 的定义可知,问题(7) ~ (9) 的解形式如下:

$$u_*(r) = AI_0(r) + BK_0(r),$$

其中 A 和 B 为待定常数,代入(8) 式和(9) 式得

$$\begin{cases} A(\alpha I_0(a) - I_1(a)) + B(\alpha K_0(a) - K_1(a)) = \alpha\bar{u}, \\ AI_1(R) - BK_1(R) = 0. \end{cases}$$

解得

$$\begin{cases} A = \alpha\bar{u}K_1(R)/(I_1(R)(\alpha(K_0(a) + K_1(a)) + K_1(R)(\alpha I_0(a) - I_1(a))), \\ B = \alpha\bar{u}I_1(R)/(I_1(R)(\alpha(K_0(a) + K_1(a)) + K_1(R)(\alpha I_0(a) - I_1(a))). \end{cases}$$

于是对任意给定的 $R > 0$,问题(7) ~ (9) 的解为

$$u_* = \alpha\bar{u}(K_1(R)I_0(r) + I_1(R)K_0(r))/(I_1(R)(\alpha K_0(a) + K_1(a)) + K_1(R)(\alpha I_0(a) - I_1(a))). \quad (11)$$

接下来验证自由边界条件,把(11) 式代入(10) 式得

$$\int_a^R r(u - \tilde{u})\,\mathrm{d}r = \alpha\bar{u}(K_1(a)I_1(R) - I_1(a)K_1(R))/(I_1(R)(\alpha(K_0(a) + K_1(a)) + K_1(R)(\alpha I_0(a) - I_1(a))) - \tilde{u}(R^2 - a^2)/2 = 0.$$

记

$$f(R) = \alpha\bar{u}(K_1(a)I_1(R) - I_1(a)K_1(R))/(I_1(R)(\alpha K_0(a) + K_1(a)) + K_1(R)(\alpha(I_0(a) - I_1(a))) - \tilde{u}(R^2 - a^2)/2.$$

对 $f(R)$ 关于 R 求导,得

$$f'(R) = a\alpha\bar{u}(I_0(a)K_1(a) + K_0(a)I_1(a))(\alpha K_0(R) \cdot I_1(R) + \alpha I_0(R)K_1(R))/(I_1(R)(\alpha K_0(a) + K_1(a)) + K_1(R)(\alpha I_0(a) - I_1(a)))^2 - \tilde{u}R.$$

显然,当 $R = a$ 时,

$$f(a) = \alpha\bar{u}(K_1(a)I_1(a) - I_1(a)K_1(a))/(I_1(a)(\alpha K_0(a) + K_1(a)) + K_1(a)(\alpha I_0(a) - I_1(a))) - \tilde{u}(a^2 - a^2)/2 = 0,$$

$$f'(a) = a\alpha^2\bar{u}(I_0(a)K_1(a) + K_0(a)I_1(a))^2/(\alpha^2(I_1(a)K_0(a) + I_0(a)K_1(a))^2) - \tilde{u}a = a(\bar{u} - \tilde{u}) > 0.$$

上面 2 式表明 $f(R)$ 在点 a 处单调递增,故 $f(R)$ 在点 a 右端大于零,从而当 r_0 足够小时,有 $f(a + r_0) > 0$.

另一方面,$\lim\limits_{R\to\infty} f(R) < 0$,由介值定理可知,至少存在一个 $R_* > 0$,使得 $f(R_*) = 0$,即问题(7) ~ (10) 存在解(u_*, R_*).

2　$R(t)$ 有界

本节假设 $\alpha(t)$ 一致有界,μ、$\bar{u}$、$\tilde{u}$ 满足 $\mu(\bar{u} - \tilde{u}) < 1$,研究问题(2) ~ (6) 的自由边界 $R(t)$ 的一致有界性.

对(2) 式关于时间 s 在$(0,t)$ 上积分,再关于 r 在$(a, R(t))$ 上积分,同时利用(3) 式得

$$\int_a^{R(t)} ru(r,t)\,\mathrm{d}r = \int_a^{R(0)} ru(r,0)\,\mathrm{d}r + \int_0^t R(s)u(R(s), s)R'(s)\,\mathrm{d}s + \int_0^t r\frac{\partial u}{\partial r}\bigg|_{r=a}^{r=R(t)}\mathrm{d}s - \int_0^t\int_a^{R(t)} ru\,\mathrm{d}r\mathrm{d}s. \quad (12)$$

由(5) 式得

$$\int_a^{R(t)} ru(r,t)\,\mathrm{d}r = R(t)R'(t)/\mu + (R^2(t) - a^2)\bar{u}/2,$$

将上式代入(12) 式,有

$$R(t)R'(t)/\mu = \int_0^t r\frac{\partial u}{\partial r}\bigg|_{r=a}^{r=R(t)}\mathrm{d}s + \int_a^{R(0)} ru(r,0)\,\mathrm{d}r + \int_0^t R(s)u(R(s),s)R'(s)\,\mathrm{d}s - (R^2(t)-a^2)/(2\mu) - \int_0^t (R^2(t)-a^2)\tilde{u}/2\mathrm{d}s - (R^2(t)-a^2)\tilde{u}/2. \tag{13}$$

引理1 假设存在一点t_0,$R'(t_0)=0$,$R''(t_0)\geqslant 0$,则有 $R(t_0)-a<2\alpha(t_0)\bar{u}/\tilde{u}$.

证 在$t=t_0$处,对(13)式关于t进行求导,得

$(R^2(t)/\mu)''|_{t=t_0} = r\partial u/\partial r|_{r=a}^{r=R(t)} - R(t_0)R'(t_0)/\mu - (R^2(t_0)-a^2)\tilde{u}/2 = R(t_0)\alpha(t_0)(\bar{u}-u(R(t_0),t_0)) - a\alpha(t_0)(\bar{u}-u(a,t_0)) - (R^2(t_0)-a^2)\tilde{u}/2 < a\alpha(t_0)\bar{u} - (R^2(t_0)-a^2)\tilde{u}/2.$

因为 $R(t)R'(t)/\mu\geqslant 0$, 从而 $R(t_0)-a< 2a\alpha(t_0)\bar{u}/((R+a)\tilde{u}) < 2\alpha(t_0)\bar{u}/\tilde{u}$.

引理2 假设 $\exists\tau_1,\tau_2$,$0\leqslant\tau_1\leqslant\tau_2$,$R'(t)\geqslant 0$,$t\in(\tau_1,\tau_2)$,$R(\tau_1)-a\geqslant 2(\sup\limits_{\tau_1<t<\tau_2}\alpha(t))\bar{u}/\tilde{u}$,则 $R(t)R'(t)/\mu|_{t=\tau_1}^{t=\tau_2}\leqslant(\bar{u}-\tilde{u}-1/\mu)(R^2(t)-a^2)|_{t=\tau_1}^{t=\tau_2}$.

证 在(13)式中令$t=t_i(i=1,2)$,可得

$$\frac{1}{\mu}R(t)R'(t)\bigg|_{t=\tau_1}^{t=\tau_2} = \int_{\tau_1}^{\tau_2} r\frac{\partial u}{\partial r}\bigg|_{r=a}^{r=R(t)}\mathrm{d}t + \int_{\tau_1}^{\tau_2} R(t)u(R(t),t)R'(t)\,\mathrm{d}t + \frac{1}{2\mu}(R^2(t)-a^2)\bigg|_{t=\tau_1}^{t=\tau_2} - \int_{\tau_1}^{\tau_2}\frac{1}{2}(R^2(t)-a^2)\tilde{u}\mathrm{d}t - \frac{1}{2}(R^2(t)-a^2)\tilde{u}\bigg|_{t=\tau_1}^{t=\tau_2} =$$

$$\int_{\tau_1}^{\tau_2} r\frac{\partial u}{\partial r}\bigg|_{r=a}^{r=R(t)}\mathrm{d}t + \int_{\tau_1}^{\tau_2} R(t)u(R(t),t)R'(t)\,\mathrm{d}t - \frac{1}{2\mu}(R^2(t)-a^2)\bigg|_{t=\tau_1}^{t=\tau_2} - \frac{1}{2\mu}(R^2(t)-R^2(0))\bigg|_{t=\tau_1}^{t=\tau_2} - \int_{\tau_1}^{\tau_2}\frac{1}{2}(R^2(t)-a^2)\bar{u}\mathrm{d}t - \frac{1}{2}(R^2(t)-a^2)\tilde{u}\bigg|_{t=\tau_1}^{t=\tau_2}.$$

由$R'(t)\geqslant 0$,有不等式

$$\int_{\tau_1}^{\tau_2} R(t)u(R(t),t)R'(t)\,\mathrm{d}t\leqslant\bar{u}(R^2(t)-a^2)\bigg|_{t=\tau_1}^{t=\tau_2},$$

于是

$$\frac{1}{\mu}R(t)R'(t)\bigg|_{t=\tau_1}^{t=\tau_2} = (\bar{u}-\tilde{u}-1/\mu)(R^2(t)-a^2)\bigg|_{t=\tau_1}^{t=\tau_2} + \int_{\tau_1}^{\tau_2} r\frac{\partial u}{\partial r}\bigg|_{r=a}^{r=R(t)}\mathrm{d}t - \int_{\tau_1}^{\tau_2}\frac{1}{2}(R^2(t)-a^2)\tilde{u}\mathrm{d}t,$$

又因为$R(\tau_1)-a\geqslant 2(\sup\limits_t\alpha(t))\bar{u}/\tilde{u}$, 则后2项小于0,故

$$\frac{1}{\mu}R(t)R'(t)\bigg|_{t=\tau_1}^{t=\tau_2}\leqslant(\bar{u}-\tilde{u}-1/\mu)(R^2(t)-a^2)\bigg|_{t=\tau_1}^{t=\tau_2}.$$

故引理2得证.

本节主要结果如下:

定理2 若$\alpha(t)$一致有界,且$\mu(\bar{u}-\tilde{u})<1$,则问题(2)~(6)的自由边界$R(t)$一致有界.

证 反证法. 假设$\sup\limits_t R(t)=+\infty$,则有以下2种情况:

(i) $\exists T_0>0$,当$t\geqslant T_0$时,$R'(t)\geqslant 0$.

(ii) 存在一个序列区间(s_n,t_n),有

$R'(t)\geqslant 0$,$t\in(s_n,t_n)$,$R(s_n)-a\leqslant B$,$R'(s_n)=0$,$R(t_n)\to+\infty$,

这里 $B=2(\sup\limits_t\alpha)\bar{u}/\tilde{u}$.

若(i)不成立,即存在一个序列$\bar{t}_n\to\infty$,使得$R(\bar{t}_n)<0$. 同时,若$\sup\limits_t R(t)=+\infty$,则意味着存在一个局部极大值点$\bar{t}_n\to\infty$的序列,使得$R(\bar{t}_n)\to\infty$. 因此,对于每一个$n$,有一个最大的序列区间$(s_n,t_n)$,使得

$R(t_n)>\max\{R(t_{n-1}),n,B\}$,$R'(s_n)=R'(t_n)=0$,$R'(t)>0$,$t\in(s_n,t_n)$.

记$R''(t)\geqslant 0$,由引理1得$R(s_n)-a<2\alpha(s_n)\bar{u}/\tilde{u}<B$.

假设(i)成立, 对于递增的T_0, 不失一般性, $R(T_0)-a\geqslant 2(\sup\limits_t\alpha)\bar{u}/\tilde{u}$,所以$\forall t>T_0$,可取$\tau_1=T_0$,$\tau_2=t$. 利用引理2,设$\rho(t)=(R^2(t)-a^2)/2$,则$\rho'(t)=R(t)R'(t)$,$(\rho'(t)-\rho'(T_0))/\mu<(\bar{u}-\tilde{u}-1/\mu)(\rho(t)-\rho(T_0))$,$\rho'(t)-\rho'(T_0)<(\mu(\bar{u}-\tilde{u})-1)(\rho(t)-\rho(T_0))$.

又因为$\mu(\bar{u}-\tilde{u})<1$,设$\beta=1-\mu(\bar{u}-\tilde{u})>0$,可得

$$\rho'(t)-\rho'(T_0)<-\beta(\rho(t)-\rho(T_0)),$$

两端同乘以$\mathrm{e}^{\beta t}$,则有

$$\mathrm{e}^{\beta t}\rho'(t)+\beta\mathrm{e}^{\beta t}\rho(t)=(\mathrm{e}^{\beta t}\rho(t))'<\mathrm{e}^{\beta t}(\rho'(T_0)+\beta\rho(T_0)).$$

对上式两端同时从T_0到t积分得

$$\mathrm{e}^{\beta t}\rho(t)-\mathrm{e}^{\beta T_0}\rho(T_0)<(\mathrm{e}^{\beta t}-\mathrm{e}^{\beta T_0})(\rho'(T_0)+\beta\rho(T_0))/\beta.$$

$\forall t>T_0$,有

$$\rho(t)<\mathrm{e}^{\beta(T_0-t)}\rho(T_0)+(1-\mathrm{e}^{\beta(T_0-t)})(\rho'(T_0)+\beta\rho(T_0))/\beta,$$

对于所有的$t>T_0$,有$\rho(t)=(R^2(t)-a^2)/2$一致收敛,因此与假设$\sup\limits_t R(t)=+\infty$矛盾.

另一方面,假设(ii)成立,用s_n'替代s_n,$s_n'\in(s_n,t_n)$,假设$R(s_n)-a=B$,利用引理2得

$\rho'(t)<-\beta(\rho(t)-\rho(s_n))+\rho'(s_n)$,$t\in(s_n,t_n)$,

上式两端同时乘以$\mathrm{e}^{\beta t}$,注意到由(5)式可得不等式

$\rho' \leqslant \mu(\bar{u} - \tilde{u})\rho$,于是有

$$(e^{\beta t}\rho(t))' < e^{\beta t}(\rho'(s_n) + \beta\rho(s_n)) = e^{\beta t}(\beta B_1) \cdot (\beta + \mu(\bar{u} - \tilde{u})),$$

记 $B_1 = \rho(s_n) = 2((\sup_t \alpha\bar{u})/\tilde{u})^2 - a^2/2$,则有

$$(e^{\beta t}\rho(t))' < e^{\beta t}(\beta B_1 + \mu(\bar{u} - \tilde{u})\rho(s_n)) \leqslant e^{\beta t}B_1(\beta + \mu(\bar{u} - \tilde{u})).$$

从 s_n 到 t_n 积分得

$$e^{\beta t_n}\rho(t_n) - e^{\beta s_n}B_1 < (e^{\beta t_n} - e^{\beta s_n})B_1(1 + \mu(\bar{u} - \tilde{u})/\beta),$$

两端同时乘以 $e^{-\beta t}$ 得

$$\rho(t_n) < e^{-\beta(t_n - s_n)}B_1 + (1 - e^{-\beta(t_n - s_n)})B_1(1 + \mu(\bar{u} - \tilde{u})/\beta) < B_1(1 + \mu(\bar{u} - \tilde{u})/\beta),$$

由此可见$\rho(t_n)$ 一致有界,这与(ii) 矛盾,故$R(t)$ 一致有界.

3　自由边界 $R(t)$ 的渐近性

在这一节中,研究问题(2) ~(6) 的自由边界 $R(t)$ 的渐近行为.

引理 3　若 $R(t)$ 一致有界,且$\lim_{t\to\infty}\alpha(t) = 0$,则 $\liminf_{t\to\infty} R(t) = a$.

证　反证法. 假设结论不成立,则存在正常数 $R_1, R_2 > a$,对所有的 $t > 0$ 有 $R_1 \leqslant R(t) \leqslant R_2$. 设 $C_* = \sup_{R_1 \leqslant r \leqslant R_2} u_*$, $c_0 = \sup_{R_1 \leqslant r \leqslant R_2} du_*/dr$. 这里 u_* 为稳态问题(7) ~(10) 的解,即

$$u_*(r) = (\alpha\bar{u}(K_1(R)I_0(r) + I_1(R)K_0(r)))/(I_1(R)(\alpha K_0(a) + K_1(a)) + K_1(R)(\alpha I_0(a) - I_1(a))),$$

$$u_*'(r) = (\alpha\bar{u}(K_1(R)I_1(r) + I_1(R)K_1(r)))/(I_1(R)(\alpha K_0(a) + K_1(a)) + K_1(R)(\alpha I_0(a) - I_1(a))) < 0.$$

取充分小的ε,满足$\varepsilon C_* < \tilde{u}/3$. 由$\lim_{t\to\infty}\alpha(t) = 0$,存在充分大的 t_0,使得

$$\alpha(t) < c_1 := -\varepsilon c_0/\bar{u}, t > t_0.$$

令 $\omega(r,t) = \bar{u}e^{-(t-t_0)} + \varepsilon u_*, t > t_0$,易验证 ω 满足

$$\partial\omega/\partial t = \Delta_r\omega - \omega,$$

$$\omega(r,t_0) = \bar{u} + \varepsilon u_* > \bar{u} \geqslant u(r,t_0),$$

故 $\partial\omega/\partial n = \varepsilon du_*/dr = 0$,在 $r = R(t)$ 处,

$$\partial\omega/\partial n + \alpha(t)(\omega - \bar{u}) > -\varepsilon du_*/dr - \alpha(t)\bar{u} > -\varepsilon c_0 - c_1\bar{u} = 0, r = a.$$

由上述讨论可见,$\omega(r,t)$ 为问题(2) ~(4) 的解,故 $u(r,t) < \omega(r,t), t > t_0$. 当 t_1 足够大时,$\bar{u}e^{-(t_1-t_0)} \leqslant \tilde{u}/3$. 于是对于 $t > t_1$,有

$$u(r,t) - \bar{u} < \omega(r,t) - \bar{u} = \bar{u}e^{-(t_1-t_0)} + \varepsilon C_* - \bar{u} < \tilde{u}/3,$$

进而对所有的 $t > t_1$ 有

$$d(R(t) - a)/dt = \frac{\mu}{R(t)}\int_a^{R(t)}(u - \tilde{u})r dr < -\mu\tilde{u}(R^2 - a)/(6R) < -\mu\tilde{u}(R - a)/3,$$

这表明当 $t\to\infty$ 时,$R(t) - a$ 以指数方式递减到0,与假设 $R_1 > a$ 矛盾,从而引理 3 的结论成立.

定理 3　若$\lim_{t\to\infty}\alpha(t) = 0$,$\mu(\bar{u} - \tilde{u}) < 1$,则当 $t\to\infty$ 时,$R(t)\to a$.

证　由定理 2 易知,$R(t)$ 是一致有界的. 假设定理 3 不成立,即$\lim_{t\to\infty}\rho(t) \neq 0$,其中 $\rho(t)$ 的定义由定理2 中给出. 由引理3 知,存在一个正数γ_0 和序列 t_n 及 $\bar{t}_n$,对所有 n 有

$$\bar{t}_n < t_n < \bar{t}_{n+1}, \rho(t_n) > \gamma_0, \rho(\bar{t}_n) < \gamma_0, \rho'(\bar{t}_n) < 0 < \rho'(t_n).$$

这里 $\rho(t) = (R^2(t) - a^2)/2$,取

$$s_n = \inf\{s' : s' < t_n, \rho'(t) > 0, t \in (s', t_n)\},$$

则 $s_n \in (\bar{t}_n, t_n)$,当 $n\to\infty$ 时,$s_n\to\infty$,$\rho'(s_n) = 0$,$\rho''(s_n) \geqslant 0$. 由引理1 得 $R(s_n) - a \leqslant 2\bar{u}\alpha(s_n)/\tilde{u}$. 从而存在不相交的序列区间$(s_n, t_n)$,有

$$\rho'(t) > 0, t \in (s_n, t_n), s_n\to\infty, \rho(s_n) \leqslant 2(\bar{u}(\sup_{(s_n,\infty)}\alpha)/\tilde{u})^2 + 2\bar{u}(\sup_{(s_n,\infty)}\alpha)/\tilde{u}\to 0. \tag{14}$$

当 $n > n_0$ 时,

$$\rho(t_n) \geqslant \gamma_0 > 2(\bar{u}(\sup_{(s_n,\infty)}\alpha)/\tilde{u})^2 + 2\bar{u}(\sup_{(s_n,\infty)}\alpha)/\tilde{u} > 0. \tag{15}$$

由(14) ~(15) 式知,$\exists s_n' \in (s_n, t_n)$,有

$$\rho(s_n') = 2(\bar{u}(\sup_{(s_n,\infty)}\alpha)/\tilde{u})^2 + 2\bar{u}(\sup_{(s_n,\infty)}\alpha)/\tilde{u}. \tag{16}$$

注意到当$n\to\infty$ 时,$s_n'\to\infty$,则(16) 式右端趋于0. 因此当 n 足够大时,

$$\rho(s_n') < \gamma_0\beta/(2\beta + \mu(\tilde{u} - \bar{u})). \tag{17}$$

结合(14)、(16) 式和引理3,取$\tau_1 = s_n'$,$\tau_2 \in [s_n', t]$,有 $\rho'(t) - \rho'(s_n') \leqslant -\beta(\rho(t) - \rho(s_n'))$,$t \in [s_n, t_n]$.

类似于定理 2 中(ii) 的证明过程,可得

$$\rho(t_n) < e^{-\beta(t_n - s_n)}\rho(s_n') + \rho(s_n')(1 + \mu(\bar{u} - \tilde{u})/\beta).$$

又由(17) 式得

$$\rho(t_n) < \rho(s_n')(2 + \mu(\bar{u} - \tilde{u})/\beta) < \gamma_0,$$

故与假设$\rho(t_n) \geqslant \gamma_0$ 相矛盾,因此,定理 3 成立.

4 参考文献

[1] Bellomo N. A survey of models for tumor-immune system dynamics [J]. Modeling, Simulation in Science Engineering, Technology, 1997, 59(5): 1023-1024.

[2] Byrne H M, Chaplain M A J. Growth of nonnecrotic tumors in the presence and absence of inhibitors [J]. Math Biosci, 1995, 130(2): 151-181.

[3] Byrne E H, Chaplain M A J. Free boundary value problems associated with the growth and development of multicellular spheroids [J]. European Journal of Applied Mathematics, 1997, 8(6): 639-658.

[4] Cui Shangbin. Analysis of a mathematical model for the growth of tumors under the action of external inhibitors [J]. Journal of Mathematical Biology, 2002, 44(5): 395-426.

[5] Zhuang Yuehong, Cui Shangbin. Analysis of a free boundary problem modeling the growth of spherically symmetric tumors with angiogenesis [J]. Acta Appl Math, 2019, 161(1): 153-169.

[6] Cui Shangbin, Friedman A. Analysis of a mathematical model of the growth of necrotic tumors [J]. Journal of Mathematical Analysis, Applications, 2001, 255(2): 636-677.

[7] Friedman A, Reitich F. Analysis of a mathematical model for the growth of tumors [J]. Journal of Mathematical Biology, 1999, 38(3): 262-284.

[8] Greenspan H P. Models for the growth of a solid tumor by diffusion [J]. Studies in Applied Mathematics, 1972, 51(4): 317-340.

[9] Ward J. Mathematical modelling of avascular-tumour growth [J]. Mathematical Medicine and Biology, 1997, 14(1): 39-69.

[10] Cristini V, Lowengrub J, Nie Qing. Nonlinear simulation of tumor growth [J]. Journal of Mathematical Biology, 2003, 46(3): 191-224.

[11] Greenspan H P. On the growth and stability of cell cultures and solid tumors [J]. Journal of Theoretical Biology, 1976, 56(1): 229-242.

[12] Friedman A, Lam K Y. Analysis of a free-boundary tumor model with angiogenesis [J]. Journal of Differential Equations, 2015, 259(12): 7636-7661.

[13] Zhou Fujun, Cui Shangbin. Well-posedness and stability of a multidimensional moving boundary problem modeling the growth of tumor cord [J]. Discrete Contin Dyn Syst, 2012, 21(3): 929-943.

[14] Wu Junde, Zhou Fujun, Cui Shangbin. Analysis of an elliptic-parabolic free boundary problem modelling the growth of non-necrotic tumor cord [J]. Journal of Mathematical Analysis and Applications, 2009, 352(1): 184-205.

[15] Hao Wenrui, Hauenstein J D, Hu Bei, et al. Bifurcation for a free boundary problem modeling the growth of a tumor with a necrotic core [J]. Nonlinear Analysis: Real World Application, 2012, 13(2): 694-709.

The Free Boundary Problem Modeling the Growth of Tumor Cord with Angiogenesis

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Abstract: In this paper, the free boundary problem modeling the growth of tumor cord with angiogenesis is studied. Assuming that the tumor grows along the outside of blood vessel, the domain of tumor considered has two boundary, the inside boundary is fixed and the outside is free. For this problem, It is proved that there is a radially stationary solution to the problem. If the angiogenesis function $\alpha(t)$ is uniformly bounded, then the free boundary $R(t)$ is uniformly bounded. If $\lim\limits_{t\to\infty}\alpha(t)=0$, the free boundary will shrink to the inner boundary, that is, the tumor disappears.

Key words: tumor cord; free boundary; stationary solution; radially symmetric solution

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