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GLOBAL STABILITY OF CELLULAR POPULATIONS WITH UNEQUAL DIVISION

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ABSTRACT. A two-phase model for the growth of a single cellular population is presented. In this model the reproduction occurs by fission into two unequal parts. The evolution of the population is described by a nonlinear partial differential equation with time delay and integral term containing maturity variable. We give conditions for global stability of the solutions of this equation.

1. Introduction. In this paper we investigate a maturity structure model of a cellular population. The cellular population number is described by a system of first order partial differential equations with time delay and a nonlocal dependence in the maturity variable due to cell replication.

The use of partial differential equations as population models has had a long history starting with the papers [**2**], [**16**], [**17**], [**19**], [**22**], [**23**]. A survey of many applications is given in the book edited by Metz and Diekmann [**15**]. In many papers on this subject, models are investigated in which reproduction is by fission into two equal parts, [**3**]–[**5**], [**7**], [**11**]–[**14**], [**18**].

In particular Mackey and Rudnicki [**13**] consider a two-phase model for the growth of a cellular population. They assume that cells are capable of simultaneous proliferation and maturation. Maturity can be size, weight, volume of a cell or concentration of some special substance. Maturity of a cell decides on the capacity of a cell for replication. The aim of this paper is to generalize results from [**13**] to a model with unequal division. In some biological situations, models with unequal division are more suitable. For example, in mutant strains of bacteria we usually observe unequal division of the size. Models with unequal division were considered in papers [**1**], [**6**], [**8**], [**9**], [**20**].

The paper is organized as follows. In Section 2 we present the model. In Section 3 we reduce the problem of asymptotic behavior of the solutions of the main equation to two simpler equations: a delay differential equation and linear partial differential equation with an integral perturbation. Section 4 gives the statement and proof of global stability. Since our paper generalizes results from [**13**], proofs of some of them are similar and we omit these.

2. Presentation of the model. We consider a model of a cell population in which the cells may be either actively proliferating or in a resting phase. Moreover, we consider here a population of cells capable of both proliferation and maturation. Each phase is represented by a partial differential equation.

2.1. Proliferating phase. After entering the proliferating phase, a cell is committed to undergo cell division a fixed time τ later. The generation time τ is assumed to consist of four phases, G_1 the pre-synthetic phase, S the DNA synthesis phase, G_2 the post-synthetic phase and M the mitotic phase. These four phases put together form the active phase. The density function of proliferating cells is denoted by $p(t,m,a)$, where $t > 0$ represents time, $m \in (0,1)$ maturity and $a \in [0,\tau]$ their age in the cycle. The cells of both types (resting and proliferating) mature with a velocity $V(m)$. We assume that $V : [0,1] \to [0,\infty)$ is a continuously differentiable function such that $V(m) > 0$ for all $m \in (0,1)$, and $V(0) = V(1) = 0$. We also assume that cells in the active phase die at a rate γ depending on maturity m. The cell density function p satisfies the following equation

$$\frac{\partial p}{\partial t} + \frac{\partial p}{\partial a} + \frac{\partial (Vp)}{\partial m} = -\gamma p \tag{1}$$

with initial conditions

$$p(0,m,a) = \Gamma(m,a) \quad \text{for } (m,a) \in (0,1) \times [0,\tau],$$

where Γ is assumed to be continuous. Finally, we define the density of proliferating cells at a given time and maturity level as follows

$$P(t,m) = \int_0^\tau p(t,m,a)\,da.$$

2.2. Resting phase. Just after the division, both daughter cells go into the resting phase called G_0-*phase*. Once in this phase, they can either return to the proliferating phase and complete the cycle or die before ending the cycle. This is why the cellular age in the resting population ranges from $a = 0$ (when cells enter this phase) to $a = +\infty$. The function $n(t, m, a)$ represents the density of the cells in the resting phase. We denote by

$$N(t, m) = \int_0^{+\infty} n(t, m, a)\, da$$

the density with arbitrary age level in the resting phase. The total number of resting cells at all age and maturity levels is given by

$$\overline{N}(t) = \int_0^{+\infty} N(t, m)\, dm.$$

In view of the above assumptions, we consider here two causes of loss, in the righthand side of the equation below.

(a) The first loss is random and has a rate δ which depends on maturity of a cell.

(b) The second one is the reintroduction of the cell into the proliferating phase with a rate β, where β depends on m and the total number of cells in the resting phase $\overline{N}$. We also assume that β is a decreasing function of $\overline{N}$.

The conservation equation is

$$\frac{\partial n}{\partial t} + \frac{\partial n}{\partial a} + \frac{\partial (Vn)}{\partial m} = -(\delta + \beta) n \tag{2}$$

with the initial condition

$$n(0, m, a) = \mu(m, a) \quad \text{for } (m, a) \in (0, 1) \times [0, +\infty) \tag{3}$$

and

$$\lim_{a \to +\infty} \mu(m, a) = 0.$$

We always assume that μ and β are continuous functions.

2.3. Boundary conditions. The first boundary condition describes biologically the fact that a mother cell can divide its maturity in an unequal manner

$$n(t, m, 0) = 2 \int_0^1 p(t, x, \tau) k(x, m)\, dx \tag{4}$$

with m representing maturity of the daughter cells at age $a = 0$ and x maturity of the mother cell at the point of cytokinesis. The function $m \mapsto k(x, m)$ is the density of maturity of a daughter cell assuming that the mother cell has maturity x. The function k is nonnegative, continuous and satisfies conservation consistency

$$\int_0^1 k(x,m)\,dm = 1 \quad \text{for every } x \in (0,1). \tag{5}$$

Moreover, we assume that there exist κ_1 and κ_2 with $0 < \kappa_1 < \kappa_2 < 1$ such that

$$k(x,m) = 0 \quad \text{for } m \le \kappa_1 x \quad \text{or } \kappa_2 x \le m. \tag{6}$$

This means that maturity of the daughter cell cannot be too small or too big.

The second boundary condition

$$p(t,m,0) = \int_0^{+\infty} \beta(\overline{N}(t),m)n(t,m,a)\,da = \beta(\overline{N}(t),m)N(t,m) \tag{7}$$

represents the population efflux from the resting compartment into the proliferative one.

2.4. Equations for N and P. In this section we recall some results from [**13**] that will be used later. First, we define the maturity flow $\pi_s m$ as the solution of the equation

$$\frac{d\pi_s m}{ds} = V(\pi_s m)$$

with the initial condition

$$\pi_0 m = m.$$

From the assumption on maturity velocity V, it follows that $\pi_s m \in (0,1)$, for all $s \ge 0$ and $m \in (0,1)$. We also define the following function

$$\varphi(m,s) = \frac{V(\pi_{-s}m)}{V(m)} \exp\left\{ -\int_{\pi_{-s}m}^{m} \frac{\gamma(y)}{V(y)}\,dy \right\}. \tag{8}$$

Using the method of characteristics we check that $p(t,m,a) = p(t-a,\pi_{-a}m,0)\varphi(m,a)$ for every $t \geq a$. From (1) and (7) it follows that

$$p(t,m,\tau) = \beta(\overline{N}(t-\tau),\pi_{-\tau}m)N(t-\tau,\pi_{-\tau}m)\varphi(m,\tau)$$

for $t \geq \tau$. Consequently

$$n(t,m,0) = 2\int_0^1 \beta(\overline{N}(t-\tau),\pi_{-\tau}x)N(t-\tau,\pi_{-\tau}x)\varphi(x,\tau)k(x,m)\,dx.$$

Now we focus on the equation (2) modelling the resting phase. Integrating (2) with respect to age a, we obtain

$$\frac{\partial N}{\partial t} + \frac{\partial(NV)}{\partial m} = -(\delta+\beta)N + n(t,m,0). \tag{9}$$

For $t \geq \tau$ the partial differential equation (9) becomes

$$\begin{aligned}\frac{\partial N}{\partial t} &+ \frac{\partial(VN)}{\partial m}\\ &= -\left(\delta(m) + \beta(\overline{N},m)\right)N\\ &\quad + 2\int_0^1 \beta(\overline{N}(t-\tau),\pi_{-\tau}x)N(t-\tau,\pi_{-\tau}x)\varphi(x,\tau)k(x,m)\,dx.\end{aligned} \tag{10}$$

Integrating (1) with respect to the age variable and using the boundary condition (7) we obtain

$$\begin{aligned}\frac{\partial P}{\partial t} + \frac{\partial(VP)}{\partial m} = &-\gamma(m)P + \beta(\overline{N},m)N - N(t-\tau,\pi_{-\tau}m)\\ &\cdot \beta(\overline{N}(t-\tau),\pi_{-\tau}m)\varphi(m,\tau)\end{aligned} \tag{11}$$

for $t \geq \tau$.

Observe that solutions of equation (11) depend on the solutions of equation (10). Moreover, knowing the asymptotic behavior of the solutions of equation (10), it is easy to forecast the behavior of the solutions of equation (11) because equation (11) can be solved by the method of characteristics. This is the reason why we will concentrate our study on equation (10).

Using similar arguments as in Section 3 of [**13**] one can prove the following proposition.

Proposition 1. *We suppose that δ, β, γ, V', Γ and $N(0,m)$ are bounded continuous functions. Then* (10) *has a unique solution.*

3. Analysis of equation (10).

3.1. Markov operator. In the following we consider the case with δ, β and γ independent of maturity m. In this case (10) takes the form

$$\frac{\partial N}{\partial t}+\frac{\partial (NV)}{\partial m} = -\left(\delta+\beta(\overline{N})\right)N+2e^{-\gamma\tau}\beta(\overline{N}(t-\tau))\mathcal{P}N(t-\tau,m), \tag{12}$$

where $N = N(t,m)$. From now on N without arguments means $N(t,m)$ and, similarly, $\overline{N} = \overline{N}(t)$. $\mathcal{P}$ is the operator defined on the space $L^1(0,1)$ given by

$$\mathcal{P}f(m) = e^{\gamma\tau}\int_0^1 \varphi(x,\tau)k(x,m)f(\pi_{-\tau}x)\,dx. \tag{13}$$

We check that $\mathcal{P}$ is a Markov operator [**10**], i.e.,

(i) $\mathcal{P}$ is a linear operator on L^1,

(ii) $f \geq 0$ implies that $\mathcal{P}f \geq 0$ and

(iii)

$$\int_0^1 \mathcal{P}f(m)\,dm = \int_0^1 f(m)\,dm.$$

Conditions (i) and (ii) are obvious. It remains to check (iii). To compute $\int_0^1 \mathcal{P}f(m)\,dm$ we substitute $x = \pi_\tau y$. As γ is independent of maturity we have

$$\varphi(\pi_\tau y,\tau) = \frac{V(y)}{V(\pi_\tau y)}\exp\{-\gamma\tau\} \tag{14}$$

and since

$$\frac{\partial}{\partial y}\pi_\tau y = \frac{V(\pi_\tau y)}{V(y)} \tag{15}$$

we obtain

$$\begin{aligned}\int_0^1 \mathcal{P}f(m)\,dm &= e^{\gamma\tau}\int_0^1\left(\int_0^1 k(x,m)\,dm\right)f(\pi_{-\tau}x)\varphi(x,\tau)\,dx\\ &= e^{\gamma\tau}\int_0^1 \varphi(\pi_\tau y,\tau)\,\frac{V(\pi_\tau y)}{V(y)}\,f(y)\,dy\\ &= \int_0^1 f(y)\,dy.\end{aligned}$$

Denote by D the subset of $L^1(0,1)$ consisting of all the densities, i.e., $f \in D$ if $f \geq 0$ and $\int_0^1 f(x)\,dx = 1$. Then $\mathcal{P}$ is a Markov operator if and only if $\mathcal{P}$ is linear and $\mathcal{P}(D) \subset D$.

3.2. Equation for $\overline{N}(t)$. Since $\mathcal{P}$ is a Markov operator, after integrating (12) with respect to maturity m, we obtain

$$\overline{N}'(t) = -\left(\delta + \beta(\overline{N})\right)\overline{N}(t) + 2e^{-\gamma\tau}\beta(\overline{N}(t-\tau))\overline{N}(t-\tau) \tag{16}$$

which corresponds exactly to (15) of [**13**]. The analysis of the behavior of the solutions of this equation is given in [**13**]. Now we recall some facts. First, all solutions are bounded. If $\delta > (2e^{-\gamma\tau} - 1)\,\beta(0)$, then the trivial solution $\overline{N} \equiv 0$ is globally asymptotically stable. This inequality has a simple biological interpretation. Namely, it holds if the death rates δ and γ are large or the phases are long (τ is large or $\beta(0)$ is small). In both cases the reproduction rate is smaller than the death rate and the population will die out.

If the above inequality does not hold and β has a typical form $\beta(x) = [b/(c+x)]$, then equation (16) has a nonzero globally stable solution $\overline{N}_0$, and $\overline{N}(t)$ converges exponentially to $\overline{N}_0$. From now on, we will assume that solutions of equation (16) have the above property.

3.3. Linear form of equation (10)**.** Let $M(t,m) = [(N(t,m))/(\overline{N}(t))]$. Then $\int_0^1 M(t,m)\,dm = 1$. Using (16) we obtain

$$\frac{\partial M}{\partial t} + \frac{\partial (VM)}{\partial m} = c(t)\left[-M(t,m) + \mathcal{P}M(t-\tau,m)\right] \tag{17}$$

with

$$c(t) = \frac{2e^{-\gamma\tau}\overline{N}(t-\tau)\beta(\overline{N}(t-\tau))}{\overline{N}(t)}. \tag{18}$$

Since $M(t,\cdot) \in D$ for every t, the solutions of (17) will be investigated in the set D. Our aim is to prove some theorem concerning asymptotic stability of equation (17). The properties of equation (17) depend on the function c. Since $\overline{N}(t)$ converges to $\overline{N}_0 > 0$ in an exponential way, the function $c(t)$ converges to some constant $c_0 > 0$ and

$$\int_0^\infty |c(t) - c_0|\, dt < \infty. \tag{19}$$

We compare the solutions of (17) with the solutions of the following linear equation

$$\frac{\partial F}{\partial t} + \frac{\partial (VF)}{\partial m} = -\, cF(t,m) + c\mathcal{P}F(t-\tau, m), \tag{20}$$

where c is a constant.

Proposition 2. *Let M and F be solutions of* (17) *and* (20), *respectively. Assume that $M(t,m) = F(t,m)$ and $M(t,\cdot) \in D$ for $t \in [t_0 - \tau, t_0]$. Then*

$$\int_0^1 |M(t,m) - F(t,m)|\, dm \le \int_{t_0}^t 2|c(s) - c|\, ds \quad \text{for } t \ge t_0. \tag{21}$$

Proof. This proposition was proved in [**13**] for the operator $\mathcal{P}$ given by the formula

$$\mathcal{P}f(m) = k'(m) f(k(m)).$$

The proof is exactly the same when $\mathcal{P}$ is an arbitrary Markov operator. So we omit it here. □

4. Stability. In this section we generalize Theorem 1 of [**13**] to the case of unequal division.

Theorem 1. *Assume that*

$$\kappa_1 > \exp(-\, V'(0)[(1/c) + \tau]). \tag{22}$$

Then there exists $f^* \in D$ *such that for every solution of* (20) *we have*

$$\lim_{t\to+\infty} \|F(t) - f^*\| = 0,$$

where $\|\cdot\|$ *is the norm in* $L^1(0,1)$.

Remark 1. This theorem implies that if (16) has a nonzero globally asymptotically stable solution $\overline{N}_0$, then all solutions of (10) converge in L^1 to $\overline{N}_0 f^*$.

Remark 2. Condition (22) has an interesting biological interpretation. It shows that the stability of the population is highly dependent on the dynamics of low mature (small) cells. Indeed, if we rewrite (22) in the following way

$$c \ln(b) < V'(0),$$

with $c = c_0 = 2e^{-\gamma\tau}\beta(\overline{N}_0) = \delta + \beta(\overline{N}_0)$ as a solution of the stationary solution of (16), and $b = (1/\kappa_1)e^{-\tau V'(0)}$. The coefficient c represents the rate of leaving of the resting phase (by being lost or by entering the proliferating phase). Using condition (6), we obtain the following inequality

$$\frac{1}{\kappa_1} > \frac{x}{m},$$

where x is the maturity of the mother cell just before dividing and m the maturity of the daughter cell at its birth. So, we obtain

$$b > \frac{xe^{-\tau V'(0)}}{m},$$

where $xe^{-\tau V'(0)}$ is the maturity of the mother at the beginning of its proliferating phase. Since $V'(0)$ is the rate at which small cells mature, condition (22) means that the maturation of a big part of small cells will increase in the next generation.

Instead of (20) we can consider a simpler equation. Let y be the solution of the following problem

$$\begin{cases} cy'(x)x = V(y(x)), \\ \quad y(1) = m_N. \end{cases} \tag{23}$$

It is easy to check that y is an increasing function from the interval $(0,\infty)$ onto the interval $(0,1)$. We make the following substitution

$$u(t,x) = y'(x)F(t,y(x)) \tag{24}$$

for $x \in (0,\infty)$. Then u satisfies the following equation

$$\frac{\partial u}{\partial t}+\frac{\partial (cxu)}{\partial x} = -\,cu(t,x)+cy'(x)\int_0^\infty u(t-\tau,r)k(\pi_\tau y(r),y(x))\,dr. \tag{25}$$

Setting

$$q(r,x) = y'(x)k(\pi_\tau y(r),y(x)), \tag{26}$$

we can check that

$$q(r,x) \ge 0 \quad \text{for all } (r,x) \quad \text{and} \quad \int_0^\infty q(r,x)\,dx = 1.$$

Now equation (25) takes the form

$$\frac{\partial u}{\partial t}+cx\,\frac{\partial u}{\partial x} = -\,2cu + c\int_0^\infty u(t-\tau,r)q(r,x)\,dr. \tag{27}$$

Since $Tf(x) = y'(x)f(y(x))$ is a linear isometric transformation from D to $D(0,+\infty)$, the set of densities of $L^1(0,+\infty)$, it is sufficient to prove the theorem for equation (27). The solutions of (27) satisfy the integral equation

$$\begin{aligned} u(t,x) &= e^{-2ct}u(0,e^{-ct}x) \\ &\quad + c\int_0^t e^{-2cs}\int_0^\infty u\left(t-\tau-s,\xi\right)q(\xi,xe^{-cs})\,d\xi\,ds. \end{aligned} \tag{28}$$

First we check that for any solutions u and $\bar{u}$ of (27) that we have $\|u(t)-\overline{u}(t)\| \to 0$ as $t\to\infty$. Then, after showing that there exists a stationary solution u_0 of (27), i.e., independent on t, we will obtain that $\|u(t)-u_0\| \to 0$ as $t\to\infty$. We prove the following lemmas.

Lemma 1. *Assume that* $\kappa_1 > \exp(-V'(0)\,[(1/c)+\tau])$. *Then there exist* $a>0$ *and* $b>2a$ *such that for every solution of* (27) *there is a time* $t_0 = t_0(u)$ *for which*

$$\int_a^b u(t,x)\,dx > \frac{1}{2} \quad \textit{for } t \ge t_0. \tag{29}$$

Proof. We first prove that for sufficiently large t, there exists $a > 0$ such that $\int_0^a u(t,x)\,dx < (1/4)$, and there exists $b > 0$ such that $\int_b^\infty u(t,x)\,dx < (1/4)$. Since $u \in D$ we will have $\int_a^b u(t,x)\,dx > (1/2)$.

We denote by D_0 the dense subset of D consisting of bounded functions f such that $\int_0^\infty x^{-r} f(x)\,dx < \infty$ with $r \in (0,1)$ and $\lim_{x\to\infty} xf(x) = 0$. Let u be a solution of (27) such that $u(t,\cdot) \in D_0$ for $t \in [-\tau, 0]$. Using (28) one can check that $u(t,\cdot) \in D_0$ for $t \geq 0$. We set

$$G(t) = \int_0^\infty x^{-r} u(t,x)\,dx.$$

From (27) the function G satisfies

$$G'(t) = -\,c(1+r)G(t) + c\int_0^\infty u(t-\tau,s)\left(\int_0^\infty x^{-r} q(s,x)\,dx\right)ds.$$

From (6) and (26) we obtain

$$\int_0^\infty x^{-r} q(s,x)\,dx = \int_{\kappa_1\pi_\tau y(s)}^1 \left(y^{-1}(z)\right)^{-r} k(\pi_\tau y(s),z)\,dz.$$

Since y^{-1} is an increasing function and $\int_{\kappa_1\pi_\tau y(s)}^1 k(\pi_\tau y(s),z)\,dz = 1$, we have

$$\int_0^\infty x^{-r} q(s,x)\,dx \leq \left(y^{-1}\left(\kappa_1\pi_\tau y(s)\right)\right)^{-r}.$$

We claim that there exists $r \in (0,1)$ such that

(30) $$\lim_{s\to 0}\left[\frac{\left(y^{-1}\left(\kappa_1\pi_\tau y(s)\right)\right)}{s}\right]^{-r} < 1 + r.$$

Indeed, from inequality $\kappa_1 > \exp(-V'(0)\,[(1/c)+\tau])$, we obtain

(31) $$\kappa_1\pi_\tau y(s) > y(e^{-1}s)$$

for sufficiently small $s > 0$. Since

$$\lim_{s\to 0}\frac{y(e^{-1}s)}{y(s)} = e^{-V'(0)/c} \quad \text{and} \quad \lim_{s\to 0}\frac{\pi_\tau y(s)}{y(s)} = \kappa_1 e^{\tau V'(0)}$$

from (31) it follows that

$$\lim_{s\to 0}\left[\frac{\left(y^{-1}\left(\kappa_1\pi_\tau y(s)\right)\right)}{s}\right] > e^{-1}.$$

Since $\lim_{r\to 0}(1+r)^{-1/r} = e^{-1}$, from the last inequality it follows that there exists $r\in(0,1)$ such that (30) holds. Thus $K < 1+r$ and $B>0$ exist such that

$$\left[\frac{\left(y^{-1}\left(\kappa_1\pi_\tau y(s)\right)\right)}{s}\right]^{-r} \le K + Bs^r$$

which gives

$$\int_0^\infty x^{-r}q(s,x)\,dx \le \left[\left(y^{-1}\left(\kappa_1\pi_\tau y(s)\right)\right)\right]^{-r} \le Ks^{-r}+B. \tag{32}$$

Hence we obtain that

$$G'(t) \le -c(1+r)G(t) + cKG(t-\tau) + Bc.$$

Let $\tilde{G}(t)$ be the solution of the differential delayed equation

$$\tilde{G}'(t) = -c(1+r)\tilde{G}(t) + cK\tilde{G}(t-\tau) + Bc, \tag{33}$$

such that $\tilde{G}(t) = G(t)$ for $t\in[-\tau,0]$. By the method of steps we can check that

$$\tilde{G}(t) \ge G(t) \quad \text{for } t \ge 0.$$

Since $K < 1+r$, the stationary solution

$$\tilde{G} = \frac{B}{1+r-K}$$

of (33) is globally asymptotically stable. Hence

$$\limsup_{t\to\infty} G(t) \le \frac{B}{1+r-K}.$$

Consequently, there exists $a>0$ independent of u such that $\int_0^a u(t,x)\,dx <$ $(1/4)$ for $t \ge t_0(u)$. We show now that there exists b such that

$\int_b^\infty u(t,x)\,dx < (1/4)$. From (26) and condition (6) it follows that if $x \geq y^{-1}(\kappa_2)$ then $q(r,x) = 0$ (where κ_2 is chosen as in Section 2.3). We set $y^{-1}(\kappa_2) = x_0$. Then for every $x \geq x_0$, (27) becomes

$$\frac{\partial u}{\partial t} + cx\,\frac{\partial u}{\partial x} = -\,2cu. \tag{34}$$

Set $U(t,x) = \int_x^\infty u(t,y)\,dy$ for $x \geq x_0$. It is easy to check that U exists and satisfies the equation

$$\frac{\partial U}{\partial t} + cx\,\frac{\partial U}{\partial x} = -\,cU. \tag{35}$$

The solution of (35) is given by

$$U(t,x) = x^{-1}x_0 U\left(t - \frac{1}{c}\,\ln\left(\frac{x}{x_0}\right), x_0\right).$$

Consequently, for $x \geq 4x_0$ and for $t \geq (1/c)\ln 4$, we have $U(t,x) \leq (1/4)$. Since D_0 is dense in D, condition (29) holds for every solution of (27). This completes the proof. □

Lemma 2. *There exists a nonnegative function $K \in L^1(0,\infty)$ with $\|K\| > 0$ such that $u(t,x) \geq K(x)$ for every solution u of* (27) *and sufficiently large t.*

Proof. Let x_0 be the same as in the proof of Lemma 1. It is easy to check by the method of characteristics that for $t \geq (1/c)\ln(x/x_0)$ and $x \geq x_0$, the solution of (34) is given by

$$u(t,x) = x^{-2}x_0^2 u\left(t - \frac{1}{c}\,\ln\left(\frac{x}{x_0}\right), x_0\right). \tag{36}$$

From (28) it follows that

$$u(t,x_0) \geq c\int_0^t e^{-2cs}\int_0^\infty u\left(t-\tau-s,\xi\right) q\left(\xi, x_0e^{-cs}\right)\,d\xi\,ds. \tag{37}$$

From (36) and (37) it follows that

$$u(t,x_0) \geq \int_{x_0}^{\bar{x}}\int_0^{t(\xi)} ce^{-2cs}\xi^{-2}x_0^2 u\left(t-\tau-s-\frac{1}{c}\,\ln\left(\frac{\xi}{x_0}\right), x_0\right) \cdot q(\xi, x_0e^{-cs})\,ds\,d\xi,$$

where $\bar{x} = x_0 e^{c(t-\tau)}$ and $t(\xi) = t - \tau - (1/c)\ln(\xi/x_0)$. Substituting $z = x_0 e^{-cs}$ in the last equation, we obtain

$$u(t, x_0) \geq \int_{x_0}^{x_0 e^{c(t-\tau)}} \int_{\xi e^{c(\tau-t)}}^{x_0} z\xi^{-2} u\left(t - \tau + \frac{1}{c}\ln\left(\frac{z}{\xi}\right), x_0\right) q(\xi, z)\, dz\, d\xi,$$

for sufficiently large t. Fix $\xi_0 > x_0$. The function $q(\xi, z)$ vanishes outside the set $D(\xi) = \left[y^{-1}\left(\kappa_1 \pi_\tau y(\xi)\right), y^{-1}\left(\kappa_2 \pi_\tau y(\xi)\right)\right]$. Since $D(\xi) \subset (0, x_0)$ and the function q is continuous, there exist $\lambda_0 > 0$, $\delta > 0$ and $z_0 \in (\xi_0 e^{c(\tau-t)} + \delta, x_0 - \delta)$ such that $q(\xi, z) > \lambda_0$ for $(\xi, z) \in \Delta_\delta$, where $\Delta_\delta = [\xi_0 - \delta, \xi_0 + \delta] \times [z_0 - \delta, z_0 + \delta]$. This implies that

$$u(t, x_0) \geq \iint_{\Delta_\delta} \lambda_0 z \xi^{-2} u\left(t - \tau + \frac{1}{c}\ln\left(\frac{z}{\xi}\right), x_0\right) d\xi\, dz.$$

Let $s_0 = \tau - (1/c)\ln(z_0/\xi_0)$ and $s = (1/c)\ln(z_0/\xi_0) - (1/c)\ln(z/\xi)$. Since z/ξ is bounded from above and below, there exist $\lambda_1 > 0$ and $\varepsilon > 0$ such that

$$\begin{aligned} u(t, x_0) &\geq \lambda_1 \int_{z_0}^{z_0+\varepsilon} \int_0^{\varepsilon} u(t - s_0 - s, x_0)\, ds\, dz, \\ &\geq \lambda_1 \varepsilon \int_0^{\varepsilon} u(t - s_0 - s, x_0)\, ds. \end{aligned}$$

for sufficiently large t. From this inequality it follows that

$$u(t, x_0) \geq \lambda_2^n \int_0^{\varepsilon} \cdots \int_0^{\varepsilon} u\left(t - ns_0 - s_1 - \cdots - s_n, x_0\right)\, ds_1 \cdots ds_n$$

for t large enough. By induction, we check that

$$u(t, x_0) \geq \lambda_2^n \left(\frac{\xi}{3}\right)^{n-1} \int_{\varepsilon(n-1)/3}^{2\varepsilon(n-1)/3} u\left(t - ns_0 - s, x_0\right)\, ds. \tag{38}$$

Now repeating arguments similar to that in the proof of Lemma 2 of [**13**], one can check that there exists a nonnegative function K with $\|K\| > 0$ such that $u(t, x) \geq K(x)$ for $t \geq t_0(u)$. □

The proof of the following lemma is the same as the proof of Lemma 3 [**13**].

Lemma 3. *Let $u(t)(x) = u(t,x)$ and $\bar{u}(t)(x) = \bar{u}(t,x)$ be two solutions of* (27)*. Then*

$$\lim_{t\to\infty} \|u(t) - \overline{u}(t)\| = 0.$$

Now we show that a stationary solution of (27) exists. From this and Lemma 3, Theorem 1 follows immediately. A density $f \in D$ is a stationary solution of (27) if it satisfies the equation

$$xf'(x) + 2f(x) = \int_0^\infty f(s)q(s,x)\,ds. \tag{39}$$

This equation can be rewritten as the integral equation

$$x^2 f(x) = \int_0^\infty f(s)\left[\int_0^x zq(s,z)\,dz\right] ds.$$

Consequently, f is a stationary solution of (26) if and only if f is a fixed point of the operator

$$\mathcal{Q}f(x) = \frac{1}{x^2}\int_0^\infty f(s)\left[\int_0^x zq(s,z)\,dz\right] ds. \tag{40}$$

It is easy to check that $\mathcal{Q} : L^1(0,\infty) \to L^1(0,\infty)$ is a Markov operator.

We show that the operator $\mathcal{Q}$ has a fixed point in the set of densities. In the proof we will use the following theorem of Socała [**21**].

Theorem 2. *A Markov operator $\mathcal{Q}$ has a fixed point in the set of densities if a density f, a set A with finite measure and a number $\delta > 0$ exist such that, for every measurable subset E of A with measure less than δ, we have*

$$\limsup_{n\to\infty} \int_{E\cup(X\setminus A)} \mathcal{Q}^n f\,dx < 1. \tag{41}$$

Lemma 4. *The operator $\mathcal{Q}$ has a fixed point in the set of densities.*

Proof. According to (32) there exist $r > 0$, $K < 1 + r$ and $B > 0$ such that

$$\int_0^\infty x^{-r} q(s,x)\,dx \le K s^{-r} + B. \tag{42}$$

Let f be a density such that $\int_0^\infty x^{-r} f(x)\,dx < \infty$. Then from (42) it follows that

$$\begin{aligned}
\int_0^\infty x^{-r} \mathcal{Q} f(x)\,dx &= \int_0^\infty f(x) \left\{ \int_0^\infty \left[x^{-r-2} \int_0^x z q(s,z)\,dz \right] ds \right\} dx \\
&= \int_0^\infty f(x) \left\{ \int_0^\infty \frac{1}{r+1}\, z^{-r} q(s,z)\,dz \right\} dx \\
&\le \int_0^\infty f(x) \left\{ \frac{K}{r+1}\, x^{-r} + B \right\} dx \\
&\le L \int_0^\infty x^{-r} f(x)\,dx + B,
\end{aligned}$$

where $L = K/(r+1)$ and $L < 1$. By an induction argument we obtain

$$\int_0^\infty x^{-r} \mathcal{Q}^n f(x)\,dx \le L^n \int_0^\infty x^{-r} f(x)\,dx + \frac{B}{1-L}.$$

Consequently

$$\limsup_{n\to\infty} \int_0^\infty x^{-r} \mathcal{Q}^n f(x)\,dx \le \frac{B}{1-L}. \tag{43}$$

Let $\varepsilon \in (0,1)$ be such that $(B/(1-L))\varepsilon^r \le (1/4)$. Then from (43) it follows that

$$\limsup_{n\to\infty} \int_0^\varepsilon \mathcal{Q}^n f(x)\,dx \le \frac{1}{4}. \tag{44}$$

Moreover, since $q(r,x) = 0$ for $x \ge y^{-1}(\kappa_2)$ we have

$$\begin{aligned}
\mathcal{Q} f(x) &= \frac{1}{x^2} \int_0^\infty f(s) \left(\int_0^{y^{-1}(\kappa_2)} z q(s,z)\,dz \right) ds \\
&\le \frac{1}{x^2}\, y^{-1}(\kappa_2).
\end{aligned} \tag{45}$$

Since the function $g(x) = (1/x^2)$ is integrable in the interval $[1, +\infty)$, there exists $M > 1$ such that

$$\limsup_{n\to\infty} \int_M^\infty \mathcal{Q}^n f(x)\, dx \le \frac{1}{4}. \tag{46}$$

From the definition of the operator $\mathcal{Q}$ it follows that

$$\mathcal{Q}^n f(x) \le \frac{M}{\varepsilon^2} \quad \text{for } x \in [\varepsilon, M]. \tag{47}$$

Now setting $A = (0, M)$ and $\delta = (\varepsilon^2/(3M))$ we obtain (41) and this completes the proof. □

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