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ON THE STABILITY OF STEADY SIZE-DISTRIBUTIONS FOR A CELL-GROWTH PROCESS WITH DISPERSION

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Abstract. The model discussed in this paper describes the evolution of the size-distribution of a population of cells in time. It is assumed that there is a degree of stochasticity in the growth process of each individual cell in the population. This manifests itself as a dispersion term in the differential equation for the evolution of the size-distribution of the overall population.

We study the stability of the Steady Size-Distributions (SSDs) of the model (the spatial components of separable solutions) and show that given a set of parameters where an SSD exists, it is unique and globally asymptotically stable.

1. Introduction

In this paper, the stability of a model for cell growth is studied. The model describes the size-distribution of a population of cells evolving in time, and assumes constant growth-rate in the cells and fixed-size cell-division. That is, the cells only divide at a fixed size $x = l$. The growth process of each individual cell is assumed to be stochastic, with white-noise superimposed over a constant mean growth-rate. This manifests itself in the model as a dispersion term, since the model describes the aggregate behaviour of many cells, rather than that of a single cell.

Let $n(x,t)$ be the density of cells of size x at time t. The partial differential equation modelling the evolution of this density is,

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$$\frac{\partial}{\partial t}n(x,t) = D\frac{\partial^2}{\partial x^2}n(x,t) - g\frac{\partial}{\partial x}n(x,t) \\ + \alpha^2 b\delta(\alpha x - l)n(\alpha x, t) - b\delta(x-l)n(x,t) - \mu n(x,t), \tag{1.1}$$

where $g > 0$ is the growth rate of the cells, $\alpha > 1$ is the number of equally sized daughter cells produced on the division of one parent cell, $\mu \geq 0$ is the death rate of cells and $D > 0$ is the dispersion coefficient of the population, which describes the population-level effect of stochastic variation in the growth of each individual cell. In cell division we always have $\alpha = 2$, but the analysis in this paper applies for general $\alpha > 1$ and, further, the model has been previously studied in [2] with general $\alpha > 1$; so here α is also kept arbitrary.

The terms $b\delta(x-l)$ and $b\delta(\alpha x - l)$ represent fixed-size cell division, where cells may only divide at a critical size $x = l$ (into α cells of size l/α). The coefficient $b > 0$ has dimension $1/[t]$ and determines how likely it is that a cell will divide as it passes through size $x = l$. Equation (1.1), with the terms $b\delta(x-l)$ and $b\delta(\alpha x - l)$ is a specific instance of the more general case where, instead of $b\delta(x-l)$ and $b\delta(\alpha x - l)$, we use the division function $B(x)$ and $B(\alpha x)$. In the discrete formulation of the model, the probability that a cell divides at any instant in time is equal to $B(x)dt$. A substitution of $b\delta(x-l)$ for $B(x)$ is made after the continuous model is derived. The governing equation (1.1) with general $B(x)$ is similar to a model formulated by Bell and Anderson [5], with the addition of the dispersion term Dn_{xx}.

The model has been considered to be a model of plankton cell growth in [2]. However, the unimodal steady size-distributions (see Figure 1 for example) of the model are also qualitatively similar to the unimodal DNA-distributions characteristic of *Escherichia coli* during exponential population growth (see [8, Fig. 1] and [9, Fig. 7]). The differences between the steady size-distributions here and the DNA-distributions in [8] and [9] might be reduced by having varying coefficients $g(x)$, $\mu(x)$ and $D(x)$, but this increases the complexity of the analysis of the model significantly. Some examples of observed steady cell-volume distributions for various mammalian cells in suspension culture with similar shape to the steady size-distributions obtained for the present model can be found in [1].

The equation (1.1) is supplemented with the initial and boundary conditions

$$0 \le n(x,0) = n_0(x), \qquad n_0 \in (C \cap L^1 \cap L^\infty)[0,\infty) \tag{1.2}$$

$$Dn_x(x,t) - gn(x,t)|_{x=0} = 0, \tag{1.3}$$

$$n(x,t) \to 0, \qquad x \to \infty, \ \ t > 0 \tag{1.4}$$

$$n_x(x,t) \to 0, \qquad x \to \infty, \ \ t > 0. \tag{1.5}$$

Solutions are sought which belong to the set CD (for ‘cell-division’), defined below:

Let $[0,T]$ be some interval, with $T > 0$, and let $l > 0$ and $\alpha > 1$ be given. We say that $f(x,t) \in CD[0,T]$ if f has the following properties

- $f(x,t)$ is continuous for $x \ge 0$ and $0 \le t \le T$.
- $f_t(x,t)$ is continuous for all $x \ge 0$ and $0 < t \le T$;
- $f_x(x,t)$ and $f_{xx}(x,t)$ are continuous in the regions

  $$x \in [0, l/\alpha], x \in [l/\alpha, l], x \in [l, \infty),$$

  and $0 < t \le T$, where the derivatives at the end points of each interval are taken either from above or below (as appropriate). Note that $f_x(x,t)$ and $f_{xx}(x,t)$ may be discontinuous at $x = l$ and $x = l/\alpha$.

Given the importance of $CD[0,\infty)$, we also define $CD = CD[0,\infty)$.

For any value of μ, we may transform equation (1.1) to the case for $\mu = 0$ by examining $\overline{n}(x,t) = n(x,t)e^{\mu t}$. Thus, we assume $\mu = 0$ for the remainder of the paper.

We also expect that at every time t there will be only a finite total number of cells. That is, we desire that

$$\int_0^\infty n(x,t)\ dx < \infty$$

for all $t \ge 0$. The set of equations (1.1)-(1.5) shall be referred to henceforth, as problem F. In Section 4, it is shown that when $n_0(x) \ge 0$ for all $x \ge 0$, there exists a non-negative solution to problem F in CD satisfying the above requirements.

The fact that we have added a dispersion term Dn_{xx} in the model means that it is possible for cells to shrink. It is intended that D, in general, should be smaller than g by several orders of magnitude, so that the number of cells shrinking at any given time will be small. A cell might shrink due to apoptosis (cell death) or due to some other (not so drastic) cause such as diffusion of some substance from the cell into the surrounding medium.

The main result in this paper, put simply, is that the Steady Size-Distributions of problem F are globally asymptotically stable. Mathematically, a

SSD of problem F is the spatial part, $y(x)$, of a separable solution,

$$N(t)y(x) = n(x,t),$$

to problem F. The solution $n(x,t) = N(t)y(x)$ maintains a constant shape described by $y(x)$ for all time, while the overall number of cells varies according to $N(t)$. A class of nonlocal differential equations, which contains those arising when investigating the SSDs for symmetric cell division with a division function $B(x)$, was studied in [3].

In [2], SSD solutions to problem F were found to exist when $\alpha b > b + g$, and to satisfy the following conditions:

$$\begin{cases} y''(x) - \gamma y'(x) + \alpha^2\beta\delta(\alpha x - l)y(\alpha x) - (\beta\delta(x-l) + \lambda)y(x) = 0, \\ y \in (C \cap L^1 \cap L^\infty)[0,\infty), \\ y'(0) - \gamma y(0) = 0, \quad y'(x), y(x) \to 0, \qquad x \to \infty. \end{cases} \tag{1.6}$$

where $\gamma = g/D$ and $\beta = b/D$ and λ is an eigenvalue of the operator

$$y(\cdot) \to y''(\cdot) - \gamma y'(\cdot) + \alpha^2\beta\delta(\alpha\cdot - l)y(\alpha\cdot) - \beta\delta(\cdot - l)y(\cdot).$$

If such an eigenvalue exists then the separable solution $N(t)y(x)$ will be of the form

$$N(t)y(x) = e^{\lambda D t}y(x), \tag{1.7}$$

with $N(t) = e^{\lambda D t}$. An example SSD is given in Figure 1, as well as the same SSD after a smoothing integral kernel has been applied, simulating error in the observation of the distribution.

We desire to know whether these SSDs are attractors. That is: does the shape of the distribution described by the model of problem F approach an SSD as $t \to \infty$. We state the main stability theorem of this paper below, but first we describe the dual problem to (1.6) and its importance.

The solution ψ of the 'dual' problem (we explain below how this is obtained) to (1.6),

$$\begin{cases} \psi''(x) + \gamma\psi'(x) + \alpha\beta\delta(x-l)\psi\left(\frac{x}{\alpha}\right) - (\beta\delta(x-l) + \lambda)\psi(x) = 0 \\ \psi'(0) = 0, \qquad 0 < \psi(x) \in L^\infty(\mathbb{R}^+), \qquad \int_0^\infty \psi(x)y(x)\ dx = 1, \end{cases} \tag{1.8}$$

has two very useful properties which help in proving the stability of the SSD y.

The first of these properties is given in Theorem 2.1, Section 2.2:

$$\int_0^\infty \psi(x)n(x,t)e^{-\lambda D t}\ dx = \int_0^\infty \psi(x)n_0(x)\ dx, \qquad t \geq 0.$$

In words: the integral on the left is not dependent on time. This gives us information about the behaviour of $n(x,t)$ we did not have before, since

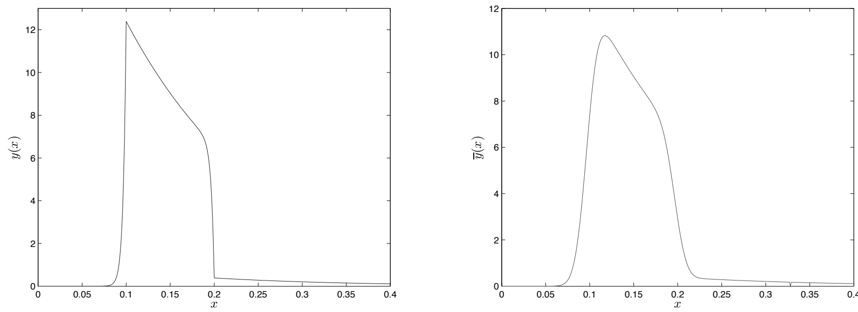

Figure 1. Plot (a) shows an example SSD, $y(x)$, with parameters $\alpha = 2$, $b = 50$, $g = 3$, $l = 0.2$ and $D = 0.01$. Plot (b) is a plot of the function $\overline{y}(x) = \int_0^\infty y(\xi)\mathcal{G}(\xi, x)\ d\xi$, where $\mathcal{G}(\xi, x)$ is the normal distribution with mean x and standard deviation $\sigma = 0.01$. Plot (b) simulates machine error in the measurement of the correct size-distribution from (a). Plot (b) is similar to the DNA distribution characteristic of *E. coli* during exponential growth (see [8, Fig. 1] and [9, Fig. 7]).

we cannot easily find the rate of change of the overall number of cells $\int_0^\infty n(x,t)\ dx$ in time. But with the help of $\psi(x)$, we have found that the quantity $\int_0^\infty \psi(x)n(x,t)\ dx$ is proportional to $e^{\lambda Dt}$.

The second is given in Theorem 2.2, Section 2.2; that is, for any two solutions $n(x,t)$, $q(x,t)$ of problem F corresponding to the initial distributions $n_0(x)$ and $q_0(x)$ respectively, we have

$$\int_0^\infty \psi(x)|n(x,t_1)-q(x,t_1)|e^{-\lambda Dt_1}dx \le \int_0^\infty \psi(x)|n(x,t_0)-q(x,t_0)|e^{-\lambda Dt_0}dx,$$

for all $0 \le t_0 < t_1$. So, with the help of $\psi(x)$, we can formulate a law which, in a sense, restricts how far apart the solutions n and q may grow in any given time. Even though it may be difficult to find a general law describing how $\int_0^\infty |n(x,t) - q(x,t)|\ dx$ varies in time.

We form the dual problem (1.8) in the following way:

Consider (1.6) expressed as $\mathcal{A}y = 0$, where $\mathcal{A}$ is the appropriate differential operator. We then find the operator $\mathcal{A}^*$ such that

$$\int_0^\infty \psi(x)[\mathcal{A}y](x)\ dx = \int_0^\infty [\mathcal{A}^*\psi](x)y(x)\ dx.$$

The operator $\mathcal{A}^*$ is formed merely by integration by parts of the left-hand-side above and a substitution of variables for the term $\delta(\alpha x - l)y(\alpha x)$. The integration by parts results in an integral plus some extra terms. Letting these extra terms equal zero provides the boundary condition $\psi'(0) = 0$ in (1.8), while the differential equation in (1.8) becomes $\mathcal{A}^*\psi = 0$.

The main convergence result of this paper is expressed as follows: If we have $m(x,t) = n(x,t)e^{-\lambda D t}$, then given the existence of y and ψ described above we find the following result in Section 3. We state it here without proof:

Theorem 3.4. *The following convergence result holds*

$$\int_0^\infty \psi(x)|m(x,t) - ky(x)|\ dx \to 0, \qquad t \to \infty.$$

Specifically, since $\psi(x) > 0$ for all $x \geq 0$, we find as an immediate consequence that $m(\cdot,t) \to ky(\cdot)$, $t \to \infty$, in $L^1_{loc}[0,\infty)$, where

$$k = \int_0^\infty \psi(x)m_0(x)\ dx = \int_0^\infty \psi(x)n_0(x)\ dx.$$

Thus, $m(x,t)$ tends to a constant multiple of $y(x)$ on any given finite interval. Thus, we should see the distribution $n(x,t)$ behave more and more like $e^{\lambda t}y(x)$ as t increases.

The method used here to prove the above convergence is based on [6, 7], where a 'general relative entropy' functional $\mathcal{H}$ is used, depending on time t, the solution n and the SSD/dual SSD pair y and ψ. The idea is that the functional $\mathcal{H}$ is non-negative, but has a non-positive derivative in time; therefore $\mathcal{H}$ must converge to some value. This gives us information about the behaviour of the solution n as $t \to \infty$. The nature of the cell-division terms $b\delta(x-l)$ and $\alpha^2 b\delta(\alpha x - l)$ makes the procedure developed in [7] hard to follow through, so in Section 3 we exploit the extra term which appears in the derivative $\mathcal{H}_t$ of the general relative entropy due to presence of dispersion $(Dn_{xx}(x,t))$ in Equation (1.1).

In [6, 7], among other applications of general relative entropy, the following cell growth equation is studied:

$$n_t(x,t) + n_x(x,t) + B(x)n(x,t) = \int_0^\infty b(y,x)n(y,t)\ dy,$$

with zero flux boundary condition $n(0,t) = 0$ for all $t \geq 0$. Here, $b(y,x)$ represents the rate of production of cells of size x from the division of cells of size y, and

$$2B(x) = \int_0^x b(x, y)\ dy.$$

The kernel $b(x, y)$ allows asymmetric cell-division, where two unequally sized daughter cells may be produced on the division of a parent cell. Letting $b(x, y) = 2B(x)\delta(y - x/2)$ gives the case of symmetric mitosis, where two equally sized daughter cells are produced on the division of a parent cell:

$$n_t(x, t) + n_x(x, t) + B(x)n(x, t) = 4B(2x)n(2x, t).$$

A sufficient condition used in [7, Section 4] when proving the stability of the above cell-division models translates, in the case of symmetric cell-division, to $B(x)$ having infinite support. In the case of problem F, however, we have a division function $B(x) = \delta(x - l)$, which does not have infinite support. Thus, the proof of convergence in Section 3 exploits the extra term which arises in the derivative $\mathcal{H}_t$ due to the presence of dispersion in problem F. This extra term occurs regardless of the division function. So, potentially, the analysis of Section 3 could be repeated for a quite general class of division functions $B(x)$, so long as in each case the solution n, SSD y and dual SSD ψ had similar properties to those of problem F with regards to positivity and integrability. Moreover, in [7, Section 4], the initial size-distribution is assumed to be bounded by a constant multiple of the SSD. This assumption is not used or needed here.

In Section 2, we show that whenever there is an SSD $y(x)$ for a given value of λ, there also exists a dual SSD $\psi(x)$. We also prove the properties of $\psi(x)$ mentioned above in Section 2. Following this, in Section 3 we prove our important result: Theorem 3.4, using the general relative entropy functional $\mathcal{H}$. The analysis in Section 3 could be applied to the more general case where $b\delta(x-l)$ is replaced by a general function $B(x)$ assuming that the SSD, dual SSD and solution of the more general case are well-behaved enough. That is, if the SSD, dual SSD and solution are such that the integrals involved in calculating $\frac{\partial}{\partial t}\mathcal{H}$ converge.

Two results regarding the existence and positivity of solutions of problem F are stated in Section 4. Wherever proofs have been left out, the reader is referred to [4].

2. The solution of the dual problem and its properties

In this section we first prove that whenever an SSD solution exists to problem F, satisfying the eigenvalue problem (1.6) for some given eigenvalue λ, then a unique solution $\psi(x)$ must exist to the dual problem (1.8). Following this we prove two useful properties of $\psi(x)$ that help in proving the stability of $y(x)$. Finally, we note two important expressions in (2.12) for $\psi(x)$ and the SSD $y(x)$ when $x \geq l$.

Given the relationship of the solution $\psi(x)$ of the dual problem (1.8) to the SSD solution $y(x)$ from (1.6), we refer to $\psi(x)$ as the dual SSD to $y(x)$, or simply the 'dual SSD' in the material that follows.

2.1. **Existence and uniqueness of the dual SSD.** In [2], the Green's function for the operator $\mathcal{L}$, where $\mathcal{L}y = y'' - \gamma y' - \lambda y$, along with the boundary conditions

$$y'(0) - \gamma y(0) = 0, \tag{2.1}$$

$$y'(x), y(x) \to 0, \qquad x \to \infty \tag{2.2}$$

is considered. Here, we consider the Green's function for the operator $\mathcal{L}^*$, with conditions $\psi'(0) = 0$ and $\psi \in L^\infty[0, \infty)$, where

$$\mathcal{L}^*\psi = \psi'' + \gamma\psi - \lambda\psi.$$

The characteristic equation associated with $\mathcal{L}^*$ has roots $(-\gamma \pm \sqrt{\gamma^2 + 4\lambda})/2$. These are the negatives of the roots r_1 and r_2 in [2]. For consistency, in this section we define r_1 and r_2 to be the roots from [2], where $r_1 > 0$ and $r_2 < 0$. That is

$$r_1 = \frac{\gamma + \sqrt{\gamma^2 + 4\lambda}}{2}; \qquad r_2 = \frac{\gamma - \sqrt{\gamma^2 + 4\lambda}}{2}.$$

The Green's function is then

$$G(x, \xi) = \frac{r_2 e^{r_2 \xi}}{r_1(r_1 - r_2)} \Big[-\frac{r_1}{r_2} e^{-r_2 x} + e^{-r_1 x} \Big] + \frac{H(x - \xi)}{r_1 - r_2} (e^{r_2(\xi - x)} - e^{r_1(\xi - x)}), \tag{2.3}$$

where H is the Heaviside function, and a formal solution to (1.8) is given by the expression

$$\psi(x) = \beta \Big[\psi(l) - \alpha\psi\Big(\frac{l}{\alpha}\Big) \Big] G(x, l). \tag{2.4}$$

We are interested only in non-trivial solutions $\psi(x)$, so $\psi(l)$ and $\psi(l/\alpha)$ must not be equal to zero. Substituting $x = l$ and $x = l/\alpha$ into the above equation gives a pair of linear equations to solve for $\psi(l)$ and $\psi(l/\alpha)$. The system may be written as:

$$\begin{bmatrix} \beta G(l, l) - 1 & -\alpha\beta G(l, l) \\ \beta G(l/\alpha, l) & -\alpha\beta G(l/\alpha, l) - 1 \end{bmatrix} \begin{bmatrix} \psi(l) \\ \psi(l/\alpha) \end{bmatrix} = \begin{bmatrix} 0 \\ 0 \end{bmatrix}. \tag{2.5}$$

For a non-trivial solution to exist, the determinant of the above matrix must be zero; that is

$$\frac{1}{\beta} = G(l,l) - \alpha G(l/\alpha, l). \tag{2.6}$$

Substituting the values for $G(l,l)$ and $G(l/\alpha, l)$ into this equation we find the following condition for a non-trivial solution to exist, namely

$$\frac{r_1(r_1 - r_2)}{\beta} = r_2 e^{r_2 l}\Big[-\frac{r_1}{r_2}(e^{-r_2 l} - \alpha e^{-r_2 l/\alpha}) + e^{-r_1 l} - \alpha e^{-r_1 l/\alpha}\Big]. \tag{2.7}$$

Now, letting $\omega = -r_2$ we can reformulate the above condition into an equation involving the positive parameters α, β, γ, l and ω, giving the same condition which was obtained in [2]:

$$\begin{aligned} F(\omega) := (\gamma+\omega)(\beta+\gamma+2\omega) - \alpha\beta(\gamma+\omega)e^{-\omega l\left(1-\frac{1}{\alpha}\right)} \\ -\beta\omega e^{-\omega l}\left(\alpha e^{-(\omega+\gamma)\frac{l}{\alpha}} - e^{-(\omega+\gamma)l}\right) = 0. \end{aligned} \tag{2.8}$$

Solving this equation for $\omega \geq 0$ gives a possible eigenvalue λ. Assume for the moment that solutions to (2.8) exist. Using the first line of the linear system in (2.5) gives us a relationship between $\psi(l)$ and $\psi(l/\alpha)$

$$\psi(l) = \frac{-\alpha\beta\psi(l/\alpha)\Phi(l)}{1 - \beta\Phi(l)}. \tag{2.9}$$

where

$$\Phi(x) = \frac{r_2 e^{r_2 l}}{r_1(r_1 - r_2)}\Big[-\frac{r_1}{r_2} e^{-r_2 x} + e^{-r_1 x}\Big] < 0.$$

It can easily be checked that if $\psi(l/\alpha) > 0$ then, according to (2.9), we must have $0 < \psi(l) < \alpha\psi(l/\alpha)$ and that the overall solution $\psi(x)$ must be positive. The function $\psi(x)$ which we have found is unique up to scaling. Thus, imposing the condition that $\int_0^\infty \psi(x)y(x)\,dx = 1$, we have found a solution to the dual problem (1.8) and the solution is unique.

The above reasoning assumed that at least one solution to (2.8) exists. If a solution does not exist, then neither an SSD nor a dual SSD exists. A sufficient condition for a solution ω to exist is given in [2]: $\alpha\beta > \beta + \gamma$. This ensures that the left hand side of (2.8) is less than zero when $\omega = 0$, and since the left hand side of (2.8) is continuous and tends to ∞ as $\omega \to \infty$, there is at least one $\omega > 0$ for which it is zero. In fact, the global convergence proved in the following sections shows that there can be at most one solution. An example of an SSD $y(x)$ and corresponding dual SSD $\psi(x)$ is given in Figure 2.

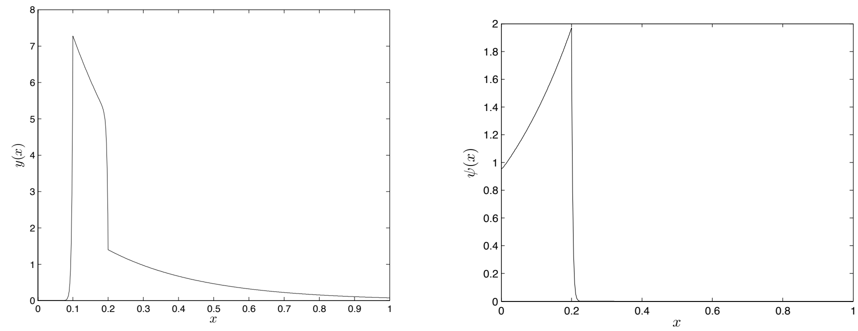

FIGURE 2. Plot (a) shows an example SSD and (b) the dual SSD for $\alpha = 2$, $b = 8$, $g = 3$, $l = 0.2$ and $D = 0.01$. The eigenvalue was found via a bisection search for a positive root of (2.7). Both functions have been scaled so that $\int_0^\infty y(x)\ dx = 1$ and $\int_0^\infty y(x)\psi(x)\ dx = 1$.

The condition $\alpha\beta > \beta + \gamma$ is equivalent to the condition $\alpha b > b + g$ and essentially means that b must be large. This corresponds to cells having a high probability of dividing when they reach the size $x = l$. This should be true in most cell populations, and so is not an unrealistic restriction to impose on the model. When $\alpha b = b + g$, there exists no non-trivial SSD, since then $y(l)$ must be zero (by Equation (2.6) of [2]), which then forces $y(x)$ to be identically zero. In cases where $\alpha b < b + g$ the expression (2.8) when investigated computationally, does not appear to have positive zeros; see Figure 3 for two examples of $F(\omega)$ for different sets of parameters. It has not, however, been proved in this paper that $\alpha b > b + g$ is a *necessary* condition for the existence of a SSD and dual SSD. Rather, we merely state that $\alpha b > b + g$ is *sufficient*. Further investigation is required to establish the necessity of the condition.

2.2. **Some nice properties of the dual SSD.** Given the existence of an eigenvalue λ, corresponding SSD $y(x)$ and dual SSD $\psi(x)$, which we have established above, the following two theorems hold.

Theorem 2.1. *The equality*

$$\int_0^\infty \psi(x) n(x,t) e^{-\lambda D t}\ dx = \int_0^\infty \psi(x) n_0(x)\ dx \tag{2.10}$$

holds for all $t > 0$.

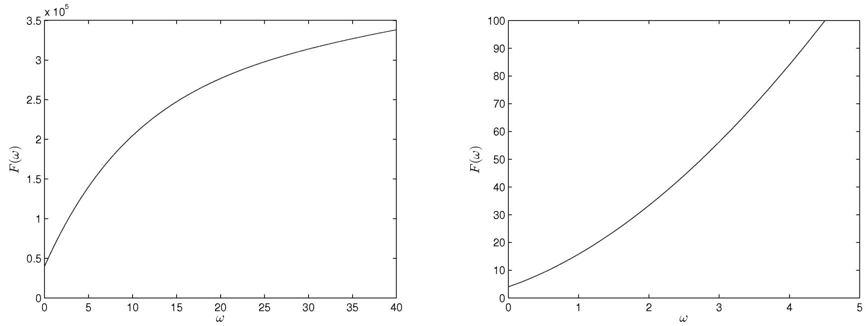

FIGURE 3. (a) A graph of $F(\omega)$ with parameters $\alpha = 2$, $b = 3$, $g = 4$, $D = 0.01$ and $l = 0.2$ (b) A graph of $F(\omega)$ with parameters $\alpha = 2$, $b = 3$, $g = 4$, $D = 1$ and $l = 0.2$. Both of these are cases where $\alpha b < b + g$ for which there seem to be no zeros of $F(\omega)$, and hence no SSD solution of problem F.

Theorem 2.2. *Let n and v be solutions to problem F with differing initial conditions $n_0(x)$ and $v_0(x)$. If $m(x,t) = n(x,t)e^{-D\lambda t}$ and $p(x,t) = v(x,t)e^{-D\lambda t}$, then*

$$\int_0^\infty \psi(x)|m(x,t_1) - p(x,t_1)|\, dx \leq \int_0^\infty \psi(x)|m(x,t_0) - p(x,t_0)|\, dx, \quad (2.11)$$

for all $t_1 > t_0 \geq 0$.

For the details of the proofs of the above two equations, see [4].

To end this section we note that from the above working and from [2], we have the following two expressions for $\psi(x)$ and $y(x)$ respectively when $x \geq l$:

$$\psi(x) = C_0 e^{-r_1 x}; \qquad y(x) = C_1 e^{r_2 x}, \quad (2.12)$$

where C_0 and C_1 are definite constants. This fact is useful in proving the convergence of integrals involving fractions such as $\psi(x)/y(x)$.

3. CONVERGENCE OF n TO A STEADY SIZE-DISTRIBUTION SOLUTION

In this section, the central result regarding the stability of the SSDs of problem F is proved. It shall be shown that given the existence of an eigenvalue λ, a corresponding SSD $y(x)$ and dual SSD $\psi(x)$ we have

$$n(\cdot,t)e^{-D\lambda t} \to ky(\cdot)$$

in $L^1_{loc}[0,\infty)$ as $t \to \infty$, where

$$k = \int_0^\infty \psi(x) n_0(x)\ dx.$$

The value of k is established in Lemma 3.3, while the main convergence result is proved in Theorem 3.4.

We presently make (without loss of generality) the substitution $m = ne^{-D\lambda t}$, so that y and ψ are stationary solutions to the differential equation ($m_t = \mathcal{B}m$) governing m and the dual equation ($m_t = -\mathcal{B}^* m$) respectively, where the equation governing the behaviour of m, and defining the differential operator $\mathcal{B}$, is given by

$$\begin{aligned} m_t(x,t) &= Dm_{xx}(x,t) - gm_x(x,t) + \alpha^2 b\delta(\alpha x - l)m(\alpha x, t) \\ &\quad - (b\delta(x-l) + D\lambda)m(x,t). \end{aligned} \tag{3.1}$$

After first establishing Lemma 3.1, regarding the behaviour of $m(x,t)$, we introduce the general relative entropy functional $\mathcal{H}(m|y,\psi)(t)$, and proceed to show that this non-negative functional is non-increasing in time. This tells us that $\mathcal{H}$ converges to some value as $t \to \infty$ and, further, that

$$\int_t^{t+T} \mathcal{H}_t(s)\ ds \to 0$$

as $t \to \infty$ for any $T > 0$. This then leads to the result given in Lemma 3.3:

$$\int_t^{t+T} ||m(\cdot,s) - ky(\cdot)||_{L^1([0,x_0])}\ ds \to 0, \qquad t \to \infty,$$

for any $x_0 > 0$ and, finally, to the main result in Theorem 3.4.

We now state the following lemma regarding the behaviour of $m(x,t)$:

Lemma 3.1. *If* $0 \le m_0(x) \le Cy(x)$, *then* $0 \le m(x,t) \le Cy(x)$ *for all* $t \ge 0$.

Note that $m_0(x) = n_0(x)$, so that if $n_0(x)$ is bounded by a constant multiple of $y(x)$, then $n(x,t)e^{-D\lambda t} = m(x,t)$ is bounded by a constant multiple of $y(x)$ for all $t \ge 0$.

Proof. Note first that (3.1) is linear, and that the boundary conditions that m satisfies are also linear. In Section 4, we prove Theorem 4.2, which tells us that solutions to problem F are non-negative when the initial conditions are non-negative. Therefore solutions to (3.1), satisfying the boundary conditions from problem F (1.3)-(1.5), will also be non-negative when the initial conditions are non-negative.

$Cy(x) - m(x,t)$ happens to be a solution to (3.1) along with the boundary conditions (1.3)-(1.5). Moreover, the initial conditions for $Cy(x) - m_0(x)$ are non-negative. Therefore, $Cy(x) - m(x,t)$ is non-negative for all $t > 0$. This is the desired result. □

Following [7], we now define the general relative entropy functional $\mathcal{H} = \mathcal{H}(m|y,\psi)(t)$

$$\mathcal{H}(m|y,\psi)(t) = \int_0^\infty \psi(x)y(x)H\Big(\frac{m(x,t)}{y(x)}\Big)\ dx; \tag{3.2}$$

for some convex function H. For the remainder of this paper we will assume the $H(x) = x^2$. We find below that $\mathcal{H}$, a non-negative quantity, has a derivative which is non-positive.

First we note the following important identity:

Lemma 3.2. *The following equality holds:*

$$\mathcal{H}_t = \int_0^\infty \frac{\partial}{\partial t}\psi(x)y(x)H\Big(\frac{m(x,t)}{y(x)}\Big)\ dx, \tag{3.3}$$

for $t > 0$.

The proof of this for $H(x) = x^2$ can be found in [4]. It follows from the fact that

$$\frac{\partial}{\partial t}\psi(x)y(x)H\Big(\frac{m(x,t)}{y(x)}\Big) \in L^1[0,\infty) \times [t_0, t_0 + T],$$

for all $t_0, T > 0$. The above result also holds when $H(x) = \max\{-x, 0\}$, which we use later to prove the positivity of the function $m(x,t)$ given positive initial conditions.

We shall now show that $\mathcal{H}_t \leq 0$ for all $t \geq 0$. In the first place, It may be found by a straightforward (if messy) calculation that for any convex H,

$$\begin{aligned}
&\frac{\partial}{\partial t}\Big[\psi(x)y(x)H\Big(\frac{m(x,t)}{y(x)}\Big)\Big] + g\frac{\partial}{\partial x}\Big[\psi(x)y(x)H\Big(\frac{m(x,t)}{y(x)}\Big)\Big] \\
&- D\frac{\partial}{\partial x}\Big[\psi(x)^2\frac{\partial}{\partial x}\frac{y(x)}{\psi(x)}H\Big(\frac{m(x,t)}{y(x)}\Big)\Big] + \alpha b\delta(x-l)\psi\Big(\frac{x}{\alpha}\Big)y(x)H\Big(\frac{m(x,t)}{y(x)}\Big) \\
&- \alpha^2 b\delta(\alpha x - l)\psi(x)y(\alpha x)H\Big(\frac{m(\alpha x,t)}{y(\alpha x)}\Big) \\
=&\alpha^2 b\delta(\alpha x - l)\psi(x)y(\alpha x)\Big[H\Big(\frac{m(x,t)}{y(x)}\Big) - H\Big(\frac{m(\alpha x,t)}{y(\alpha x)}\Big)
\end{aligned} \tag{3.4}$$

$$+ H'\Big(\frac{m(x,t)}{y(x)}\Big)\Big\{\frac{m(\alpha x,t)}{y(\alpha x)} - \frac{m(x,t)}{y(x)}\Big\}\Big]$$
$$- D\psi(x)y(x)\Big(\frac{\partial}{\partial x}\frac{m(x,t)}{y(x)}\Big)^2 H''\Big(\frac{m(x,t)}{y(x)}\Big).$$

We now make use of our choice $H(x) = x^2$ for the convex function H. Integrating both sides of (3.4) from 0 to ∞ with respect to x for $t > 1$ gives, after applying Theorem 3.2,

$$\begin{aligned}\frac{d}{dt}\mathcal{H} = \alpha b\psi(l/\alpha)y(l)\Bigg[\Big(\frac{m(l/\alpha,t)}{y(l/\alpha)}\Big)^2 - \Big(\frac{m(l,t)}{y(l)}\Big)^2 \\ +2\Big(\frac{m(l/\alpha,t)}{y(l/\alpha)}\Big)\Big\{\frac{m(l,t)}{y(l)} - \frac{m(l/\alpha,t)}{y(l/\alpha)}\Big\}\Bigg] \\ - 2\int_0^\infty D\psi(x)y(x)\Big(\frac{\partial}{\partial x}\frac{m(x,t)}{y(x)}\Big)^2\, dx \le 0.\end{aligned} \tag{3.5}$$

We know the integral term in Equation (3.5) converges by virtue of the fact that the integral of the left hand side of (3.4) converges when $H(x) = x^2$. To see that the integral of the left hand side of (3.4) converges, we make use of the expressions in (2.12), which tell us that the following terms all tend to zero as $x \to \infty$:

$$\frac{\psi(x)}{y(x)}, \frac{\psi'(x)}{y(x)}, \frac{\psi(x)y'(x)}{y^2(x)}. \tag{3.6}$$

The integrability of the term $\frac{\partial}{\partial t}\big[\psi(x)y(x)H\big(\frac{m(x,t)}{y(x)}\big)\big]$ is proved as part of the proof of Lemma 3.2.

If we assume that $m_0(x)$ is bounded by a constant multiple of $y(x)$, then instead of using the fact that the terms from (3.6) tend to zero as $x \to \infty$, we only require that

$$\psi'(x)y(x) \to 0 \tag{3.7}$$

as $x \to \infty$, in addition to the restrictions on ψ and y which have already been imposed (such as $\psi(x) \in L^\infty[0,\infty)$ and $y(x) \to 0$ as $x \to \infty$). The final integral term in (3.5) only appears when dispersion is present in the model.

The fact that $\mathcal{H}_t \le 0$ is due to the following property of any differentiable convex function H:

$$H'(x)(y - x) \le H(y) - H(x).$$

Now, since $\mathcal{H}$ is non-negative but $\frac{d}{dt}\mathcal{H}$ is non-positive, it must be the case that $\mathcal{H}$ tends to some limit as $t \to \infty$. This implies that for any $T > 0$,

$$\int_t^{t+T} \frac{d}{dt}\mathcal{H}(m|y,\psi)(s)\ ds \to 0, \qquad t \to \infty. \tag{3.8}$$

Specifically, with our choice $H(x) = x^2$, we find that

$$\int_t^{t+T} \int_0^{x_0} \psi(x)y(x)\Big(\frac{\partial}{\partial x}\frac{m(x,s)}{y(x)}\Big)^2\ dxds \to 0, \qquad t \to \infty. \tag{3.9}$$

for any $x_0 > 0$. Moreover, since $\psi(x)$ and $y(x)$ are strictly positive (and applying Jensen's inequality),

$$\int_t^{t+T} \int_0^{x_0} \Big|\frac{\partial}{\partial x}\frac{m(x,s)}{y(x)}\Big| dxds \to 0, \qquad t \to \infty. \tag{3.10}$$

Now, consider the integral of $|m(x,t) - k(t)y(x)|$ between $x = 0$ and $x = x_0$, where $k(t) = m(0,t)/y(0)$. Manipulating this integral we obtain

$$\begin{aligned}\int_0^{x_0} |m(x,t) - k(t)y(x)|\, dx &= \int_0^{x_0} y(x)\Big|\frac{m(x,t)}{y(x)} - k(t)\Big| dx \\ &\le \int_0^{x_0} M\Big|\frac{m(x,t)}{y(x)} - k(t)\Big| dx,\end{aligned} \tag{3.11}$$

where $M = \sup_{0\le x\le x_0} y(x)$. But

$$\begin{aligned}\int_0^{x_0} \Big|\frac{m(x,t)}{y(x)} - k(t)\Big| dx &= \int_0^{x_0} \Big|\int_0^x \frac{\partial}{\partial z}\frac{m(z,t)}{y(z)}\ dz\Big| dx \\ &\le x_0 \int_0^{x_0} \Big|\frac{\partial}{\partial z}\frac{m(z,t)}{y(z)}\Big| dz,\end{aligned} \tag{3.12}$$

and the right hand expression integrated from t to $t + T$ tends to zero as $t \to \infty$. Therefore, we see that for any $x_0 > 0$, there holds

$$\int_t^{t+T} ||m(\cdot,s) - k(s)y(\cdot)||_{L^1([0,x_0])}\ ds \to 0, \qquad t \to \infty. \tag{3.13}$$

The following theorem is now asserted:

Theorem 3.3. *For any $T > 0$,*

$$\int_t^{t+T} ||m(\cdot,s) - ky(\cdot)||_{L^1[0,x_0]}\ ds \to 0, \qquad t \to \infty$$

where k is the constant defined by:

$$k = \int_0^\infty \psi(x) m_0(x)\ dx = \int_0^\infty \psi(x) m(x,t)\ dx, \qquad t > 0.$$

Proof. First note that since $y(x)$ is strictly positive and $m_0(x)$ is essentially bounded, for any $x^* > 0$ we can choose a C such that $Cy(x) > m_0(x)$ for all $0 \le x \le x^*$. Therefore it is possible to decompose $m_0(x)$ into a sum of two parts

$$m_0(x) = m_b(x) + m_u(x),$$

where $m_b(x)$ is bounded by $Cy(x)$ for some C and $m_u(x)$ is not. Specifically, for any $\varepsilon > 0$ we may choose some $x^* > 0$ such that

$$m_b(x) = m_0(x), \qquad 0 \le x \le x^*,$$

and $m_b(x)$ is less than a constant multiple of $y(x)$ for all $x^* < x < \infty$. Then $m_u(x) = m_0(x) - m_b(x)$, and we can make x^* large enough that

$$\int_0^\infty \psi(x) m_u(x,t)\ dx = \int_0^\infty \psi(x) m_u(x)\ dx < \varepsilon,$$

where $m_u(x,t)$ and $m_b(x,t)$ denote the solutions for m obtained respectively from the initial conditions $m_u(x)$ and $m_b(x)$.

Now, for any $\varepsilon > 0$ it is possible to pick x^* large enough so that

$$\left| k - \int_0^{x^*} \psi(x) m(x,t)\ dx \right| = \left| \int_{x^*}^\infty \psi(x) m(x,t)\ dx \right| < \varepsilon/2T, \tag{3.14}$$

$$\frac{1}{1+\varepsilon} < \int_0^{x^*} \psi(x) y(x)\ dx \le 1.$$

The second inequality may be satisfied because $\int_0^\infty \psi(x)y(x)\ dx = 1$. The first of these inequalities may be satisfied because we can decompose $m(x,t)$ into $m_b(x,t)$ and $m_u(x,t)$, so that

$$\begin{aligned} \left| \int_{x^*}^\infty \psi(x) m(x,t)\ dx \right| &\le \left| \int_{x^*}^\infty \psi(x) m_b(x,t)\ dx \right| + \left| \int_{x^*}^\infty \psi(x) m_u(x,t)\ dx \right|, \\ &\le \left| \int_{x^*}^\infty \psi(x) m_b(x,t)\ dx \right| + \left| \int_0^\infty \psi(x) m_u(x,t)\ dx \right|, \end{aligned}$$

with m decomposed into m_u and m_b such that

$$\left| \int_0^\infty \psi(x) m_u(x,t)\ dx \right| < \frac{\varepsilon}{4T}.$$

Then, since $m_b(x,t)$ is bounded by $Cy(x)$, we may choose x^* large enough so that

$$\Big|\int_{x^*}^{\infty} \psi(x) m_b(x,t)\ dx\Big| < \frac{\varepsilon}{4T},$$

thus satisfying the first inequality of (3.14)

Now, since $\psi(x)$ is bounded and the convergence from (3.13) holds, we may pick $t_0 > 0$ large enough so that

$$\int_t^{t+T}\int_0^{x^*} \psi(x)|m(x,s) - k(s)y(x)|\ dxds < \frac{\varepsilon}{2}$$

for all $t \geq t_0$. But then

$$\int_t^{t+T}\Big|\int_0^{x^*} \psi(x)m(x,s)\ dx - k(s)\int_0^{x^*} \psi(x)y(x)\ dx\Big|\ ds < \frac{\varepsilon}{2},$$

and using the properties in (3.14), we find that

$$\int_t^{t+T}\Big|k - \frac{k(s)}{1+\rho}\Big| ds < \varepsilon,$$

for some $\rho < \varepsilon$ and all $t \geq t_0$. Multiplying both sides of the above inequality by $(1+\rho)$, using the triangle inequality and the fact that $\rho < \varepsilon$, we find that for any $\varepsilon > 0$ it is possible to choose some $t_0 > 0$ such that

$$\int_t^{t+T} |k - k(s)|\ ds < \varepsilon(1+\varepsilon+kT), \qquad t \geq t_0.$$

The desired result then follows from the fact that

$$\begin{aligned}\int_t^{t+T} ||m(\cdot,s) - ky(\cdot)||_{L^1[0,x_0]}\ ds \quad &\leq \quad \int_t^{t+T} ||m(\cdot,s) - k(s)y(\cdot)||_{L^1[0,x_0]} \\ &\quad + |k-k(s)|\int_0^{x_0} y(x)\ dx\ ds,\end{aligned}$$

for any $x_0 > 0$, where the expression on the right-hand-side tends to zero as $t \to \infty$. □

We are now ready to prove the main stability result of this paper.

Theorem 3.4. *The following convergence result holds*

$$\int_0^{\infty} \psi(x)|m(x,t) - ky(x)|\ dx \to 0, \qquad t \to \infty. \tag{3.15}$$

Specifically, since $\psi(x) > 0$ *for all* $x \geq 0$*, we find as an immediate consequence that*

$$m(\cdot,t) \to ky(\cdot), \qquad t \to \infty,$$

in $L^1_{loc}[0,\infty)$. *Where*

$$k = \int_0^\infty \psi(x)m_0(x)\ dx = \int_0^\infty \psi(x)n_0(x)\ dx.$$

Proof. By the linearity of problem F and the positivity of y, we may decompose $m_0(x)$, in the same way as in the proof of Theorem 3.3, into 'bounded' and 'unbounded' components $m_b(x)$ and $m_u(x)$ such that

$$m_0(x) = m_b(x) + m_u(x),$$

and $m_b(x)$ is bounded by a constant multiple of $y(x)$. Moreover, for any $\varepsilon > 0$, we may choose $m_b(x)$ and $m_u(x)$ such that $\int_0^\infty \psi(x)m_u(x,t)\ dx < \varepsilon$ for all $t \geq 0$.

Let $m_b(x,t)$ and $m_u(x,t)$ be solutions for m obtained from the initial conditions $m_b(x)$ and $m_u(x)$ respectively and let

$$k^* = \int_0^\infty \psi(x)m_b(x)\ dx.$$

Then $|k^* - k| < \varepsilon$.

By Theorem 3.3, we know that

$$\int_t^{t+T} ||m_b(\cdot,s) - k^*y(\cdot)||_{L^1[0,x_0]} \to 0$$

as $t \to \infty$ for any $x_0, T > 0$. Let us assume now, by way of contradiction, that the desired result does not hold for $m_b(x,t)$. Then, since

$$\int_0^\infty \psi(x)|m_b(x,t) - k^*y(x)|\ dx$$

is non-increasing in time (by Theorem 2.2) we find that

$$\int_0^\infty \psi(x)|m_b(x,t) - k^*y(x)|\ dx > \varepsilon > 0, \qquad t \geq 0,$$

for some $\varepsilon > 0$.

Since $m_b(x,t) < Cy(x)$ for some $C > 0$ and all $t \geq 0$, we can choose ρ large enough such that

$$\int_\rho^\infty \psi(x)|m_b(x,t) - k^*y(x)|\ dx < \varepsilon/2.$$

Thus, there exists a $\rho > 0$ such that

$$\int_0^\rho \psi(x)|m_b(x,t) - k^*y(x)|\ dx > \varepsilon/2 > 0, \qquad t \geq 0,$$

Let M be the maximum of $\psi(x)$ for $0 \leq x \leq \rho$. Then we find that

$$\int_0^\rho |m_b(x,t) - k^* y(x)| \, dx > \frac{\varepsilon}{2M}, \qquad t \geq 0.$$

But then

$$\int_t^{t+T} ||m_b(\cdot,s) - k^* y(\cdot)||_{L^1([0,\rho])} \, ds > \frac{\varepsilon T}{2M} > 0, \qquad t \geq 0,$$

which contradicts Theorem 3.3. The original assumption that the desired result does not hold for $m_b(x,t)$ must therefore be incorrect.

We have now shown that the desired result holds for $m_b(x,t)$. To show that it holds for $m(x,t)$, we note that

$$\begin{aligned}\int_0^\infty \psi(x)|m(x,t) - ky(x)| \, dx \leq & \int_0^\infty \psi(x)|m_b(x,t) - k^* y(x)| \, dx \\ & + \int_0^\infty \psi(x)|m_u(x,t)| \, dx \\ & + |k^* - k| \int_0^\infty \psi(x) y(x) \, dx.\end{aligned}$$

Therefore, for any $\varepsilon > 0$ we may choose $m_b(x)$ and $m_u(x)$ as above such that

$$\lim_{t\to\infty} \int_0^\infty \psi(x)|m(x,t) - ky(x)| \, dx \leq \varepsilon.$$

But since ε may be arbitrarily small, we find that Equation (3.15) holds for $m(x,t)$. □

We have now shown that for any given set of parameters, if an SSD solution exists to the problem F, then it is a global attractor. That is, given any non-negative initial conditions, the function $m(x,t) = n(x,t)e^{-D\lambda t}$ will tend to a constant multiple, k, of the SSD, with k given in the statement of the theorem. The fact that the convergence is global implies that there can be at most one SSD.

In the proof of Theorem 3.4, we only needed Theorem 3.3 for a function $m_b(x,t)$ with initial conditions $m_b(x)$ bounded by a constant multiple of $y(x)$. The fact that we could work with solutions $m_b(x,t)$ bounded by a constant multiple of $y(x)$ was a result of Lemma 3.1 and the fact that $y(x)$ is strictly positive. Lemma 3.1 was, in turn, a result of the non-negativity of the solutions $m(x,t)$ to (3.1) when given non-negative initial conditions.

Thus, for the above result to hold we only need the following:

- Strict positivity of $y(x)$ and $\psi(x)$, although it should be possible to weaken this assumption on $\psi(x)$, giving slightly weaker results.
- Non-negativity of solutions to problem F when the initial conditions are non-negative,
- The assumption from (3.7), that $\psi'(x)y(x) \to 0$ in order to calculate $\mathcal{H}_t$,
- The integrability of $n_t(x,t)$ on $[0,\infty) \times [t_0, t_0+T]$ for $t_0, T > 0$. (this leads immediately to Lemma 3.2 when $n(x,t)$ is bounded by a constant multiple of $y(x)$).

This is important if we wish to consider applying the analysis here to the more general problem, where we replace the δ-distributions in Equation (1.1) with arbitrary cell-division functions $B(x)$.

4. Existence of the solution n to problem F

We state here two results regarding the existence and properties of the solution n to problem F.

Theorem 4.1 (Existence)**.** *Given initial conditions $n(x,0) = n_0(x) \in (C \cap L^1 \cap L^\infty)[0,\infty)$, there exists a unique solution $n(x,t) \in CD$ to problem F.*

For detailed proof see [4].

Theorem 4.2 (Positivity)**.** *Solutions of problem F with non-negative initial conditions are non-negative.*

Proof. Let $H(x) = \max\{-x, 0\}$ in the expression for $\mathcal{H}$. We find that $\mathcal{H}_t \leq 0$ (for $t > 0$)in a similar way to the case where $H(x) = x^2$. Thus, $\mathcal{H} \geq 0$ and is non-increasing in time when $t > 0$. We can also show that $\mathcal{H}(t)$ is continuous for all $t \geq 0$:

Take any $t_0 \geq 0$ and choose some $T > t_0$. Then $m(x,t)$ is bounded in the region $[0,\infty) \times [0,T]$ (see [4]). Therefore, let $|m(x,t)| \leq M$ on $[0,\infty) \times [0,T]$ for some constant $M > 0$. For any $t \in [0,T]$, we have

$$|\mathcal{H}(t) - \mathcal{H}(t_0)| \leq \int_0^\infty \psi(x)y(x)\Big|H\Big(\frac{m(x,t)}{y(x)}\Big) - H\Big(\frac{m(x,t_0)}{y(x)}\Big)\Big|dx.$$

Splitting this integral into two parts and using the bound on $|m(x,t)|$ gives,

$$|\mathcal{H}(t) - \mathcal{H}(t_0)| \leq \int_0^X \psi(x)y(x)\Big|H\Big(\frac{m(x,t)}{y(x)}\Big) - H\Big(\frac{m(x,t_0)}{y(x)}\Big)\Big|\ dx + 2M\int_X^\infty \psi(x)\ dx,$$

for any $X > 0$ (recall that for this result we are using $H(x) = \max\{-x, 0\}$).

Now, from the above inequality, it can be seen that for any $\varepsilon > 0$, we can choose $X > 0$ such that

$$|\mathcal{H}(t) - \mathcal{H}(t_0)| \leq \int_0^X \psi(x)y(x)\Big|H\Big(\frac{m(x,t)}{y(x)}\Big) - H\Big(\frac{m(x,t_0)}{y(x)}\Big)\Big|\, dx + \varepsilon.$$

Moreover, by the fact that $m(x,t)$ is continuous for all $t \geq 0$, we find that $m(x,t)$ is uniformly continuous on $[0,X] \times [0,T]$. Therefore we may pick $\delta > 0$ small enough such that when $|t - t_0| \leq \delta$, we have $t < T$, and

$$|\mathcal{H}(t) - \mathcal{H}(t_0)| \leq 2\varepsilon,$$

Thus, we have shown that $\mathcal{H}(t)$ is continuous at any point $t_0 \geq 0$.

Returning to the main proof, we find that when the initial conditions are non-negative we have $\mathcal{H}(0) = 0$. But then, by the continuity of $\mathcal{H}$ and the fact that it is non-increasing for $t > 0$, we must have $\mathcal{H}(t) = 0$ for all $t \geq 0$. This implies that $m(x,t) \geq 0$ for all $t \geq 0$ when the initial conditions are non-negative, and consequently $n(x,t) \geq 0$ for all $t \geq 0$, where the function $n(x,t)$ is the solution to problem F. □

5. Concluding remarks

We have studied problem F, described by Equations (1.1)-(1.5), and it has been shown that for a given set of parameters, any SSD is globally asymptotically stable; that is, any initial distribution will give a solution which tends to the SSD. This global stability implies that there can be at most one SSD.

A sufficient condition for the existence of SSDs is given by $\alpha b > b + g$. This condition implies that there is a high probability of a cell dividing when it reaches size $x = l$, and is expected to apply to most real cell populations. Computational experiment seems to show that there is no SSD when $\alpha b < b + g$; while in the case where $\alpha b = b + g$ there is no non-trivial SSD (by Equation (2.6) of [2]).

It should be noted that most of the analysis in Section 3 could be applied in the case where a general division function $B(x)$ was used in the place of $b\delta(x - l)$. The main points which need to be established are as follows (from the end of Section 3):

- Strict positivity of $y(x)$ and $\psi(x)$, although it should be possible to weaken this assumption on $\psi(x)$, giving slightly weaker results.
- The assumption from (3.7), that $\psi'(x)y(x) \to 0$,
- The integrability of $n_t(x,t)$ on $[0,\infty) \times [t_0, t_0 + T]$.

The last two points are needed in order to show that $\mathcal{H}_t \leq 0$. (The integrability condition on $n_t(x,t)$ leads immediately to Lemma 3.2 when $n(x,t)$ is bounded by a constant multiple of $y(x)$)

In the present case, where $B(x) = b\delta(x-l)$, an estimate of the probability of cell division when passing through $x = l$ is given by:

$$\frac{(\text{added flux at } x = l/\alpha)/\alpha}{\text{flux into } x = l}.$$

The added flux at $x = l/\alpha$ comes from daughter cells produced by cell division at $x = l$ and is found by integrating Equation (1.1) about $x = l/\alpha$. We then find that,

$$-Dn_x\Big(\frac{l}{\alpha}^{+}, t\Big) + gn\Big(\frac{l}{\alpha}, t\Big) = -Dn_x\Big(\frac{l}{\alpha}^{-}, t\Big) + gn\Big(\frac{l}{\alpha}, t\Big) + \alpha bn(l.t).$$

Therefore the added flux from cell division is $\alpha bn(l,t)$. But this flux is due to some definite number k of growing cells, and was therefore the result of k/α cell divisions. Thus, $\alpha bn(l,t)$ is α times the total flux of cells which divide as they pass through $x = l$. The probability of cell division has thus been found to be

$$\frac{bn(l,t)}{\text{flux into } x = l}.$$

Let f denote the flux into $x = l$. Then

$$f = \begin{cases} -Dn_x(l^-,t) + gn(l,t), & -Dn_x(l^-,t) + gn(l,t) > 0, \\ & Dn_x(l^+,t) - gn(l,t) \leq 0, \\ Dn_x(l^+,t) - gn(l,t), & -Dn_x(l^-,t) + gn(l,t) \leq 0, \\ & Dn_x(l^+,t) - gn(l,t) > 0, \\ Dn_x(l^+,t) - Dn_x(l^-,t), & -Dn_x(l^-,t) + gn(l,t) > 0, \\ & Dn_x(l^+,t) - gn(l,t) > 0. \end{cases}$$

One of the three cases above must hold, since if we integrate Equation (1.1) about $x = l$ we find that

$$bn(l,t) = [-Dn_x(l^-,t) + gn(l,t)] + [Dn_x(l^+,t) - gn(l,t)]. \tag{5.1}$$

Therefore, when $n(l,t) > 0$ at least one of the terms $[-Dn_x(l^-,t) + gn(l,t)]$ or $[Dn_x(l^+,t) - gn(l,t)]$ must be positive. When $n(l,t) = 0$ we find that the derivatives $n_x(l^-,t) = n_x(l^+,t)$ and thus they must both equal zero, otherwise the solution would be negative at some point, in contradiction with Theorem 4.2. Hence, when $n(l,t) = 0$ the flux into $x = l$ is also zero and the probability of cell division is undefined.

Note that from (5.1) we have $Dn_x(l^+,t) - Dn_x(l^-,t) = bn(l,t)$. Therefore we find that

$$f = \begin{cases} -Dn_x(l^+,t) + (b+g)n(l,t), & -Dn_x(l^-,t) + gn(l,t) > 0, \\ & Dn_x(l^+,t) - gn(l,t) \le 0, \\ Dn_x(l^-,t) + (b-g)n(l,t), & -Dn_x(l^-,t) + gn(l,t) \le 0, \\ & Dn_x(l^+,t) - gn(l,t) > 0, \\ bn(l,t), & -Dn_x(l^-,t) + gn(l,t) > 0, \\ & Dn_x(l^+,t) - gn(l,t) > 0. \end{cases}$$

In the first case we find that since $Dn_x(l^+,t) - gn(l,t) \le 0$, we must have the flux into $x = l$ at least $bn(l,t)$. In the second case, since $-Dn_x(l^-,t) + gn(l,t) \le 0$, we again find that the flux into $x = l$ must be at least $bn(l,t)$. In the third case we have found that the flux into $x = l$ is exactly $bn(l,t)$. We therefore find that the probability of an individual cell dividing as in passes through $x = l$ is given by:

$$\begin{cases} \frac{b}{-D\frac{n_x(l^+,t)}{n(l,t)}+(b+g)}, & -Dn_x(l^-,t) + gn(l,t) > 0, Dn_x(l^+,t) - gn(l,t) \le 0, \\ \frac{b}{D\frac{n_x(l^-,t)}{n(l,t)}+(b-g)}, & -Dn_x(l^-,t) + gn(l,t) \le 0, Dn_x(l^+,t) - gn(l,t) > 0, \\ 1, & -Dn_x(l^-,t) + gn(l,t) > 0, Dn_x(l^+,t) - gn(l,t) > 0, \end{cases}$$

and this probability is, of course, less than or equal to one in all cases. If we then set b much greater than g and D very small, the probability of division approaches one.

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