

## A MODEL FOR ASYMMETRICAL CELL DIVISION

ALI ASHHER ZAIDI

Institute of Natural and Mathematical Sciences  
Massey University, Auckland, New Zealand

BRUCE VAN BRUNT

Institute of Fundamental Sciences  
Massey University, Palmerston North, New Zealand

GRAEME CHARLES WAKE

Institute of Natural and Mathematical Sciences  
Massey University, Auckland, New Zealand

(Communicated by Andrei Korobeinikov)

**ABSTRACT.** We present a model that describes the growth, division and death of a cell population structured by size. The model is an extension of that studied by Hall and Wake (1989) and incorporates the asymmetric division of cells. We consider the case of binary asymmetrical splitting in which a cell of size  $\xi$  divides into two daughter cells of different sizes and find the steady size distribution (SSD) solution to the non-local differential equation. We then discuss the shape of the SSD solution. The existence of higher eigenfunctions is also discussed.

**1. Introduction.** Population models have long been used to analyze various biological and physical phenomena. The human population growth was analyzed by Malthus [13] through an unstructured population model. McKendrick [14] presented an age-structured population model in terms of a partial differential equation. Following Diekmann *et al.* [15] and others, Hall and Wake [9] formulated a size structured population model (where the size could be the volume, mass, DNA content or any attribute that quantifies the physical dimension of a cell) and considered the case where a cell divides into daughter cells of the same size. Hall *et al.* [10]; Basse *et al.* [2]; Begg *et al.* [4] used this model to describe cell growth in plants. Basse *et al.* [1] used the same model for tumor cell growth. Hall and Wake's model, however, did not cover the asymmetric division of cells, in which a cell divides into daughter cells of different sizes. Early antecedents of this work are found in the papers of Diekmann *et al.* [8] and Heijmans [11]. We provide some explicit construction of the eigenfunctions given in [11]. Michel, Mischler and Perthame [16] considered the general scattering equation and the age, size and maturity structured population models and showed a common relative entropy structure. Perthame and Ryzhik [19] discussed the fragmentation equation and the evolution of the density of cells that grow and divide. A binary fragmentation of cell division was considered by

---

2010 *Mathematics Subject Classification.* Primary: 34K08, 35L02, 34L10; Secondary: 92C37.

*Key words and phrases.* Functional differential equations, eigenfunctions, cell biology, hyperbolic partial differential equations.

Michel, Mischler and Perthame [17]. Laurençot and Perthame [12] described the growth-fragmentation equation which allowed for the cell growth and its division into any number of pieces. Cáceres, Cañizo and Mischler [5], [6] then studied the asymptotic behavior of the growth-fragmentation equation. Suebcharoen *et al.* [20] developed a model for the asymmetrical cell division and gave an example of the occurrence of such a division in the embryos of *C. elegans* (worms) and *Drosophila* (flies). This is described in Neumüller and Knoblich [18], where it states “Besides *C. elegans*, the fruitfly *Drosophila melanogaster* is the model organism of choice for the analysis of asymmetric cell division”. Here the property of asymmetric cell division is less precisely defined, but in order to be able to quantify these attributes we think of size as physical quantities like mass, volume or diameter. Cells of different sizes may have different potential. Since the size of the daughter cells may reflect on their future, it is important to understand the impact of asymmetrical division on the evolutionary future path of the cohort. These models (mentioned above), however, did not focus on the biological interpretation of the splitting kernel. The papers [5], [6] do not consider the effect of requiring conservation of cell mass before and after division. We extend Hall and Wake’s model to cater for the asymmetric division of cells and establish the model directly from a biological interpretation of the splitting kernel.

**2. Model derivation.** We assume here that the system is deterministic. Let the horizontal axis represent the size and let  $n(x, t)$  be the number density of cells of size  $x$  at time  $t$ . If the units of  $x$ ,  $[x] = M$  then  $[n] = M^{-1}$ . Consider the interval

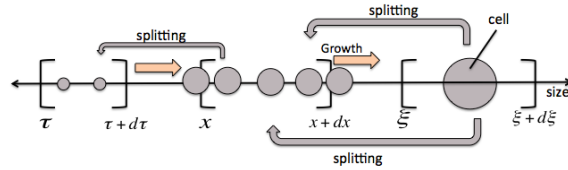


FIGURE 1. Cell growth and division for the cohort

$(x, x + dx)$  (as shown in Figure 1). In the absence of division or death, the rate of change of the cell number density in the size-interval  $dx$  equals the rate of the cell number density “convected” into  $dx$  minus the rate of the cell number density “convected” out of  $dx$ . This gives

$$\frac{\partial n}{\partial t} = -\frac{\partial}{\partial x}(gn), \quad (1)$$

where  $g(x)$  is the per capita growth rate,  $[g] = MT^{-1}$ , and  $T = [t]$ . The incoming rate of change of cell density in the interval  $(x, x + dx)$  (because of the splitting of cells of larger size) is

$$\int_x^\infty b(\xi)W(x, \xi)n(\xi, t)d\xi, \quad (2)$$

where  $W(x, \xi)$  is the number density of cells of size  $x$  produced when one cell of size  $\xi$  divides ( $[W] = M^{-1}$ ) and  $b(\xi)$  ( $[b] = T^{-1}$ ) is the frequency at which the cells of size  $\xi$  divide to give the cells of size  $x$ . The term  $\tau W(\tau, x)d\tau$  is the biomass of the

cells in the interval  $(\tau, \tau + d\tau)$  that arrive from the interval  $(x, x + dx)$  when one cell of size  $x$  divides. Thus,  $\frac{\tau}{x}W(\tau, x)d\tau$  gives the number of cells of size  $x$  formed from this biomass. The out going cell density rate due to the splitting of cells in the interval  $(x, x + dx)$  is therefore

$$- \left( \int_0^x b(x) \frac{\tau}{x} W(\tau, x) d\tau \right) n(x, t), \quad (3)$$

where the minus sign indicates that the cells are leaving the interval  $(x, x + dx)$ . Also, the contribution due to the death rate of cells in the interval  $(x, x + dx)$  is  $-\mu n(x, t)$  where  $\mu(x)$  is the specific death rate ( $[\mu] = T^{-1}$ ). Incorporating the cell division and death, equation (1) becomes

$$\begin{aligned} \frac{\partial n}{\partial t} + \frac{\partial}{\partial x}(gn) &= \int_x^\infty b(\xi)W(x, \xi)n(\xi, t)d\xi \\ &- \left( \int_0^x b(x) \frac{\tau}{x} W(\tau, x) d\tau \right) n(x, t) - \mu n(x, t). \end{aligned} \quad (4)$$

At any time  $t$ , it is biologically reasonable to expect the number density of cells of size zero to be zero, i.e., for all  $t \geq 0$

$$n(0, t) = 0. \quad (5)$$

Although no size limit is placed on cells in this model, it is also reasonable to impose the condition

$$\lim_{x \rightarrow \infty} n(x, t) = 0, \quad (6)$$

for all  $t \geq 0$ . The cell population model is studied from an initial number density distribution,

$$n(x, 0) = n_0(x), \quad (7)$$

where  $n_0$  is a given non-negative function satisfying equations (5)-(6). The problem is thus an initial-boundary value problem that consists of solving the integro-differential equation (4) subject to conditions (5)-(7). As noted the size  $x$  of a cell can be volume, mass, DNA content etc. Here, we shall make the choice that the size corresponds to a quantity that is conserved during the division, e.g. DNA content or biomass. We simply refer to this as “biomass”. Since  $\tau W(\tau, x)d\tau$  is the biomass of the cells in the interval  $(\tau, \tau + d\tau)$  that arrive from the interval  $(x, x + dx)$  when one cell of size  $x$  divides, the mass balance requires the equation

$$x = \int_0^x \tau W(\tau, x) d\tau, \quad (8)$$

which is a Volterra integral equation with many solutions. Further, for binary division (two daughter cells) we need

$$\int_0^\xi W(x, \xi) dx = 2. \quad (9)$$

Equations (8) and (9) together provide restrictions on the admissible functions possible for  $W$ . We introduce the most feasible  $W$  in the next section. Using the mass balance equation (8), equation (4) then simplifies to

$$\frac{\partial n}{\partial t} + \frac{\partial}{\partial x}(gn) = \int_x^\infty b(\xi)W(x, \xi)n(\xi, t)d\xi - (b(x) + \mu)n(x, t), \quad (10)$$

This, together with appropriate boundary and initial conditions is the problem to be addressed here.

**3. Qualitative results and SSD solutions.** The asymmetric cell division occurs when a cell divides into daughter cells of different sizes. Here, we study the case in which a cell of size  $\xi$  divides into two daughter cells of (different) sizes  $\frac{\xi}{\alpha}$  and  $\frac{\xi}{\beta}$  (the asymmetrical binary splitting), where  $\alpha > \beta > 1$ . Since a cell divides only when its size is a multiple of  $\alpha$  or  $\beta$ ,  $W(x, \xi)$  in this case becomes

$$W(x, \xi) = \delta\left(\frac{\xi}{\alpha} - x\right) + \delta\left(\frac{\xi}{\beta} - x\right), \quad (11)$$

where  $\delta$  denotes the Dirac delta function. The above choice of  $W$  and the mass balance equation simplify equation (4) to

$$\frac{\partial n}{\partial t} + g\frac{\partial n}{\partial x} = \alpha bn(\alpha x, t) + \beta bn(\beta x, t) - (\mu + b)n(x, t). \quad (12)$$

Here we took for simplicity  $g$  and  $b$  to be constant. Moreover, the mass balance equation (8) implies

$$\frac{1}{\alpha} + \frac{1}{\beta} = 1, \quad (13)$$

i.e.,

$$\beta = \frac{\alpha}{\alpha - 1}. \quad (14)$$

We focus on the solutions of equation (12), subject to the conditions given by equations (5)-(7), that correspond to the steady size distribution (SSD) (of constant shape). Perthame *et al.* [19] proved the existence of a stable steady distribution (first positive eigenfunction) and exponential convergence of solutions toward such a steady state for large times. Hall and Wake [9] considered separated solutions of the form  $n(x, t) = y(x)N(t)$ , where  $N(t) = \int_0^\infty n(x, t)dx$  is the total population at time  $t$  and  $y(x)$  (i.e.,  $y$  is time invariant) is a probability density function with  $\int_0^\infty y(x)dx = 1$ . They called such solutions “steady size distributions”. SSD solutions are thus separable solutions of the form  $n(x, t) = N(t)y(x)$  which lead to solutions of the form

$$n(x, t) \sim e^{-\lambda t}y(x), \quad (15)$$

where  $\lambda$  is a separation constant (to be found) and  $y$  satisfies

$$gy' = \alpha by(\alpha x) + \beta by(\beta x) - (\mu + b - \lambda)y(x), \quad (16)$$

along with the conditions

$$y(0) = 0 = \lim_{x \rightarrow \infty} y(x). \quad (17)$$

Clearly, we require that  $y(x) \geq 0$  for all  $x \geq 0$ . We further require that  $y$  be integrable on  $[0, \infty)$  and without loss of generality we can assume that  $y$  is a probability density function (pdf) so that

$$\int_0^{\infty} y(x) dx = 1. \quad (18)$$

Equation (16) can be integrated with respect to  $x$  from 0 to  $\infty$  and using conditions (17) and (18) this yields

$$\lambda = \mu - b. \quad (19)$$

Equation (16) thus reduces to

$$y' + \frac{2b}{g}y(x) = \frac{b}{g}(\alpha y(\alpha x) + \beta y(\beta x)). \quad (20)$$

The solution to equation (20) subject to the conditions (17) and (18) can be found by the technique used by Suebcharoen, van-Brunt and Wake [20]. The solution is a double Dirichlet series

$$y(x) = \sum_{k=0}^{\infty} \sum_{j=0}^{\infty} c_{k,j} e^{-\frac{2b}{g} \alpha^k \beta^j x}, \quad (21)$$

where,

$$c_{0,0} = \frac{2b}{g} + \left(\frac{b}{g}\right) \sum_{k=1}^{\infty} \frac{2^k (\alpha^{-k} + \beta^{-k})}{\prod_{s=1}^k (2 - \alpha^{-s} - \beta^{-s})}, \quad (22)$$

$$c_{k,0} = \frac{(-1)^k \alpha^k}{2^k \prod_{s=1}^k (\alpha^s - 1)} c_{0,0}, \quad (23)$$

$$c_{0,j} = \frac{(-1)^j \beta^j}{2^j \prod_{s=1}^j (\beta^s - 1)} c_{0,0}, \quad (24)$$

$$c_{k,j} = \frac{-1}{2(\alpha^k \beta^j - 1)} (\alpha c_{k-1,j} + \beta c_{k,j-1}), \quad (25)$$

for  $k, j \in \mathbb{N}$ . The convergence of equations (22)-(25) and uniqueness of the double Dirichlet series solution (21) along with the positivity can also be proved in a way similar to that used by Suebcharoen, van-Brunt and Wake [20]. No closed form solution for  $c_{k,j}$  can be obtained.

**4. Shape of the SSD solution.** The shape of the SSD solution is not obvious from the Dirichlet series (21). Numerical experiments, however, suggest strongly that the SSD solution is unimodal (see later). Rather than use the Dirichlet series directly, we will use the equation (20) to show that the function  $y$  must be unimodal. As noted in the last section, it can be shown that  $y(x) > 0$  for all  $x > 0$ .

The proof of unimodality for the single nonlocal term, the basic pantograph equation, was established by da Costa *et al.* [7]. The symmetric case  $\alpha = \beta = 2$  is covered by this analysis. If  $\alpha \neq 2$ , then the presence of a second nonlocal term complicates the analysis and certain arguments valid in the one term case break down for the two term case. To show the unimodality of the pdf solution  $y$  analytically, we suppose on the contrary that  $y$  is a pdf solution to equation (20) that is not unimodal. Without loss of generality we can assume

$$\alpha > 2 > \beta > 1.$$

Then there exists at least one local minimum. Let  $\{m_n\}$  be a strictly increasing sequence of points where  $y$  has a local minimum and  $\{M_n\}$  be a strictly increasing sequence where  $y$  has a local maximum. Since  $y'$  is also a Dirichlet series, local maxima and minima are confined to be bounded in  $x$ . Accordingly, neither  $m_n$  nor  $M_n$  tends to infinity as  $n$  tends to infinity. Also,  $\{m_n\}$  and  $\{M_n\}$  have no limit points since  $y'$  is holomorphic in the half plane and a limit point of extrema implies  $y'(z) = 0$  for all  $\operatorname{Re}(z) > 0$  which is clearly not true. We thus conclude that the sequences are finite. Note that  $y$  cannot be piecewise constant in any interval  $(a, b)$ ,  $a < b$  of the positive real axis by the same argument and this means  $y$  must be strictly decreasing after the last maximum.

Let  $m_f$  and  $M_f$  be the locations of the last local minimum and maximum respectively i.e.  $\max \{m_n\} = m_f$  and  $\max \{M_n\} = M_f$ . Then

$$y(m_f) > 0, y'(m_f) = 0, y''(m_f) \geq 0, \quad (26)$$

and equation (20) implies

$$2y(m_f) = \alpha y(\alpha m_f) + \beta y(\beta m_f). \quad (27)$$

Since  $\alpha > 2$  and  $y(m_f) > 0$ , we have

$$y(m_f) > y(\alpha m_f). \quad (28)$$

The last maximum at  $M_f$  must occur after the last minimum at  $m_f$ , and equation (28) implies that

$$m_f < M_f < \alpha m_f. \quad (29)$$

In particular,  $y'(\alpha m_f)$  cannot be positive as this would induce another local maximum beyond  $M_f$ . Also, at the last maximum  $M_f$ , equation (20) implies

$$2y(M_f) = \alpha y(\alpha M_f) + \beta y(\beta M_f). \quad (30)$$

Since

$$2y(m_f) < 2y(M_f), \quad (31)$$

Equations (27) and (30) give

$$\alpha y(\alpha m_f) + \beta y(\beta m_f) < \alpha y(\alpha M_f) + \beta y(\beta M_f). \quad (32)$$

The function is decreasing after the last maximum and  $\alpha m_f < \alpha M_f$ , hence,

$$y(\alpha m_f) > y(\alpha M_f). \quad (33)$$

Inequalities (32) and (33) give,

$$\begin{aligned} \alpha y(\alpha m_f) + \beta y(\beta m_f) &< \alpha y(\alpha M_f) + \beta y(\beta m_f) \\ &< \alpha y(\alpha M_f) + \beta y(\beta M_f), \end{aligned} \quad (34)$$

which implies  $\beta y(\beta m_f) < \beta y(\beta M_f)$ , i.e.,

$$y(\beta m_f) < y(\beta M_f). \quad (35)$$

Now  $\beta m_f < \beta M_f$  and  $y$  is decreasing after the last maximum, consequently,

$$m_f < \beta m_f < M_f < \alpha m_f, \quad (36)$$

so that,

$$y(m_f) < y(\beta m_f). \quad (37)$$

Equation (30) and inequality (33) give,

$$\begin{aligned} 2y(M_f) &= \alpha y(\alpha M_f) + \beta y(\beta M_f) \\ &< \alpha y(\alpha m_f) + \beta y(\beta M_f). \end{aligned} \quad (38)$$

Adding and subtracting  $\beta y(\beta m_f)$  to equation (38) gives,

$$2y(M_f) < \alpha y(\alpha m_f) + \beta y(\beta M_f) + \beta y(\beta m_f) - \beta y(\beta m_f),$$

which, using equation (27), yields

$$2(y(M_f) - y(m_f)) < \beta(y(\beta M_f) - y(\beta m_f)), \quad (39)$$

and since  $1 < \beta < 2$ , Inequalities (37) and (39) imply,

$$\begin{aligned} y(M_f) - y(m_f) &< y(\beta M_f) - y(\beta m_f) \\ &< y(\beta M_f) - y(m_f). \end{aligned} \quad (40)$$

Inequality (40) implies,

$$y(M_f) < y(\beta M_f), \quad (41)$$

which contradicts the fact that  $M_f$  is the last maximum. This proves that  $y$  is unimodal for all  $\alpha > 2 > \beta > 1$ .

**5. Existence and uniqueness of higher eigenfunctions.** SSD solutions are of central interest in this model since they can be easily matched to data for the size distribution of cells for large time. They are special solutions to the nonlocal p.d.e. (12). In particular, given an initial distribution  $n(x, 0) = n_0(x)$ , the SSD solution does not give the complete solution (unless  $n_0(x) = y(x)$ ) and this prompts one to consider other techniques to solve the more general problem.

This means that there is a set of solutions for equation (16) with homogeneous boundary conditions, that is,  $\lambda$  has the role of an eigenvalue as discussed in van Brunt *et al* [21]. We note that even in the single nonlocal term case, the general solution to the p.d.e. is not known. It may be possible that a class of solutions  $y_m$  for  $m = 0, 1, \dots$  can be obtained using an eigenfunction expansion. Specifically, we can use the conditions given by the successive moments (that is, the Mellin transform),

$$\int_0^\infty x^{m-1} y_m(x) dx = 0, \quad \int_0^\infty x^m y_m(x) dx \neq 0 \quad (42)$$

to calculate some further solutions to equation (16). These conditions give rise to a class of eigenfunctions and are sufficient in this respect. At this stage it is not clear whether there are other eigenfunctions. The idea mimics that used by van-Brunt and Vlieg-Hulstman [22], and leads to the spectrum (see Figure 2)

$$\lambda_m = \mu - b \left( \frac{1}{\alpha^m} + \frac{1}{\beta^m} - 1 \right), \quad (43)$$

for  $m = 0, 1, 2, \dots$ . Here  $y = y_m$  is the solution to equation (16) when  $\lambda = \lambda_m$ . We note that equation (43) gives equation (19) when  $m = 0$ , the first eigenfunction which is, of course, the SSD.

We note that there are a countable number of real eigenvalues in the interval  $[\mu - b, \mu + b]$ , increasing with  $m$ , with point of accumulation  $\lambda = \mu + b$ . These eigenvalues lead to equations of the form

$$y'_m + \frac{b}{g}(\alpha^{-m} + \beta^{-m})y_m(x) = \frac{b}{g}(\alpha y_m(\alpha x) + \beta y_m(\beta x)). \quad (44)$$

Of course, there may be other eigenvalues and eigenfunctions. These eigenfunctions

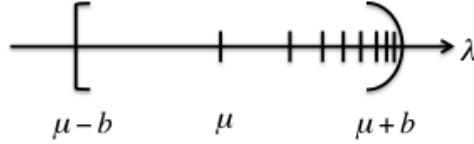


FIGURE 2. Spectrum of Eigenvalues

$y_m$  are the solutions to equation (44) subject to equation (42) and

$$y_m(0) = 0 = \lim_{x \rightarrow \infty} y_m(x),$$

The first eigenfunction is the pdf solution  $y_0$  given by equation (21). The higher eigenfunctions (as shown in Figure 4) can be found by following the procedure used by Suebcharoen, van-Brunt and Wake [20]. The solutions are

$$y_m(x) = \sum_{k=0}^{\infty} \sum_{j=0}^{\infty} c_{k,j} e^{-\alpha^k \beta^j \frac{b}{g} (\alpha^{-m} + \beta^{-m})x}, \quad (45)$$

where,

$$c_{0,0} = (-1)^m \left( \frac{b}{g} (\alpha^{-m} + \beta^{-m}) \right)^{m+1} + (-1)^m \left( \frac{b}{g} \right)^{m+1} \sum_{k=1}^{\infty} \frac{((\alpha^{-m} + \beta^{-m}))^{k+m} a_m(\alpha^{-(k+m)} + \beta^{-(k+m)})}{\prod_{r=1}^k (\alpha^{-m} + \beta^{-m} - \alpha^{-(m+r)} - \beta^{-(m+r)}), \quad (46)$$

$$c_{k,0} = \frac{(-1)^k \alpha^k c_{0,0}}{(\alpha^{-m} + \beta^{-m})^k \prod_{s=1}^k (\alpha^s - 1)}, \quad (47)$$



$$c_{0,j} = \frac{(-1)^j \beta^j c_{0,0}}{(\alpha^{-m} + \beta^{-m})^j \prod_{s=1}^j (\beta^s - 1)}, \quad (48)$$

$$c_{k,j} = \frac{-1}{(\alpha^k \beta^j - 1)(\alpha^{-m} + \beta^{-m})} (\alpha c_{k-1,j} + \beta c_{k,j-1}), \quad (49)$$

for  $k, j \in \mathbb{N}$ . Here  $a_m$  is a constant which can be chosen arbitrarily. In Figure 4, we have chosen  $a_m$  so that  $\int_0^\infty x y_1(x) dx = 1$ . The convergence of equations (46)-(49) and uniqueness of the double Dirichlet series solution (45) can also be proved on a pattern similar to that followed by Suebcharoen, van-Brunt and Wake [20]. No closed form solution for  $c_{k,j}$  can be obtained.

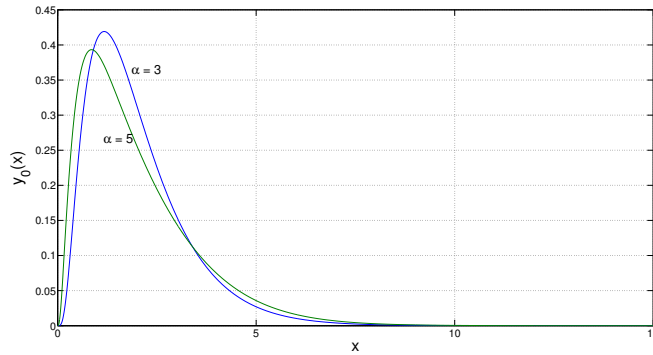


FIGURE 3. The solution  $y_0(x)$  given by the Dirichlet series (21) for  $m = 0$ ,  $g = 2$ ,  $b = 1$ ,  $\alpha = 3$ ,  $\beta = \frac{3}{2}$

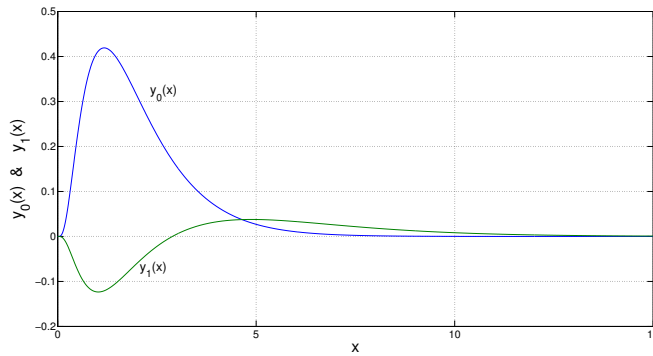


FIGURE 4. The solutions  $y_0(x)$  and  $y_1(x)$  given by the Dirichlet series (45) for  $m = 0, 1$ ,  $g = 2$ ,  $b = 1$ ,  $\alpha = 3$ ,  $\beta = \frac{3}{2}$

**6. Conclusions.** This model provides a quantitative basis of estimating the evolutionary path of the cell population cohort and determining the subsequent size distribution. The case of symmetrical division,  $\alpha = \beta = 2$ , can be used as a basis to compare with more general cell division with  $\alpha > \beta > 1$  but satisfying equation (13). The question of whether the set of the above solutions are complete is still open. Suppose that  $n$  is a function of the form

$$n(x, t) = \sum_{m=0}^{\infty} c_m y_m(x) e^{-\lambda_m t}, \quad (50)$$

where the above series is uniformly convergent for  $x \geq 0$ . Then it is straightforward to show that such a function is a solution to equation (12). The problem, however, is that in order to satisfy condition (7), the coefficients  $c_m$  must satisfy

$$n_0(x) = \sum_{m=0}^{\infty} c_m y_m(x), \quad (51)$$

and this brings to the fore the crucial question about what function space is spanned by the eigenfunctions. This question and other properties of these eigenfunctions remain to be explored, and this will be the subject of future papers.

If, as we conjecture that, equation (50) is the full solution to equation (12), then clearly  $n(x, t) \sim c_0 y_0 e^{-\lambda_0 t}$  for large time, showing the steady size distribution is proportional to  $y_0(x)$ . This is given in equation (21) and is shown in Figure 3 and Figure 4. The latter also includes  $y_1(x)$ , the second eigenfunction.

Now we have the means, through equation (50), to calculate the evolutionary path of the cell population cohort. Although  $y_m(x)$  is not mono-signed for  $m > 0$ , we expect that  $n(x, t)$  remain positive for all  $x, t > 0$  but we have not proved this here. It is to be addressed in a future paper.

**Acknowledgments.** The authors would like to thank Professor Helen Byrne, University of Oxford, for pointing out the need of mass conservation which leads to equation (8). We also thank the referees for their comments which led to an improved version of this paper.

## REFERENCES

- [1] B. Basse, B. Baguley, E. Marshall, W. Joseph, B. Van-Brunt, G. C. Wake and D. Wall, [Modelling cell death in human tumor cell lines exposed to the anticancer drug paclitaxel](#), *J. Math. Biol.*, **49** (2004), 329–357.
- [2] Basse, G. C. Wake, D. J. N. Wall and B. Van-Brunt, [On a cell-growth model for plankton](#), *Mathematical medicine and biology*, **21** (2004), 49–61.
- [3] R. Begg, *Cell-population Growth Modeling and Functional Differential Equations*, Ph.D thesis, University of Canterbury, New Zealand, 2007.
- [4] R. Begg, D. J. N. Wall and G. C. Wake, [On a functional equation model of transient cell growth](#), *Mathematical medicine and biology*, **22** (2005), 371–390.
- [5] M. J. Cáceres, J. A. Cañizo and S. Mischlerl, [Rate of convergence to self similarity for the fragmentation equation in  \$L^1\$  spaces](#), *Communications in Applied and Industrial Mathematics*, **1** (2010), 299–308.
- [6] M. J. Cáceres, J. A. Cañizo and S. Mischlerl, [Rate of convergence to an asymptotic profile for the self-similar fragmentation and growth-fragmentation equations](#), *Journal de Mathématiques Pures et Appliquée*, **96** (2011), 334–362.
- [7] F. P. Da Costa, M. Grinfeld and J. B. Mcleod, [Unimodality of steady size distributions of growing cell populations](#), *J. evol. equ.*, **1** (2001), 405–409.
- [8] O. Diekmann, H. J. A. M. Heijmans and H. R. Thieme, [On the stability of the cell size distribution](#), *Jour. Math. Biol.*, **19** (1984), 227–248.

- [9] A. J. Hall and G. C. Wake, [A functional differential equation arising in modelling of cell growth](#), *J. Aust. Math. Soc. Ser. B*, **30** (1989), 424–435.
- [10] A. J. Hall, G. C. Wake and P. W. Gandar, [Steady size distributions for cells in one dimensional plant tissues](#), *J. Math. Biol.*, **30** (1991), 101–123.
- [11] H. J. A. M. Heijmans, [On the stable size distribution of populations reproducing by fission into two unequal parts](#), *Mathematical Biosciences*, **72** (1984), 19–50.
- [12] P. Laurençot and B. Perthame, [Exponential decay for the growth-fragmentation/cell-division equation](#), *Commun. Math. Sci.*, **7** (2009), 503–510.
- [13] T. R. Malthus, *An Essay on the Principle of Population*, St. Paul's London, 1798.
- [14] A. G. McKendrick, Applications of mathematics to medical problems, *Proc. Edinburgh Math. Soc.*, **44** (1926), 98–130.
- [15] J. A. J. Metz and O. Diekmann, *The Dynamics of Physiologically Structured Populations*, Lecture Notes in Biomathematics, 68. Springer-Verlag, Berlin, 1986.
- [16] P. Michel, S. Mischler and B. Perthame, [General entropy equations for structured population models and scattering](#), *Comptes Rendus Mathématique*, **338** (2004), 697–702.
- [17] P. Michel, S. Mischler and B. Perthame, [General relative entropy inequality: An illustration on growth models](#), *J. Math. Pures Appl.*, **84** (2005), 1235–1260.
- [18] R. A. Neumüller and J. A. Knoblich, Dividing cellular asymmetry: Asymmetric cell division and its implications for stem cells and cancer, *Genes Dev.*, **23** (2009), 2675–2699.
- [19] B. Perthame and L. Ryzhik, [Exponential decay for the fragmentation or cell-division equation](#), *Journal of Differential Equations*, **210** (2005), 155–177.
- [20] T. Suebcharoen, B. Van-Brunt and G. C. Wake, Asymmetric cell division in a size-structured growth model, *Differential and Integral Equations*, **24** (2011), 787–799.
- [21] B. Van-Brunt, G. C. Wake and H. K. Kim, [A singular Sturm-Liouville problem involving an advanced functional differential equation](#), *European Journal of Applied Mathematics*, **12** (2001), 625–644.
- [22] B. Van-Brunt and M. Vlieg-Hulstman, [An eigenvalue problem involving a functional differential equation arising in a cell growth model](#), *ANZIAM J.*, **51** (2010), 383–393.

Received August 05, 2014; Accepted November 13, 2014.

E-mail address: [a.a.zaidi@massey.ac.nz](mailto:a.a.zaidi@massey.ac.nz)

E-mail address: [B.vanBrunt@massey.ac.nz](mailto:B.vanBrunt@massey.ac.nz)

E-mail address: [g.c.wake@massey.ac.nz](mailto:g.c.wake@massey.ac.nz)