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A Fokker–Planck equation for growing cell populations

C. V. M. van der Mee[1] and P. F. Zweifel[2]

[1] Department of Mathematics, Texas Tech University Lubbock, TX 79409, USA
[2] Center for Transport Theory and Mathematical Physics, Virginia Polytechnic Institute and State University, Blacksburg, VA 24061, USA

Abstract. Closed form solutions are obtained for a Fokker–Planck model for cell growth as a function of maturation velocity and degree of maturation. For reproduction rules where daughter cells inherit their parent's maturation velocity the complete solution is derived in terms of Airy functions. For more complicated reproduction rules partial results are obtained. Emphasis is given to the relationship of these problems to time dependent linear transport theory.

Key words: Fokker–Planck — Cell population — Reproduction rules

1. Introduction

In a recent article Rotenberg [1] derived a diffusion equation which describes the number of cells with a certain degree of maturity as a function of maturation velocity and time. This equation is the partial differential equation

$$\frac{\partial f}{\partial t} + v\frac{\partial f}{\partial \mu} = D\frac{\partial^2 f}{\partial v^2}, \tag{1}$$

where $t \in (0, \infty)$ is time, $v \in (0, \infty)$ the maturation velocity, $\mu \in (0, 1)$ the degree of maturation and D a (positive) diffusion coefficient. It was derived from a linear integrodifferential equation describing the same quantities using the Fokker–Planck approximation that the transition rate which specifies the transition of cells from one maturation velocity to another is symmetric and highly peaked about conservation of maturation velocity. As boundary conditions (in the maturation velocity v) one takes

$$\frac{\partial}{\partial v} f(\mu, v, t)|_{v=0} = 0 \tag{2}$$

and

$$\lim_{v \to \infty} f(\mu, v, t) = 0, \tag{3}$$

since these are necessary to produce a continuity equation without sources,

$$\frac{\partial}{\partial t}\int_0^\infty f(\mu, v, t)\,dv+\frac{\partial}{\partial \mu}\int_0^\infty vf(\mu, v, t)\,dv=0. \tag{4}$$

According to Rotenberg [1], there is no known closed solution to Eq. (1) with initial condition

$$f(\mu, v, 0)=\delta(\mu)\delta(v-w) \tag{5}$$

and boundary conditions (2) and (3). The purpose of the present article is to supply such closed solutions.

On separating off the time variable t, by means of the Ansatz

$$f(\mu, v, t)=e^{-\lambda t}\varphi_\lambda(\mu, v), \tag{6}$$

one obtains the eigenvalue equation

$$v\frac{\partial f}{\partial \mu}-D\frac{\partial^2 f}{\partial v^2}=\lambda f(\mu, v), \tag{7}$$

subject to the boundary conditions (2) and (3). Further separation of variables, viz.

$$\varphi_\lambda(\mu, v)=e^{\rho\mu}g_{\lambda,\rho}(v), \tag{8}$$

gives the ordinary differential equation

$$Dg''_{\lambda,\rho}(v)-\lambda g_{\lambda,\rho}(v)=\rho v g_{\lambda,\rho}(v) \tag{9}$$

with boundary conditions

$$g'_{\lambda,\rho}(0)=0, \qquad \lim_{v\to\infty} v g_{\lambda,\rho}(v)=0. \tag{10}$$

We shall consider Eq. (9) on the Hilbert space $L_2(\mathbb{R}_+; v\,dv)$. Then the Sturm-Liouville differential operation $g|\to Dg''-\lambda g$ is regular at $v=0$ and singular of limit-point type at $v=+\infty$ (cf. [2, 3]); a normal and, for $\lambda\in\mathbb{R}$, a selfadjoint boundary value problem arises by imposing the first boundary condition (10) and replacing the second one by $g_{\lambda,\rho}\in L_2(\mathbb{R}_+; v\,dv)$. For fixed λ one then has to find the (regular and singular) eigenvalues ρ and the corresponding eigenfunctions and eigendistributions as to obtain a complete set in $L_2(\mathbb{R}_+; v\,dv)$. Since this may be done for any λ the conditions (2) and (3) do not suffice to specify the solution $f(\mu, v, t)$ to Eq. (1) uniquely. In order to accomplish well-posedness, an additional boundary condition involving μ should be imposed which specifies the (regular and singular) time eigenvalues λ and allows one to solve the corresponding initial-boundary value problem by expansion with respect to the eigenfunctions and eigendistributions corresponding to λ, given $f(\mu, v, 0)$.

It is clear from the above that an additional boundary condition must be imposed as to make Eqs. (1) to (4) well-posed. For this condition we take a *reproduction rule* which expresses the cell distribution of birth ($\mu=0$) in the distribution at mitosis ($\mu=1$). The simplest reproduction rule stipulates complete inheritance of the maturation velocity from parent cell to daughter cell on mitosis,

$$f(0, v, t)=pf(1, v, t), \tag{11}$$

where $p \in (0, 2]$ is the average number of viable daughters per mitosis. Lebowitz and Rubinow [4] have introduced a class of more general reproduction rules given by

$$vf(0, v, t) = p \int_0^\infty k(v, v')v'f(1, v', t)\, dv', \tag{12}$$

where $k(v, v')$ is nonnegative and satisfies the normalization condition

$$\int_0^\infty k(v, v')\, dv = 1. \tag{13}$$

For $k(v, v') = \delta(v - v')$ we will retrieve (11). Other special cases were discussed in Rotenberg [1], such as the reproduction rule assigning maturation velocities to daughter cells independent of the velocity distribution at mitosis,

$$k(v, v') = k(v), \qquad \int_0^\infty k(v)\, dv = 1, \tag{14}$$

and the reproduction rule giving a fixed initial maturation velocity w,

$$k(v, v') = \delta(v - w). \tag{15}$$

We also mention the separated kernel

$$k(v, v') = \sum_{j=1}^{M} k_j(v) l_j(v'), \qquad \sum_{j=1}^{M} \kappa_j l_j(v') = 1 \quad \textit{where}\ \kappa_j = \int_0^\infty k_j(v)\, dv. \tag{16}$$

For the "perfect memory rule" (11) we shall give a complete solution of the time-dependent transport equation. Except for this rather elementary reproduction rule, where the eigenvalues λ and eigenfunctions can be given without resorting to complicated series expansions, we shall give a detailed discussion of the completeness of the eigenfunctions and the distribution of the eigenvalues which will appear as the zeros of a "dispersion" function.

We attack the solution of Eq. (1), with boundary condition (2), (3) (plus one of the reproduction rules (11), (12), (14), (15) or (16)) as follows. We begin, in Sect. 2, by solving Eq. (9), assuming $\lambda \in \mathbb{C}$ fixed, in terms of Airy functions. Having obtained the eigensolutions $\varphi_{n,\lambda}$, we go on to show how arbitrary functions of v may be expanded in terms of the $\varphi_{n,\lambda}$ with expansion coefficients g_n. Next, we consider $f(\mu, v, 0) = f_0(\mu, v)$ and expand it using the eigenvalue expansion of $f_0(0, v)$. If λ (still assumed fixed) is an eigenvalue of the original transport equation, (1), the function $f_0(\mu, v)$ has to satisfy the reproduction rule. Considering first the general rule, Eq. (12), one gets an expression for the expansion coefficients g_n, which is a complicated equation in which λ is contained implicitly, through $\varphi_{n,\lambda}$, $\rho_n(\lambda)$ and C_n^λ. To study it, we consider the simplest rule, corresponding to perfect memory, which leads to an explicit solution for ρ_s, while each ρ_s leads to an infinite sequence of eigenvalues $\lambda_{n,s}$. For $0 < p < 1$ the corresponding eigenfunctions $\varphi_{n,s}$ are complete ($s \in Z$, $n \in \mathbb{N}$). The final solution to Eq. (1) is obtained by expanding $f_0(\mu, v, 0)$ in terms of the $\varphi_{n,s}$ and inserting the appropriate time exponents. For $p \geqslant 1$, the term $s = 0$ concerns continuous spectrum and the sum over n must be replaced by an integral.

For more complicated reproduction rules, one can proceed in an analogous manner, but the procedure is much more complicated and we have obtained only a partial answer. In all cases this leads to a dispersion formula which contains λ implicitly and must be solved for λ. When the λ have been obtained, the procedure sketched above for the simplest case can be followed to obtain the solution for the present case. This would undoubtedly require numerical techniques.

The above problem has much in common with time-dependent transport theory problems (see [5-8] for references), since for $p=1$ condition (11) reduces to a so-called periodic boundary condition. Due to the complicated nature of the equation, one usually employs semigroup techniques to study the long-time behavior of their solutions. Only for some simplified equations and for periodic boundary conditions, closed form results have been obtained (for instance, [9]). The eigenfunction method itself is commonplace in transport theory (see [10]).

2. Eigenfunctions of the boundary value problem in maturation velocity

On substituting $z=(\rho v+\lambda)/\alpha$ where $\alpha^3=D\rho^2$ and $\rho\neq 0$, into Eqs. (9) and (10) and putting $G(z)=g_{\lambda,\rho}((\alpha z-\lambda)/\rho)$ we obtain the Airy equation [11] with boundary conditions

$$G''(z)=zG(z), \qquad \arg(z)=\arg(\rho/\alpha), \tag{17}$$

$$G'(\lambda/\alpha)=0, \qquad G\in L_2((\rho/\alpha)\mathbb{R}_+;|z|\,dz). \tag{18}$$

The Airy equation (17) has two linearly independent solutions $Ai(z)$ and $Bi(z)$, satisfying ([11], 10.4.59 and 10.4.63)

$$Ai(z)\sim\tfrac{1}{2}\pi^{-1/2}z^{-1/4}e^{-\zeta}\sum_{k=0}^{\infty}(-1)^k c_k\zeta^{-k} \qquad (|\arg z|<\pi) \tag{19}$$

and

$$Bi(z)\sim\pi^{-1/2}z^{-1/4}e^{\zeta}\sum_{k=0}^{\infty}c_k\zeta^{-k} \qquad (|\arg z|<(\pi/3)), \tag{20}$$

where $c_0=1$, $c_k=(2k+1)(2k+3)\cdots(6k-1)/(216^k\cdot k!)$ and $\zeta=(2z^{3/2}/3)$. Hence, if $|\arg(\rho/\alpha)|<(\pi/3)$, then $G(z)\simeq Ai(z)$ where ρ must be chosen in such a way that λ/α is a zero of $Ai'(z)$. Since $Ai'(z)$ has all its zeros on the negative real line and these are simple and may be denoted as $0>a_1'>a_2'>\cdots>-\infty$, we find a discrete set of values $\rho_{n,0}$ and corresponding $\alpha_{n,0}$ with $\alpha_{n,0}^3=D\rho_{n,0}^2$ and $|\arg(\rho_{n,0}/\alpha_{n,0})|<(\pi/3)$, satisfying $\alpha_{n,0}=(\lambda/a_n')$ where $n\in\mathbb{N}$. Next, if $(\pi/3)<\arg(\rho/\alpha)<\pi$, then $G(z)\simeq Ai(z/\varepsilon)$ with $\varepsilon=\exp[2\pi i/3]$, where ρ is chosen as to get $(\lambda/\alpha\varepsilon)$ as a zero of $Ai'(z)$; thus one must select a discrete set of values $\rho_{n,1}$ and $\alpha_{n,1}^3=D\rho_{n,1}^2$, $(\pi/3)<\arg(\rho_{n,1}/\alpha_{n,1})<\pi$ and $\alpha_{n,1}=(\lambda/\varepsilon a_n')$ where $n\in\mathbb{N}$. If $\pi<\arg(\rho/\alpha)<(5\pi/3)$, then $G(z)\simeq Ai(\varepsilon z)$, where ρ is chosen such that $(\varepsilon\lambda/\alpha)$ is a zero of $Ai'(z)$; thus a discrete set of values $\rho_{n,2}$ and $\alpha_{n,2}$ should be selected for which $\alpha_{n,2}^3=D\rho_{n,2}^2$, $\pi<\arg(\rho_{n,2}/\alpha_{n,2})<(5\pi/3)$ and $\alpha_{n,2}=(\varepsilon\lambda/a_n')$ where $n\in\mathbb{N}$. The corresponding eigenfunctions are given by

$$h_{n,k}(v)=Ai\left(\frac{\rho_{n,k}}{\alpha_{n,k}}\frac{v}{\varepsilon^k}+a_n'\right), \qquad n\in\mathbb{N} \textit{ and } k=0,1,2. \tag{21}$$

It remains to discuss the case when $\arg(\rho/\alpha)=\pm(\pi/3)$ or (π). The asymptotic expansion (19) indicates that $Ai(\cdot)\notin L_2(\varepsilon\mathbb{R}_+;|z|\,dz)$. Since every solution of

Eq. (17) is a linear combination of $Ai(z)$ and $Ai(\varepsilon z)$ ([11], 10.4.1), it is not difficult to see that no nonzero solution of Eq. (17) belongs to $L_2(\varepsilon\mathbb{R}_+; |z|\,dz)$, whence no eigenfunctions will be found if $\arg(\rho/\alpha) = \pm(\pi/3)$ or (π). If $\rho = 0$, we consider Eqs. (9) and (10) themselves and easily derive that no eigenfunction exists for this case. Putting $\beta_k = \arg(\rho_{n,k}/\alpha_{n,k})$ and observing $\arg(\rho_{n,k}) = 3\beta_k$, the eigenvalue equation

$$(\rho_{n,k}/\alpha_{n,k}) = (\varepsilon^k a_n'/\lambda)\rho_{n,k}, \qquad n \in \mathbb{N} \textit{ and } k = 0, 1, 2, \tag{22}$$

yields

$$\arg(\lambda) = 2\beta_k + \pi + (2\pi k/3), \tag{23}$$

where $-(\pi/3) < \beta_k + (2\pi k/3) < (\pi/3)$. Hence, the eigenvalues λ belong to the region

$$(\pi/3) < \arg(\lambda) < (5\pi/3) \tag{24}$$

and $\beta_k = \pm(\pi/3) + (2\pi k/3)$ (the no eigenvalue case) corresponds to $\arg(\lambda) = \pm(\pi/3)$. Thus if $\lambda \neq 0$ satisfies the condition (24), one must consider each of the three choices of β_k, all satisfying $\beta_k = \beta_0 + (2\pi k/3)$ with $|\beta_0| < (\pi/3)$ and leading to the same [cf. (21)] sequence of eigenfunctions

$$\varphi_{n,\lambda}(v) \overset{\text{def}}{=} h_{n,0}(v) = Ai\left(\frac{\rho_n}{\alpha_n} v + a_n'\right), \qquad n \in \mathbb{N}, \tag{25}$$

where $\rho_n = \rho_{n,0}$ and $\alpha_n = \alpha_{n,0}$. For $\lambda = 0$ or $\arg\lambda = \pm(\pi/3)$ the Sturm–Liouville problem (9)–(10) has continuous spectrum $\rho \in (-\infty, 0]$. The set of eigenfunctions (25) has the orthogonality property

$$\int_0^\infty v\varphi_{n,\lambda}(v)\overline{\varphi_{m,\lambda}(v)}\,dv = C_n^\lambda \delta_{nm} \tag{26}$$

and the completeness property

$$\int_0^\infty v|g(v)|^2\,dv = \sum_{n=1}^\infty C_n^\lambda |g_n|^2 \quad \textit{where } g_n = \frac{1}{C_n^\lambda}\int_0^\infty vg(v)\overline{\varphi_{n,\lambda}(v)}\,dv.$$

As a result every function $g \in L_2(\mathbb{R}_+; v\,dv)$ may be expanded as

$$g(v) = \sum_{n=1}^\infty g_n\varphi_{n,\lambda}(v) \tag{27}$$

in the sense that

$$\lim_{L\to\infty}\int_0^\infty v\left|g(v) - \sum_{n=1}^L g_n\varphi_{n,\lambda}(v)\right|^2 dv = \lim_{L\to\infty}\sum_{n=L+1}^\infty C_n^\lambda |g_n|^2 = 0,$$

where

$$C_n^\lambda = \int_0^\infty v|\varphi_{n,\lambda}(v)|^2\,dv.$$

3. Eigenfunctions of the transport operator

In our study of the boundary value problem (7)-(2)-(3)-(12) we introduce the Banach space $\mathbb{B}$ of functions $h:[0,1]\times\mathbb{R}_+\to\mathbb{C}$ which are continuous in $\mu\in[0,1]$, measurable in $v\in\mathbb{R}_+$ and bounded with respect to the norm

$$\|h\|_{\mathbb{B}}=\max_{0\leq\mu\leq 1}\left[\int_0^\infty v|h(\mu,v)|^2\,dv\right]^{1/2}.$$

We may consider $\mathbb{B}$ to be the Banach space of continuous functions $\hat{h}:[0,1]\to L_2(\mathbb{R}_+;v\,dv)$ with supremum norm, the correspondence given by $\hat{h}(\mu)(v)=h(\mu,v)$. Searching for a time eigenvalue λ satisfying (22) and corresponding eigenfunction $f_0(\mu,v)(\in\mathbb{B})$, we first make the expansion

$$f_0(\mu,v)=\sum_{n=1}^\infty g_n e^{\rho_n\mu}\varphi_{n,\lambda}(v),\tag{28}$$

where

$$\|f_0\|_{\mathbb{B}}^2=\max_{0\leq\mu\leq 1}\sum_{n=1}^\infty C_n^\lambda\,e^{2\mu(\operatorname{Re}\rho_n)}|g_n|^2<\infty.\tag{29}$$

On substituting (28) in (12) we obtain

$$v\sum_{n=1}^\infty g_n\varphi_{n,\lambda}(v)=p\sum_{n=1}^\infty g_n e^{\rho_n}\int_0^\infty k(v,v')v'\varphi_{n,\lambda}(v')\,dv',\tag{30}$$

whence (cf. (13))

$$\sum_{n=1}^\infty g_n l_n^\lambda=p\sum_{n=1}^\infty e^{\rho_n}g_n l_n^\lambda,\tag{31}$$

where

$$l_n^\lambda=\int_0^\infty v'\varphi_{n,\lambda}(v')\,dv'.$$

On multiplying (28) by $\overline{\varphi_{m,\lambda}(v)}$ and integrating we find

$$g_m C_m^\lambda=p\sum_{n=1}^\infty g_n e^{\rho_n}\int_0^\infty\int_0^\infty k(v,v')v'\varphi_{n,\lambda}(v')\overline{\varphi_{m,\lambda}(v)}\,dv'\,dv,\tag{32}$$

which must be satisfied for a nontrivial sequence $(g_m)_{m=1}^\infty$ having the property (29) in order that λ is a time eigenvalue. For $\lambda=0$ or $\arg(\lambda)=\pm(\pi/3)$ one uses the continuous analogs of (28) and (29) and obtains (32) where the summation has been replaced by (another) integration.

Let us first analyze the "perfect memory rule" (11) where $k(v,v')=\delta(v-v')$. Equation (32) reduces to the algebraic equation

$$(1-p\,e^{\rho_m})g_m C_m^\lambda=0,\tag{33}$$

whence

$$\rho^s=\ln(1/p)+2\pi is,\qquad s\in Z.$$

For every $s \in Z$ and every $0<p\leq 2$, exempting $s=0$ and $1\leq p\leq 2$ where $-\infty< \rho_m^s \leq 0$, we find the eigenvalues

$$\lambda_{n,s} = a_n' D^{1/3}[\ln^2(1/p)+4\pi^2 s^2]^{1/3}\exp[i\varphi_s], \tag{34}$$

where

$$\varphi_s = \arg[\ln(1/p)+2\pi i s]^{2/3}\begin{cases} \textit{belongs to } \left(-\frac{\pi}{3},\frac{\pi}{3}\right) & \textit{if } 0<p<1 \\ \textit{equals } \frac{\pi}{3}\operatorname{sgn}(s) & \textit{if } p=1 \\ \textit{belongs to } \left(\frac{-2\pi}{3},\frac{-\pi}{3}\right)\cup\left(\frac{\pi}{3},\frac{2\pi}{3}\right) & \textit{if } 1<p\leq 2. \end{cases}$$

In all cases $\operatorname{sgn}\varphi_s = \operatorname{sgn} s$ and $\lim_{s\to\pm\infty}\varphi_s = \pm(\pi/3)$ (except for $s=0$ and $0<\beta<1$ where $\varphi_s=0$). For $0<p\leq 1$ none and for $1<p\leq 2$ at most finitely many classes of eigenvalues having the same s (exempting $s=0$ for $p\leq 1$) belong to the closed left half-plane. The eigenfunctions are given by

$$\varphi_{n,s}(\mu, v) = \varphi_{\lambda_{n,s}}(\mu, v) = \frac{1}{p^{\mu}}\, e^{2\pi i\mu s} Ai(\sigma_s v + a_n') \tag{35}$$

where

$$\sigma_s = D^{-1/3}[\ln^2(1/p)+4\pi^2 s^2]^{1/6}\exp[\tfrac{1}{2}i\varphi_s]. \tag{36}$$

For $s=0$ and $1\leq p\leq 2$ the time eigenvalue problem in the Banach space $\mathbb{B}$ has continuous spectrum. Next we shall discuss the reproduction rule (14). Putting

$$k_m^\lambda = \int_0^\infty k(v)\varphi_{m,\lambda}(v)\,dv,$$

Eq. (31) reduces to the algebraic equation

$$\sum_{n=1}^{\infty}\left(\delta_{nm} - p\, e^{\rho_n}\frac{k_m^\lambda l_n^\lambda}{\sqrt{C_m^\lambda}\sqrt{C_n^\lambda}}\right)\sqrt{C_n^\lambda}g_n = 0, \tag{37}$$

which must be solved for $\{\sqrt{C_n^\lambda}g_n\}_{n=1}^\infty \in l_2$[cf. (29)]. We easily derive

$$\sum_{m=1}^{\infty}\frac{|k_m^\lambda|^2}{C_m^\lambda} = \int_0^\infty \frac{k(v)^2}{v}\,dv, \qquad \sum_{n=1}^{\infty}\frac{|l_n^\lambda|}{C_n^\lambda} = \int_0^\infty v\,dv = \infty.$$

Hence, on assuming $\int_0^\infty (k(v)^2/v)\,dv<\infty$, we obtain λ as a time eigenvalue if at least the summability condition

$$\sum_{n=1}^{\infty} e^{2\operatorname{Re}\rho_n}\frac{|l_n^\lambda|}{C_n^\lambda}<\infty$$

and the dispersion relation

$$\frac{1}{p} = \sum_{n=1}^{\infty} e^{\rho_n}\frac{k_n^\lambda l_n^\lambda}{C_n^\lambda} \tag{38}$$

are satisfied for λ. The coefficients g_n must then be taken as $g_n = (k_n^\lambda / C_n^\lambda)$, whence

$$f_0(\mu, v) = \sum_{n=1}^{\infty} \frac{k_n^\lambda}{C_n^\lambda} e^{\rho_n \mu} \varphi_{n,\lambda}(v) \tag{39}$$

is an eigenfunction in $\mathbb{B}$ if it satisfies

$$\|f_0\|_{\mathbb{B}}^2 = \max_{0 \le \mu \le 1} \sum_{n=1}^{\infty} |k_n^\lambda|^2 e^{2\mu \operatorname{Re} \rho_n} < \infty. \tag{40}$$

Thus if condition (40) is fulfilled with the corresponding series absolutely convergent, then the function given by (39) is an eigenfunction at the time eigenvalue λ if (and only if) the summability condition (40) is satisfied. For $\lambda = 0$ or $\arg(\lambda) = \pm(\pi/3)$ one must use the continuous analogue of (32) leading to a complete analog of conditions (38)-(40) for λ to be a time eigenvalue.

For the reproduction law (15) where $k(v) = \delta(v - w)$ we do not have $\int_0^\infty (k(v)^2/v)\, dv < \infty$. Therefore we shall do a separate computation. Putting

$$H^\lambda = \sum_{n=1}^{\infty} g_n e^{\rho_n} l_n^\lambda,$$

Eq. (32) leads to the algebraic equation

$$g_m C_m^\lambda = p H^\lambda \overline{\varphi_{m,\lambda}(w)}.$$

Since $H^\lambda \neq 0$ to get an eigenfunction, we obtain the dispersion relation

$$\sum_{n=1}^{\infty} e^{\rho_n} \frac{l_n^\lambda}{C_n^\lambda} \overline{\varphi_{n,\lambda}(w)} = \frac{1}{p} \tag{41}$$

to be satisfied for λ, with corresponding eigenfunction

$$f_0(\mu, v) = \sum_{n=1}^{\infty} \frac{1}{C_n^\lambda} \overline{\varphi_{n,\lambda}(w)}\, e^{\rho_n \mu} \varphi_{n,\lambda}(v), \tag{42}$$

provided it satisfies the normalization condition

$$\|f_0\|_{\mathbb{B}}^2 = \max_{0 \le \mu \le 1} \sum_{n=1}^{\infty} |\varphi_{n,\lambda}(w)|^2 e^{2\mu \operatorname{Re} \rho_n} < \infty. \tag{43}$$

For $\lambda = 0$ or $\arg(\lambda) = \pm(\pi/3)$ one uses the continuous analogs of (32).

Finally, let us consider the reproduction law (16). Putting

$$k_{j,m}^\lambda = \int_0^\infty k_j(v) \overline{\varphi_{m,\lambda}(v)}\, dv, \qquad l_{j,n}^\lambda = \int_0^\infty v' l_j(v') \varphi_{n,\lambda}(v')\, dv',$$

we may reduce Eq. (32) to the algebraic equation

$$\sum_{n=1}^{\infty} \left(\delta_{nm} - p\, e^{\rho_n} \sum_{j=1}^{M} \frac{k_{j,m}^\lambda l_{j,n}^\lambda}{\sqrt{C_m^\lambda}\sqrt{C_n^\lambda}} \right) \sqrt{C_n^\lambda} g_n = 0 \tag{44}$$

to be solved for $\{\sqrt{C_n^\lambda} g_n\}_{n=1}^\infty \in l_2$ in a nontrivial way. One easily computes

$$\sum_{n=1}^{\infty} \frac{|k_{j,m}^\lambda|^2}{C_m^\lambda} = \int_0^\infty \frac{k_j(v)^2}{v}\, dv, \qquad \sum_{n=1}^{\infty} \frac{|l_{j,n}^\lambda|^2}{C_n^\lambda} = \int_0^\infty v |l_j(v)|^2\, dv.$$

Hence, on assuming, for $j=1,2,\dots,M$, $\int_0^\infty (k_j(v)^2/v)\,dv<\infty$, one obtains λ as a time eigenvalue if at least the summability conditions

$$\sum_{n=1}^{\infty} e^{2\operatorname{Re}\rho_n} \frac{|l_{j,n}^\lambda|}{C_n^\lambda}<\infty$$

are satisfied as well as the dispersion relation

$$\det\left(\delta_{jk}-p\sum_{n=1}^{\infty} e^{\rho_n}\frac{k_{j,n}^\lambda l_{k,n}^\lambda}{C_n^\lambda}\right)_{j,k=1}^{M}=0. \tag{45}$$

If the latter holds true for λ and

$$\sum_{k=1}^{M}\left(\delta_{jk}-p\sum_{n=1}^{\infty} e^{\rho_n}\frac{k_{j,n}^\lambda l_{k,n}^\lambda}{C_n^\lambda}\right)\xi_k=0, \qquad j=1,2,\dots,M,$$

for a nontrivial vector $(\xi_k)_{k=1}^M$, then one may choose $g_m=\sum_{j=1}^M \xi_j(k_{j,m}^\lambda/C_m^\lambda)$ and

$$f_0(\mu,v)=\sum_{j=1}^{M}\xi_j\sum_{n=1}^{\infty}\frac{k_{j,n}^\lambda}{C_{j,n}^\lambda}e^{\rho_n\mu}\varphi_{n,\lambda}(v) \tag{46}$$

is an eigenfunction in $\mathbb{B}$ at the eigenvalue λ, provided

$$\|f_0\|_{\mathbb{B}}^2=\max_{0\leq\mu\leq 1}\sum_{n=1}^{\infty}\left|\sum_{j=1}^{M}\xi_j k_{j,n}^\lambda\right|^2 e^{2\mu\operatorname{Re}\rho_n}<\infty.$$

For $\lambda=0$ or $\arg(\lambda)=\pm(\pi/3)$ one has to employ the continuous analogue of (32).

4. The time-dependent transport equation

In this section we discuss the solution of the transport equation (1) for $f(.,.,t)\in\mathbb{B}$ under the boundary conditions (2), (3), and (12), assuming the solution at $t=0$ given. Let us first treat the case $k(v,v')=\delta(v-v')$, where all eigenfunctions have been computed explicitly. For $0<p<1$ we expand the initial density $f(\mu,v,0)$ as

$$f(\mu,v,0)=\sum_{s=-\infty}^{+\infty}\sum_{n=1}^{\infty}C_{n,s}\frac{1}{p^\mu}e^{2\pi i\mu s}Ai(\sigma_s v+a_n'), \tag{48}$$

where σ_s is given by (36) and

$$C_{n,s}=\int_0^1\int_0^\infty vp^\mu e^{-2\pi i\mu s}\overline{Ai(\sigma_s v+a_n')}f(\mu,v,0)\,dv\,d\mu\Big/\int_0^\infty v|Ai(\sigma_s v+a_n')|^2\,dv.$$

The cell population density at time t is then given by

$$f(\mu,v,t)=\sum_{s=-\infty}^{+\infty}\sum_{n=1}^{\infty}C_{n,s}e^{\lambda_{n,s}t}\frac{1}{p^\mu}e^{2\pi i\mu s}Ai(\sigma_s v+a_n'). \tag{49}$$

For $1\leq p\leq 2$ the situation is more complicated. For the density we first write

$$f(\mu,v,t)=\frac{1}{p^\mu}f_{\|}(v,t)+f_\perp(\mu,v,t), \tag{50}$$

where

$$\int_0^1 p^\mu f_\perp(\mu,v,t)\,d\mu=0. \tag{51}$$

Repeating the previous calculation we obtain

$$f_\perp(\mu, v, t) = \sum_{\substack{s=-\infty \\ s\neq 0}}^{+\infty} \sum_{n=1}^{\infty} C_{n,s}\, e^{\lambda_{n,s} t} \frac{1}{p^\mu} e^{2\pi i\mu s} Ai(\sigma_s v + a_n'),$$

where

$$C_{n,s} = \int_0^1 \int_0^\infty v p^\mu e^{-2\pi i \mu s} Ai(\sigma_s v + a_n') f_\perp(\mu, v, 0)\, dv\, d\mu \Big/ \int_0^\infty v |Ai(\sigma_s v + a_n')|^2\, dv.$$

For the "parallel" density one obtains the boundary value problem

$$\left.\begin{aligned} &\frac{\partial}{\partial t} f_{\|}(v, t) = D \frac{\partial^2}{\partial v^2} f_{\|}(v, t) - \ln\left(\frac{1}{p}\right) v f_{\|}(v, t) \\ &f_{\|}(v, 0) \textit{ given and } \int_0^\infty v |f_{\|}(v, t)|^2\, dv < \infty \\ &\frac{\partial}{\partial v} f_{\|}(v, t)|_{v=0} = 0 \end{aligned}\right\} \tag{52}$$

which for $p = 1$ reduces to the heat equation. For $p = 1$ standard Fourier transform techniques [12] lead to the solution

$$f_{\|}(v, t) = \int_0^\infty \cos(sv)\, e^{-s^2 D t} \hat{f}_{\|}(s)\, ds, \tag{53}$$

where $f_{\|}(v, 0) = \int_0^\infty \cos(sv) \hat{f}_{\|}(s)\, ds$; it is then advantageous mathematically to require $\int_0^\infty |f(v, t)|^2\, dv < \infty$, since one then has $\int_0^\infty |\hat{f}(s)|^2\, ds < \infty$. For $1 < p \leq 2$ we introduce $Ci_s(z)$ as the unique solution of the boundary value problem

$$Ci_s''(z) = -z Ci_s(z), \qquad Ci_s(s) = 1, \qquad Ci_s'(s) = 0,$$

where $s \in (0, \infty)$. In fact, in terms of Airy and associated Airy functions [11] we have

$$Ci_s(z) = \frac{Ai(-z) Bi'(-s) - Ai'(-z) Bi(-s)}{Ai(-s) Bi'(-s) - Ai'(-s) Bi(-s)}.$$

For $Q = -\ln(1/p) > 0$ we have

$$f_{\|}(v, t) = \int_0^\infty Ci_s\left(\left(\frac{Q}{D}\right)^{1/3} v + s\right) \exp(-D^{1/3} Q^{2/3} s t) \hat{f}_{\|}(s)\, ds, \tag{54}$$

where $f_{\|}(v, 0) = \int_0^\infty Ci_s((Q/D)^{1/3} v + s) \hat{f}_{\|}(s)\, ds$. The complete cell density $f(\mu, v, t)$ then follows using (50).

For more complicated reproduction rules it is not straightforward to solve the time-dependent transport equation. In the case when the transport operator

$$(Ah)(\mu, v) = v\frac{\partial h}{\partial \mu} - D\frac{\partial^2 h}{\partial v^2} \tag{55}$$

defined on a suitable domain of functions $h \in \mathbb{B}$ satisfying $(\partial h/\partial v)(v=0)=0$ as well as condition (12) generates a strongly continuous semigroup on $\mathbb{B}$, written e^{tA} (cf. [13] for semigroup theory), the unique solution may be written formally as

$$f(\mu, v; t) = [e^{tA}f(.,.,0)](\mu, v), f(.,.,0) \in \mathbb{B}. \tag{56}$$

For the "perfect memory" rule this procedure can be implemented without modification for $0<p<1$. For $1 \leq p \leq 2$ we must replace $\mathbb{B}$ by

$$\mathbb{B}_{0,p} \oplus Q_p[\mathbb{B}] \quad \text{where } (Q_p h)(\mu, v) = h(\mu, v) - \int_0^1 p^\nu h(\nu, v)\, d\nu$$

and $\mathbb{B}_{0,p} = L_2(\mathbb{R}_+; d\mu_p(v))$ for a suitable measure $d\mu_p(v)$. If A has a compact resolvent and its eigenfunctions and generalized eigenfunctions form a complete set (in the sense that the span is a dense linear subspace of $\mathbb{B}$), one can express the formal solution (56) in terms of a series involving eigenfunctions of A. A more complicated situation arises if either A has a compact resolvent but its eigenfunctions do not form a complete set, or part of the spectrum of A is continuous. The latter occurs, for instance, for perfect memory reproduction with $1 \leq p \leq 2$. In the latter case one may still solve the time-dependent transport problem explicitly if one has an explicit representation of A, possibly on a modified solution space, as exemplified for "perfect memory" and $1 \leq p \leq 2$.

5. Discussion

For the simple reproduction rule (11) we have given the complete solution of the time-dependent transport equation. For more complicated rules our result is far from complete, since we did not solve completely three basic problems: (i) existence and uniqueness of the solution which requires a proof that the operator A in (55) generates a strongly continuous semigroup, either on $\mathbb{B}$ or on a modified Banach solution space, (ii) a complete determination of the spectrum of A, i.e. eigenvalues, continuous and residual spectrum, and (iii) a spectral representation of A which allows for the solution to be written down by series and/or integral expansion. The bulk of time-dependent transport theory (cf. [5-8]) centers around the first and second problems and usually does not lead to closed form solutions. The latter is almost solely restricted to very simple problems and in most cases to periodic boundary conditions (i.e. condition (11) for $p=1$), as exemplified by recent work of Protopopescu [9]. Time-dependent Fokker-Planck equations are almost virgin territory (cf. [14] for one such problem, having $v \in \mathbb{R}$ and different boundary conditions, for which (i) could be treated).

From the perfect memory example it is easily seen that the spectrum of A, $\sigma(A)$, is contained in the open left half-plane if $0<p<1$. At the same time the solution decays in $\mathbb{B}$-norm at least as fast as e^{-rt} where $(-r) = \sup\{\operatorname{Re}\lambda \mid \lambda \in \sigma(A)\} < 0$. For $p=1$ the solution is bounded as $t \to +\infty$, while for

$1 < p \leq 2$ the solution may increase exponentially in time if one of the discrete eigenvalues belongs to the right half-plane. This is to be expected as p represents the average number of viable daughters per mitosis. In neutron transport theory the corresponding quantity, c, is the average number of secondary neutrons per collision and, in fact, a similar phenomenon occurs.

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References

1. Rotenberg, M.: Transport theory for growing cell populations. J. Theor. Biol. **103**, 181 (1983)
2. Coddington, E. A., Levinson, N.: Theory of ordinary differential equations. New York: McGraw-Hill 1955
3. Hille, E.: Lectures on ordinary differential equations. London: Addison-Wesley 1969
4. Lebowitz, J. L., Rubinow, S. I.: A theory for the age and generation time distribution of a microbial population. J. Math. Biol. **1**, 17 (1974)
5. Larsen, E. W., Zweifel, P. F.: On the spectrum of the linear transport operator. J. Math. Phys. **15**, 1987 (1974)
6. Palczewski, A.: Spectral properties of the space nonhomogeneous linearized Boltzmann operator. Transp. Theor. Stat. Phys. **13**, 409 (1984)
7. Beals, R., Protopopescu, V.: Abstract time-dependent transport equation. J. Math. Anal. Appl., to appear
8. Greenberg, W., van der Mee, C. V. M., Protopopescu, V.: Boundary value problems in abstract kinetic theory. Basel: Birkhäuser, in preparation, cf. Chaps. 12–14
9. Protopopescu, V.: On the spectral decomposition of the transport operator with anisotropic scattering and periodic boundary conditions. Transp. Theor. Stat. Phys. **14**, 103 (1985)
10. Case, K. M., Zweifel, P. F.: Linear transport theory. Reading (Mass.): Addison-Wesley 1967
11. Abramowitz, M., Stegun, I. A.: Handbook of mathematical functions. New York: Dover 1964
12. Weinberger, H. F.: Partial differential equations. Waltham (Mass.): Blaisdell 1965
13. Kato, T.: Perturbation theory for linear operators. Heidelberg: Springer 1966
14. Beals, R., Protopopescu, V.: Half-range completeness for the Fokker-Planck equation. J. Stat. Phys. **32**, 565 (1983)

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