

Long Time Behavior of Solution to Equal Mitosis PDE

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Abstract: In this work, we are interested in the long time behavior of a solution to equal mitosis partial differential equation with positive and periodic coefficients. First, we prove the existence and uniqueness of solution of Floquet eigenvalue and its adjoint eigenvalue problem to the equal mitosis equation by using the fixed point theorem in the suitable L^1 weighted space under general division rate hypotheses. Let us recall that the Floquet exponent measures the growth rates of the population and understanding an eigenfunction is crucial for proving the long run behavior of the Cauchy problem. Then we apply the generalized relative entropy method to derive such long time asymptotic behavior of the population density.

Keywords: Equal Mitosis Equation, Floquet Theory, Entropy Method

1. Introduction

The first stage in modeling population dynamics is to determine the important variables that allow a population to be divided into homogeneous subgroups. This is used to explain how various groups interact with one another. Size is one of the most natural and important parameters for structuring a population. Equal mitosis concept is utilized in population

dynamics to explain how cell population grows through cell division. To model the evolution of the population over time, one uses a partial differential equations [7].

In this paper, we are interested in equal mitosis partial differential equation with positive and periodic coefficients, which provides the model of a population cells in which cells of size x split into two equal pieces of size $\frac{x}{2}$. It is governed by the equation that follows, for $t, x \geq 0$,

$$\begin{cases} \frac{\partial}{\partial t} n(t, x) + \frac{\partial}{\partial x} n(t, x) + K(t, x)n(t, x) = 4K(t, 2x)n(t, 2x), \\ n(t, x = 0) = 0, \quad t > 0 \\ n(t = 0, x) = n^0(x), \quad x \geq 0 \end{cases} \quad (1)$$

where $n(t, x)$ represents the population density of cells of size x at time t and a division rate K satisfies

1. K is T -periodic,
2. $0 < K \in W^{1,\infty}$,
3. and

$$1 < \inf_{t \in (0, T)} \int_0^\infty K(., x) e^{-\int_0^x K(., -x+y, y) dy} dx,$$

and

$$\sup_{t \in (0, T)} \int_0^\infty K(., x) e^{-\int_0^x K(., -x+y, y) dy} dx < \infty.$$

Time dependence between this equation's coefficients is introduced for a number of reasons. Representing seasonality is a popular justification. Another is in cancer treatments like resonance and chrono-therapy, which are based on modeling circadian rhythms, the assumption of time periodic dependency of the division rate is motivated by the need to model cell division [2].

The long run behavior of this equation is strongly related to the existence of distribution of steady size. In most circumstances, the solutions behave asymptotically like the steady size distribution. Since the pioneering work in [5], numerous authors have used various approach to demonstrate the property known as asynchronous exponential growth [17]. It has been proved in the case of equal mitosis by means

of spectral semigroups [1, 5, 14] or general relative entropy approach [4, 13]. The technique of general relative entropy is a sophisticated and powerful method to derive the convergence to the Perron eigenfunction [15]. This technique was just expanded to the growth-fragmentation equation's measure solutions with a smooth fragmentation kernel [4], but this isn't applicable to the singular case of the mitosis kernel. The equation (1) can be expressed as evolution equation

$$\begin{cases} \frac{\partial}{\partial t} n = An \\ n(0, x) = n^0(x) \end{cases}$$

by using the operator

$$(An(., x))(t) = -\frac{\partial}{\partial x} n(t, x) - K(t, x)n(t, x) + 4K(t, 2x)n(t, 2x)$$

defined on the space $\mathcal{D}'((0, \infty) \times (0, \infty))$. We notice that this operator is T -periodic since K is assumed to be T -periodic. With a T -periodic operator A , this enables us to solve the linear differential equation on a Banach space using

the Floquet theory (see [9]).

This work's primary result is the existence and uniqueness of $(\lambda_{\text{per}}, N, \phi)$ of the related Floquet eigenvalue problem of the equation (1) which is provided by, for all $t, x \geq 0$,

$$\begin{cases} \frac{\partial}{\partial t} N(t, x) + \frac{\partial}{\partial x} N(t, x) + (\lambda_{\text{per}} + K(t, x))N(t, x) = 4K(t, 2x)N(t, 2x) \\ N(t, x = 0) = 0 \\ N(t, x) > 0, T\text{-periodic}, \int_0^T \int_0^\infty N(t, x) dx dt = 1 \end{cases} \quad (2)$$

Furthermore, its adjoint eigenvalue problem which is provided by

$$\begin{cases} -\frac{\partial}{\partial t} \phi(t, x) - \frac{\partial}{\partial x} \phi(t, x) + (\lambda_{\text{per}} + K(t, x))\phi(t, x) = 2K(t, x)\phi(t, \frac{x}{2}) \\ \phi(t, x) > 0, T\text{-periodic}, \int_0^\infty N(t, x)\phi(t, x) dx = 1. \end{cases} \quad (3)$$

Theorem 1.1. With the assumptions on K ; there is a unique $\lambda_{\text{per}} > 0$ and $N, \phi \in C(\mathbb{R}_+, L^1(\mathbb{R}_+; \phi(., x)dx))$ of the Floquet eigenvalue problem (2) and its adjoint eigenvalue problem (3).

Additionally, the entropy technique provides the following long run asymptotic behavior.

Theorem 1.2. Under the assumptions on K and assume that $n^0 \in L^1(\mathbb{R}_+, \phi(0, x)dx)$. Then one has

$$\int_0^\infty |n(t, x)e^{-\lambda_{\text{per}} t} - \rho N(t, x)| \phi(t, x) dx \xrightarrow{t \rightarrow \infty} 0$$

where $\rho = \int_0^\infty n^0(x)\phi(0, x)dx$.

2. Eigenvalue Problem

This section will demonstrate Theorem 1.1, which follows from the Floquet theory described in [9] and the following theorem.

Theorem 2.1. Let $\mu > 0$. Then there is a unique solution $n \in C(\mathbb{R}_+, L^1(\mathbb{R}_+; \phi(., x)dx))$ to the equation

$$\begin{cases} \frac{\partial}{\partial t} n(t, x) + \frac{\partial}{\partial x} n(t, x) + (\mu + K(t, x))n(t, x) = 4K(t, 2x)n(t, 2x) \\ n(t, x = 0) = 0 \\ n(t = 0, x) = n^0(x) \in L^1(\mathbb{R}_+; \phi(0, x)dx). \end{cases}$$

Proof First, let $X = C([0, T], L^1(\mathbb{R}_+; dx))$ be a Banach space with the norm

$$\|n\|_X = \sup_{t \in [0, T]} \|n(t, .)\|_{L^1(\mathbb{R}_+)}.$$

Using the Banach Fixed Point theorem, we will demonstrate that $n(t, x)$ is a fixed point of a contraction operator. This is

accomplished by defining the operator U as follows:

$$\begin{aligned} U : X &\rightarrow X \\ m &\mapsto n = U(m) \end{aligned}$$

where n is a solution of the following partial differential equation

$$\begin{cases} \frac{\partial}{\partial t} n(t, x) + \frac{\partial}{\partial x} n(t, x) + (\mu + K(t, x))n(t, x) = 4K(t, 2x)m(t, 2x) \\ n(t, x = 0) = 0, \\ n(t = 0, x) = n^0(x). \end{cases}$$

Let $m_1, m_2 \in X$ and $n_i = U(m_i), i = 1, 2$. Consequently, the difference $n = n_1 - n_2$ satisfies

$$\begin{cases} \frac{\partial}{\partial t} n(t, x) + \frac{\partial}{\partial x} n(t, x) + (\mu + K(t, x))n(t, x) = 4K(t, 2x)m(t, 2x) \\ n(t, x = 0) = 0 \\ n(t = 0, x) = 0 \end{cases}$$

with $m = m_1 - m_2$. The characteristics technique provides for $x < t$,

$$n(t, x) = \int_0^x 4K(t - x + y, 2y)m(t - x + y, 2y) \times e^{-\int_y^x (\mu + K)(t - x + y', y') dy'} dy.$$

As a consequence,

$$\|n(t, \cdot)\|_{L^1(\mathbb{R}_+)} \leq \int_0^t \left| \int_0^x 4K(t - x + y, 2y)m(t - x + y, 2y) \times e^{-\int_y^x (\mu + K)(t - x + y', y') dy'} dy \right| dx \leq tM \|m(t, \cdot)\|_{L^1(\mathbb{R}_+)}.$$

Hence,

$$\begin{aligned} \|n\|_X &= \sup_{t \in [0, T]} \|n(t, \cdot)\|_{L^1(\mathbb{R}_+)} \\ &\leq \sup_{t \in [0, T]} tM \|m(t, \cdot)\|_{L^1(\mathbb{R}_+)} \\ &= TM \|m\|_X. \end{aligned}$$

In other words, $U : X \rightarrow X$. After selecting T such that $TM \leq \frac{1}{2}$, we have

$$\|U(m_1) - U(m_2)\|_X \leq \frac{1}{2} \|m_1 - m_2\|_X.$$

$$\begin{cases} \frac{\partial}{\partial t} \tilde{n}_k(t, x) + \frac{\partial}{\partial x} \tilde{n}_k(t, x) + (\mu + K(t, x))\tilde{n}_k(t, x) = 4K(t, 2x)\tilde{n}_k(t, 2x) \\ \tilde{n}_k(t, x = 0) = 0. \end{cases}$$

Let $\tilde{n} = \tilde{n}_k - \tilde{n}_l$, then

$$\begin{cases} \frac{\partial}{\partial t} (\tilde{n}(t, x)\phi(t, x)) + \frac{\partial}{\partial x} (\tilde{n}(t, x)\phi(t, x)) + (\mu + K(t, x))\tilde{n}(t, x)\phi(t, x) = 4\phi(t, x)K(t, 2x)\tilde{n}(t, 2x) - 2\phi(t, \frac{x}{2})K(t, x)\tilde{n}(t, x) \\ \tilde{n}(t, x = 0)\phi(0, x) = 0. \end{cases}$$

Additionally, it holds that

$$\begin{cases} \frac{\partial}{\partial t} (|\tilde{n}(t, x)|\phi(t, x)) + \frac{\partial}{\partial x} (|\tilde{n}(t, x)|\phi(t, x)) + (\mu + K(t, x))|\tilde{n}(t, x)|\phi(t, x) \leq 4\phi(t, x)K(t, 2x)|\tilde{n}(t, 2x)| \\ \quad - 2\phi(t, \frac{x}{2})K(t, x)|\tilde{n}(t, x)| \\ |\tilde{n}(t, x = 0)|\phi(0, x) = 0. \end{cases}$$

This demonstrates the existence of the fixed point by indicating that U is contraction in the Banach space X . We can repeat this process on intervals $[T, 2T], [2T, 3T], \dots$. Such a solution can be constructed in $C(\mathbb{R}_+, L^1(\mathbb{R}_+; dx))$. It then completes the proof using the density argument. Let us take $n^0 \in L^1(\mathbb{R}_+; \phi(0, x)dx)$, $\exists n_k^0 \in L^1(\mathbb{R}_+; dx)$ that satisfies $n_k^0 \rightarrow n^0$ in $L^1(\mathbb{R}_+; \phi(0, x)dx)$ and $\tilde{n}_k$ be a solution of the partial differential equation that follows.

By integrating with respect to x , it yields

$$\frac{d}{dt} \int_0^\infty |\tilde{n}(t, x)| \phi(t, x) dx \leq 0.$$

It follows from this that

$$\int_0^\infty |\tilde{n}_k - \tilde{n}_l| \phi(t, x) dx \leq \int_0^\infty |n_k^0 - n_l^0| \phi(0, x) dx.$$

Therefore, $\tilde{n}_k$ is a Cauchy sequence in a Banach space $C(\mathbb{R}_+; L^1(\mathbb{R}_+; \phi(\cdot, x) dx))$. Thus, $\tilde{n}_k$ converges in the space to a solution in the distributional sense.

The existence and uniqueness of the solution to the Floquet eigenvalue and its adjoint may now be demonstrated. Theorem

1.1 can be restated as follows.

Theorem 2.2. With the assumptions on K ; there is a unique $\lambda_{\text{per}} > 0$ and $N, \phi \in C(\mathbb{R}_+; L^1(\mathbb{R}_+; \phi(\cdot, x) dx))$ of the Floquet eigenvalue problem (2) and its adjoint eigenvalue problem (3).

Proof Let $\mu = \lambda_{\text{per}} > 0$. Then by Theorem 2.1, there exists a unique solution $N(t, x) \in C(\mathbb{R}_+; L^1(\mathbb{R}_+; \phi(\cdot, x) dx))$ satisfying

$$\frac{\partial}{\partial t} N(t, x) + \frac{\partial}{\partial x} N(t, x) + (\lambda_{\text{per}} + K(t, x)) N(t, x) = 4K(t, 2x) N(t, 2x).$$

Similarly, its adjoint is provided by

$$-\frac{\partial}{\partial t} \phi(t, x) - \frac{\partial}{\partial x} \phi(t, x) + (\lambda_{\text{per}} + K(t, x)) \phi(t, x) = 2K(t, x) \phi(t, \frac{x}{2})$$

where $\phi(t, x) \in C(\mathbb{R}_+; L^1(\mathbb{R}_+; \phi(\cdot, x) dx))$. Furthermore, since K is assumed to T -periodic, the operator U described in Theorem 2.1 is T -periodic and strictly positive. The Arzela-Ascoli theorem shows that the operator U is compact because $\sup \{ \|U(n)\|_X; \|n\|_X \leq 1 \}$ is uniformly bounded

and equicontinuous. The spectral radius of U , $r(\mu) = 1$, and up to renormalization N, ϕ are unique according to Corollary 1.11 and Corollary 1.14 in [9] with $\mu = \lambda_{\text{per}}$. Finding μ so that $r(\mu) = 1$ completes the proof. Because r is a decreasing function that vanishes at infinity and

$$r(0) \geq \inf_{t \in (0, T)} \int_0^\infty K(\cdot, x) e^{-\int_0^x K(\cdot, -x+y, y) dy} dx > 1.$$

Consequently, $r(\lambda_{\text{per}}) = 1$ for a unique λ_{per} .

3. Long Time Behavior Using Entropy Method

This section uses the generalized relative entropy approach [12, 13, 15] to demonstrate the long-term asymptotic decay of the equal mitosis equation solution.

Theorem 3.1. With the assumptions on K and for all convex functions H and for all $t > 0$, one has

$$\frac{d}{dt} \int_0^\infty \phi(t, x) N(t, x) H\left(\frac{\tilde{n}(t, x)}{N(t, x)}\right) dx = -D_H(\tilde{n})(t) \leq 0$$

where $\tilde{n}(t, x) = n(t, x) e^{-\lambda_{\text{per}} t}$ and

$$\begin{aligned} D_H(\tilde{n})(t) &= 4 \int_0^\infty K(t, 2x) \phi(t, x) N(t, 2x) \\ &\quad \times \left[H\left(\frac{\tilde{n}(t, 2x)}{N(t, 2x)}\right) - H\left(\frac{\tilde{n}(t, x)}{N(t, x)}\right) - H'\left(\frac{\tilde{n}(t, x)}{N(t, x)}\right) \left(\frac{\tilde{n}(t, 2x)}{N(t, 2x)} - \frac{\tilde{n}(t, x)}{N(t, x)}\right) \right] dx. \end{aligned}$$

Proof The equations (1), (2) and (3) give

$$\frac{\partial}{\partial t} \left(\frac{\tilde{n}(t, x)}{N(t, x)} \right) + \frac{\partial}{\partial x} \left(\frac{\tilde{n}(t, x)}{N(t, x)} \right) = 4K(t, 2x) \left(\frac{\tilde{n}(t, 2x)}{N(t, x)} - \frac{\tilde{n}(t, x) N(t, 2x)}{N^2(t, x)} \right)$$

and

$$\frac{\partial}{\partial t} H\left(\frac{\tilde{n}(t, x)}{N(t, x)}\right) + \frac{\partial}{\partial x} H\left(\frac{\tilde{n}(t, x)}{N(t, x)}\right) = 4K(t, 2x)H'\left(\frac{\tilde{n}(t, x)}{N(t, x)}\right)\left(\frac{\tilde{n}(t, 2x)}{N(t, x)} - \frac{\tilde{n}(t, x)N(t, 2x)}{N^2(t, x)}\right).$$

Consequently,

$$\begin{aligned} & \frac{\partial}{\partial t} \left[\phi(t, x)N(t, x)H\left(\frac{\tilde{n}(t, x)}{N(t, x)}\right) \right] + \frac{\partial}{\partial x} \left[\phi(t, x)N(t, x)H\left(\frac{\tilde{n}(t, x)}{N(t, x)}\right) \right] \\ &= N(t, x)H\left(\frac{\tilde{n}(t, x)}{N(t, x)}\right)\left(\frac{\partial}{\partial t}\phi(t, x) + \frac{\partial}{\partial x}\phi(t, x)\right) + \phi(t, x)H\left(\frac{\tilde{n}(t, x)}{N(t, x)}\right)\left(\frac{\partial}{\partial t}N(t, x) + \frac{\partial}{\partial x}N(t, x)\right) \\ & \quad + \phi(t, x)N(t, x)\left[\frac{\partial}{\partial t}H\left(\frac{\tilde{n}(t, x)}{N(t, x)}\right) + \frac{\partial}{\partial x}H\left(\frac{\tilde{n}(t, x)}{N(t, x)}\right)\right] \\ &= 4K(t, 2x)\phi(t, x)N(t, 2x)H\left(\frac{\tilde{n}(t, x)}{N(t, x)}\right) - 2K(t, x)\phi(t, \frac{x}{2})N(t, x)H\left(\frac{\tilde{n}(t, x)}{N(t, x)}\right) + 4K(t, 2x)N(t, 2x)\phi(t, x) \\ & \quad \times H'\left(\frac{\tilde{n}(t, x)}{N(t, x)}\right)\left(\frac{\tilde{n}(t, 2x)}{N(t, 2x)} - \frac{\tilde{n}(t, x)}{N(t, x)}\right). \end{aligned}$$

Integrating with respect to x implies that

$$\begin{aligned} & \frac{d}{dt} \int_0^\infty \phi(t, x)N(t, x)H\left(\frac{\tilde{n}(t, x)}{N(t, x)}\right)dx \\ &= 4 \int_0^\infty K(t, 2x)\phi(t, x)N(t, 2x)H\left(\frac{\tilde{n}(t, x)}{N(t, x)}\right)dx - 2 \int_0^\infty K(t, x)\phi(t, \frac{x}{2})N(t, x)H\left(\frac{\tilde{n}(t, x)}{N(t, x)}\right)dx \\ & \quad + 4 \int_0^\infty K(t, 2x)N(t, 2x)\phi(t, x) \times H'\left(\frac{\tilde{n}(t, x)}{N(t, x)}\right)\left(\frac{\tilde{n}(t, 2x)}{N(t, 2x)} - \frac{\tilde{n}(t, x)}{N(t, x)}\right)dx \\ &= -4 \int_0^\infty K(t, 2x)\phi(t, x)N(t, 2x)\left[H\left(\frac{\tilde{n}(t, 2x)}{N(t, 2x)}\right) - H\left(\frac{\tilde{n}(t, x)}{N(t, x)}\right) - H'\left(\frac{\tilde{n}(t, x)}{N(t, x)}\right)\left(\frac{\tilde{n}(t, 2x)}{N(t, 2x)} - \frac{\tilde{n}(t, x)}{N(t, x)}\right)\right]dx. \\ &= -D_H(\tilde{n})(t). \end{aligned}$$

Therefore, $-D_H(\tilde{n})(t)$ is nonpositive due to the convexity of H .

Theorem 1.2, which is rewritten as follows, can now be proved.

Theorem 3.2. With the assumptions on K and assume that $n^0 \in L^1(\mathbb{R}_+, \phi(0, x)dx)$, one has

$$\int_0^\infty |\tilde{n}(t, x) - \rho N(t, x)|\phi(t, x)dx \xrightarrow{t \rightarrow \infty} 0$$

where $\rho = \int_0^\infty n^0(x)\phi(0, x)dx$.

Proof Let $h(t, x) = \tilde{n}(t, x) - \rho N(t, x)$; it follows that h satisfies the partial differential equation that follows

$$\begin{cases} \frac{\partial}{\partial t} h(t, x) + \frac{\partial}{\partial x} h(t, x) + (\lambda_{\text{per}} + K(t, x))h(t, x) = 4K(t, 2x)h(t, 2x) \\ h(t, x = 0) = 0. \end{cases} \quad (4)$$

Moreover, it holds

$$\begin{aligned} & \frac{\partial}{\partial t} (|h(t, x)|\phi(t, x)) + \frac{\partial}{\partial x} (|h(t, x)|\phi(t, x)) \\ & \leq 4\phi(t, x)K(t, 2x)|h(t, 2x)| - 2\phi(t, \frac{x}{2})K(t, x)|h(t, x)|. \end{aligned}$$

Integrating with respect to x yields

$$\frac{d}{dt} \int_0^\infty |h(t, x)|\phi(t, x)dx \leq 0.$$

As a result, $\int_0^\infty |h(t, x)|\phi(t, x)dx$ is positive and decaying, convergent to some value $L \geq 0$. We still need to demonstrate that $L = 0$. Let's now define the sequence of functions $h_k(t, x) = h(t + k, x)$; it also satisfies (4). Then $h_k(t, x)$ is bounded in $L^1(\mathbb{R}_+; \phi(\cdot, x)dx)$. Thus, $h_k \rightharpoonup g$ weakly up to the subsequence. We can work on the entropy dissipation of $h(t, x)$, and the relative entropy condition for a convex function $H(s) = s^2$ provides

$$\int_0^\infty \int_0^\infty K(t, 2x)\phi(t, x)N(t, 2x) \times \left(\frac{h(t, x)}{N(t, x)} - \frac{h(t, 2x)}{N(t, 2x)} \right)^2 dx dt \leq C.$$

Hence, as $k \rightarrow \infty$,

$$\begin{aligned} & \int_0^\infty \int_0^\infty K(t, 2x)\phi(t, x)N(t, 2x) \times \left(\frac{h_k(t, x)}{N(t, x)} - \frac{h_k(t, 2x)}{N(t, 2x)} \right)^2 dx dt \\ &= \int_k^\infty \int_0^\infty K(t, 2x)\phi(t, x)N(t, 2x) \times \left(\frac{h(t, x)}{N(t, x)} - \frac{h(t, 2x)}{N(t, 2x)} \right)^2 dx dt \rightarrow 0. \end{aligned}$$

Taking the weak limit results in

$$\int_0^\infty \int_0^\infty K(t, 2x)\phi(t, x)N(t, 2x) \times \left(\frac{g(t, x)}{N(t, x)} - \frac{g(t, 2x)}{N(t, 2x)} \right)^2 dx dt = 0.$$

In other words, $\frac{g(t, x)}{N(t, x)} = \frac{g(t, 2x)}{N(t, 2x)}$ almost everywhere on the support of K . However, in the limits, the entropy dissipation for g/N goes to zero, thus we get

$$\frac{\partial}{\partial t} \left(\frac{g(t, x)}{N(t, x)} \right) + \frac{\partial}{\partial x} \left(\frac{g(t, x)}{N(t, x)} \right) = 0.$$

According to Lemma 4.5 in [15, p.100], $g(t, x) = \text{constant}$ and from the condition $\int_0^\infty g(t, x)\phi(t, x)dx = 0$ it follows that $g = 0$ and so we can conclude that $L = 0$.

4. Conclusion

In this work, we investigated the mathematical properties of the solution to the equal mitosis partial differential equation with the positive and periodic coefficients. The aim of this work was twofold. On one hand, we proved the existence and uniqueness of the associated eigenvalue problem and its adjoint eigenvalue problem for the periodic operator on Banach space. The Banach fixed point theorem on the suitable weighted Banach space L^1 under the general hypotheses on the growth rate K yields the unique λ_{per} , the Floquet exponent, which measures the growth rate of the population. On the other hand, the long run asymptotic exponential decay of the solution of the equal mitosis PDE has been established by using an elegant and powerful method: the generalized relative entropy method.

A possible extension of the present work is to apply the Floquet theory on Banach space to establish the proof of the well-posedness and the long-time behavior of the solution of evolution partial differential equations that govern more sophisticated models of mitosis [10].

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Abbreviations

PDE Partial Differential Equation

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Author Contributions

Meas Len is the sole author. The author read and approved the final manuscript.

Conflicts of Interest

The author declares no conflicts of interest.

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