Existence and global attractivity of positive ω -periodic solutions for discrete hematopoiesis models

(離散造血モデルにおける正のω周期解の存在性及び大域的吸収性)

Yan Yan

March 2020

Interdisciplinary Graduate School of Science and Engineering Shimane University

Acknowledgments

I would like to thank my supervisor Professor Jitsuro Sugie for his careful guidance and many useful discussions in the preparation of this thesis.

I would also like to thank Professor Daishi Kuroiwa, Professor Takeshi Wada and Professor Takumi Yamada for their critical reading of the manuscript and useful comments for improvement.

Moreover, I wish to express my sincere gratitude to Professor Hideaki Matsunaga of Osaka Prefecture University for his many grateful discussions in details and many pieces of invaluable advice.

Finally, I would like to express my thanks to seniors who have graduated and to juniors who study hard together now.

Contents

Acknowledgments Preface			iii 1
	1.1	First order nonlinear difference equation with time delays	5
	1.2	Continuation theorem of coincidence degree theory	6
	1.3	Schauder fixed point theorem	8
2	Existence of positive ω -periodic solutions		9
	2.1	Previous research and main result	9
	2.2	Parametric delay difference equation	17
	2.3	Proof of main result	21
	2.4	Examples	28
	2.5	The case that $0 < n \le 1$	34
3	Glo	Global asymptotic stability of a unique positive ω -periodic solution	
	3.1	Main result	37
	3.2	Upper and lower limit values on positive solutions	39
	3.3	Proof of main result	45
	3.4	On the condition of Theorem 3.1	51
	3.5	Examples	53
4	Global attractivity of a unique positive ω -periodic solution		61
	4.1	Main result	61
	4.2	Basic fact	62
	4.3	Equivalence transformation	66
	4.4	Proof of main result	66
\mathbf{R}	References		

Preface

As an important component of blood, blood cells are divided into three types: erythrocytes (red blood cells), leukocytes (white blood cells) and thrombocytes (platelets). They play a vital role in the human body. Erythrocytes are the most numerous of the blood cells. The primary function of erythrocytes is the transport of oxygen and carbon dioxide. Although leukocytes are generally larger than erythrocytes, they are fewest in number. Leukocytes are immune system cells who can defend the body against both infectious disease and foreign invaders. Thrombocytes are the smallest of the three types of blood cells. The principal function of platelets is that aggregate at the wound and formate blood cot, when the blood vessel wall is damaged, to prevent bleeding. It is well known that abnormality in the number of these three kinds of blood cells causes disease and leads to death.

Mature blood cells are produced in the bone marrow. They develop from hematop oietic stem cells that have the capacity to self-replicate and differentiate into other blood cells. These hematopoietic stem cells differentiate into myeloid progenitor cells and lymphoid progenitor cells as an intermediate stage in order to become various immature blood cells who will fully mature in the bone marrow. When the immature blood cells grow into mature blood cells and become functional, they will leave the bone marrow and enter into the blood circulation. In the whole production process of blood cells, hematopoietic stem cells, immature blood cells at various stages that they are proliferating and differentiating and mature blood cells that have just been completed are coexisted. All blood cells have inherent life spans. The life span of a blood cell will be terminated when it is normally phagocytized by macrophages of splenic and hepatic sinusoids, etc. as an aged blood cell. For the basic knowledge of the specific production process of blood cells, for example, see the book [4, Chap. 18].

The production process of blood cells is well-known as hematopoiesis process. In 1977, Mackey and Glass [18] proposed the hematopoiesis model

$$x'(t) = -a x(t) + \frac{bx(t-\tau)}{1+x^n(t-\tau)}$$

with n > 0, which describes the hematopoiesis process. Here, the coefficients a, band the delay τ are positive constants. Let

$$f(u) = \frac{u}{1+u^n} \quad \text{for } u \ge 0.$$

We can rewrite the above equation as

$$x'(t) = -a x(t) + bf(x(t-\tau)).$$

The function f is also called by the production function. It is well known that the periodic environmental changes due to seasonal variations have important influence on the dynamics of blood cell number. This impact can not be considered by autonomous differential equation with constant coefficients and constant delay. On the other words, the coefficients a, b and the delay τ should be assumed as periodic functions rather than constants. The second term with a time lag τ on the right-hand of the above model represents the production term in hematopoiesis process. In the clinical studies, it has been confirmed that the time for immature blood cells to become mature blood cells (time lag) is different depending on the type of blood cells. It can be said that a hematopoiesis model that only consider one production term is not accurate. Blood cells are in fact discrete entities, they work effectively one by one and are represented by the number contained in one microliter of blood. They are never continua. In that sense, a discrete model is more suitable than a continuous model to study the dynamics of the number of blood cells.

Taking the above reasons into account, this thesis concerns a discrete hematopoie-

sis model with periodic coefficients and multiple production terms dominated by different delays. We consider

$$\Delta x(k) = -a(k)x(k) + \sum_{i=1}^{m} b_i(k)f(x(k - \tau_i(k)))$$
(H)

with n > 1 and $m \in \mathbb{N}$, where $\Delta x(k) = x(k+1) - x(k)$, and $a : \mathbb{Z} \to (0,1)$, $b_i : \mathbb{Z} \to (0,\infty)$ and $\tau_i : \mathbb{Z} \to \mathbb{Z}^+ \stackrel{\text{def}}{=} \mathbb{N} \cup \{0\} (1 \le i \le m)$ are ω -periodic discrete functions with $\omega \in \mathbb{N}$. The function f is defined by $f(u) = u/(1+u^n)$ for $u \ge 0$. Specifically, we focus on the positive periodic solutions of (H). The purpose of this thesis is to investigate the existence and global asymptotic stability of positive periodic solution. This thesis is divided into four chapters.

In Chapter 1, theoretical knowledge needed for mathematical analysis is given. We first introduce a nonlinear delay difference equation with periodic coefficients. Some basic stability definitions of the zero solution and a positive periodic solution of this equation are presented. The continuation theorem of coincidence degree theory often used to explore the existence of positive periodic solutions is given afterwards. Finally, we present the well-known Schauder fixed point theorem.

In Chapter 2, we study existence of positive ω -periodic solutions of hematopoiesis model (*H*). A sufficient condition is established for the existence of positive ω periodic solutions. This sufficient condition is constructed by the relationship between coefficient a(k) and $\sum_{i=1}^{m} b_i(k)$ for $k = 1, 2, \ldots, \omega$. The existence region of positive ω -periodic solutions is also clarified. To achieve the above goals, the parametric delay difference equation

$$\Delta x(k) = -\lambda a(k)x(k) + \lambda \sum_{i=1}^{m} b_i(k)f(x(k-\tau_i(k)))$$
(L)

for each parameter $\lambda \in (0, 1)$ is considered. We estimate the upper bound and lower bound of any positive ω -periodic solution of (L) under a proper condition. In fact, the upper and lower bounds of positive ω -periodic solution of (L) ensure that we can make clear the region where positive ω -periodic solutions of (H) located in. In Chapter 3, a new theorem of the global asymptotic stability of a unique positive ω -periodic solution of (H) is presented by the mathematical analysis method. Obviously, this theorem shows that equation (H) has the exactly one positive ω periodic solution. It is undoubted that we get global asymptotic stability of the unique positive ω -periodic solution based on the existence result given in Chapter 2. In order to complete the investigation of this section, the information about the fluctuation range of general positive solutions of (H) is needed. By using this information, we estimate the difference between any positive solution and a certain positive ω -periodic solution. Thereby, the result that this certain positive ω -periodic solution is globally asymptotically stable can be obtained. That is to say, the unique positive ω -periodic solution is globally asymptotically stable.

In Chapter 4, we obtain a result of global attractivity of a unique positive ω periodic solution of (H) by Schauder fixed point theorem, which is different from
the method used to get the global asymptotic stability in Chapter 3. It is worth
mentioning that the global attractivity of the unique positive ω -periodic solution is
obtained only under the condition for the existence of positive ω -periodic solutions.
This means that as long as positive ω -periodic solutions exist (maybe only one
exists), then all positive periodic solutions are globally attractive. On the other
words, equation (H) has the unique positive ω -periodic solution which is globally
attractive.

Chapter 1

Preliminaries

1.1 First order nonlinear difference equation with time delays

Consider the general first order nonlinear delay difference equation

$$\Delta x(k) = -a(k)x(k) + \sum_{i=1}^{m} b_i(k)F(x(k-\tau_i(k)))$$
(1.1)

for $k \in \mathbb{Z}$ and $m \in \mathbb{N}$. Here, Δ is the forward difference operator defined by $\Delta x(k) = x(k+1) - x(k)$ for $k \in \mathbb{Z}$. In equation (1.1), $a: \mathbb{Z} \to (0, 1), b_i: \mathbb{Z} \to (0, \infty)$ and $\tau_i: \mathbb{Z} \to \mathbb{Z}^+ \stackrel{\text{def}}{=} \mathbb{N} \cup \{0\} (1 \le i \le m)$ are ω -periodic discrete functions with $\omega \in \mathbb{N}$. The function $F: \mathbb{R} \to \mathbb{R}$ is continuous.

Since τ_i $(1 \le i \le m)$ are ω -periodic, we can get the maximum value $\overline{\tau}$ of them; namely,

$$\overline{\tau} = \max_{1 \le i \le m} \left\{ \max_{1 \le k \le \omega} \tau_i(k) \right\} \in \mathbb{Z}^+.$$

For any given discrete initial function $\phi : [-\overline{\tau}, 0] \cap \mathbb{Z} \to \mathbb{R}$, we assume that there exists a unique solution of (1.1). We denote it by $x(\cdot; \phi)$. A solution $x(\cdot; \phi)$ of (1.1) is said to be the zero solution, if $x(k; \phi) \equiv 0$ for all $k \in \mathbb{Z}$. We assume F(0) = 0, then it is obvious that equation (1.1) has the zero solution. About the zero solution of (1.1), we introduce the definition of global attractivity.

Definition 1.1. The zero solution of (1.1) is said to be globally attractive, if for any initial function ϕ , the solution $x(\cdot; \phi)$ of (1.1) satisfies

$$\lim_{k\to\infty} x(k;\phi) = 0$$

Next, we consider the positive ω -periodic solution of (1.1). To distinguish a positive ω -periodic solution of (1.1) from other solutions, we denote it by $x_*(\cdot; \psi)$. Of course, the positive ω -periodic solution $x_*(\cdot; \psi)$ satisfies $x_*(k + \omega; \psi) = x_*(k; \psi)$ for all $k \in \mathbb{Z}$. Assume $x(\cdot, \phi)$ is an arbitrary solution of (1.1). With regards to a positive ω -periodic solution, we introduce the following important definitions.

Definition 1.2. A positive ω -periodic solution $x_*(\cdot; \psi)$ is said to be stable, if for any $\varepsilon > 0$, there exists a $\delta(\varepsilon) > 0$ such that $\|\phi - \psi\| < \delta$ implies

$$|x(k;\phi) - x_*(k;\psi))| < \varepsilon \quad for \ k \in \mathbb{N}$$

The norm $\|\cdot\|$ above denotes the maximum norm $\|\phi\| = \max_{-\overline{\tau} \le k \le 0} |\phi(k)|$.

Definition 1.3. A positive ω -periodic solution $x_*(\cdot; \psi)$ is said to be globally attractive, if any solution $x(\cdot; \phi)$ of (1.1) satisfies

$$\lim_{k \to \infty} \left| x(k;\phi) - x_*(k;\psi) \right| = 0.$$

Definition 1.4. A positive ω -periodic solution $x_*(\cdot; \psi)$ is said to be globally asymptotically stable, if it is stable and globally attractive.

1.2 Continuation theorem of coincidence degree theory

In the exploration of the existence of positive periodic solutions for difference equation in the form (1.1), there are many methods that can be utilized. The two common are Krasnoselskii's fixed point theorem and the fixed point theorem in cone for decreasing operator. However, in the case that F included in equation (1.1) is unimodal, the above two methods are not applicable. The unimodal function mentioned above means a function which has different monotonicity at left side and right side of the point where the only one peak of the function is obtained. A different approach which has less special restrictions and more wider range of use is urgently needed to solve such equation. The continuation theorem of coincidence degree theory [9] is one of efficient methods.

Definition 1.5. Let X be a Banach space and L: Dom $L \subset X \to X$ a linear mapping. The mapping L is said to be a Fredholm mapping of index zero if

- dim Ker $L = \operatorname{codim} \operatorname{Im} L < +\infty$,
- $\operatorname{Im} L$ is closed in X.

Throughout this thesis, we assume that X always represents a Banach space. It is well known that if L is a Fredholm mapping of index zero and $P, Q: X \to X$ are continuous projectors such that

 $\operatorname{Im} P = \operatorname{Ker} L;$ $\operatorname{Ker} Q = \operatorname{Im} L = \operatorname{Im}(I - Q),$

where I is the identity mapping from X to X, then the restriction L_P : Dom $L \cap$ Ker $P \to \text{Im } L$ is invertible. We denote the inverse of the restriction by K_P : Im $L \to$ Dom $L \cap \text{Ker } P$.

Definition 1.6. Let $N: X \to X$ be a continuous mapping and Ω an open bounded subset of X. The mapping N is said to be L-compact on $\overline{\Omega}$ if

- $QN(\overline{\Omega})$ is bounded,
- $K_P(I-Q)N:\overline{\Omega}\to X$ is compact.

Lemma 1.1. Let L be a Fredholm mapping of index zero and let N be L-compact on $\overline{\Omega}$. Suppose that

- for each parameter $\lambda \in (0, 1)$, every solution x of $Lx = \lambda Nx$ satisfies $x \notin \partial \Omega$;
- $QNx \neq 0$ for each $x \in \partial \Omega \cap \text{Ker } L$ and

$$\deg \{QN, \Omega \cap \operatorname{Ker} L, 0\} \neq 0.$$

Then the equation Lx = Nx has at least one solution staying in $X \cap \overline{\Omega}$.

Remark 1.1. A significant advantage of continuation theorem of coincidence degree theory is that the existence range of positive periodic solutions can be evaluated.

1.3 Schauder fixed point theorem

In this section, we introduce the well known Schauder fixed point theorem [2].

Definition 1.7. A subset U of Banach space Ω is said to be convex, if for all $\lambda \in [0, 1], x \in U$ and $y \in U$, the segment $\lambda x + (1 - \lambda)y$ also belongs to U.

For more details of a convex set, we refer to [22].

Definition 1.8. A subset U of Banach space Ω is said to be relatively compact, if any sequence in U has a convergent subsequence in Ω .

Theorem A. (Schauder fixed-point theorem). Let U be a closed convex subset of Banach space Ω . Suppose T is a mapping such that T(U) is a subset of U. If T is continuous and T(U) is relatively compact, then T has a fixed point in U.

Chapter 2

Existence of positive ω -periodic solutions

2.1 Previous research and main result

To express the hematopoiesis process, the first order nonlinear delay differential equation

$$x'(t) = -a x(t) + \frac{bx(t-\tau)}{1+x^n(t-\tau)}$$
(2.1)

with n > 0 was proposed by Mackey and Glass [18] as a hematopoiesis model. Here, the coefficients a, b and the delay τ are positive constants. To be exact, the variable x is the density of mature blood cells in the blood circulation; the coefficient a is the rate of blood cells lost by the circulation; the second term of the right-hand is the influx of blood cells into the blood circulation from hematopoietic stem cells; the coefficient b is positive; the number τ is the time delay that immature cells made in the bone marrow are released into the circulating blood stream as mature cells. Let

$$f(u) = \frac{u}{1+u^n} \quad \text{for } u \ge 0.$$

Equation (2.1) can be rewritten as

$$x'(t) = -a x(t) + bf(x(t - \tau)).$$

This model is composed with an extinction term and a production term. The function f in the production term is called as production function of model (2.1). It is a unimodal function who increases monotonically at the beginning and then decreases monotonically. Hence, it has only one peak. The extensive research of (2.1) can be referred to [3, 10–12, 15, 21, 24, 25, 30].

Although the fact that blood cells are discrete entities, they are usually treated as a continuum because of their enormous number. Hence, a hematopoiesis model is usually governed by a differential equation in many studies. However, blood cells play a role one by one, and they are represented by the number contained in one microliter of blood. They are never continua. In that sense, a discrete hematopoiesis model is more suitable than a continuous one to investigate the dynamics of the blood cells number. Moreover, from the perspective of continuously obtaining historical data of the blood cell count in actual measurement work, the fact that discrete hematopoiesis model are superior to continuous hematopoiesis model can also be confirmed. Why can we say something like that? In fact, to solve differential equation (2.1) using the method of steps (or step by step method), we need an initial function ϕ defined on $[-\tau, 0]$ that is continuous and satisfies the property that

$$\phi(s) \ge 0$$
 for $-\tau \le s \le 0$ and $\phi(0) > 0$.

For a given initial function ϕ , let

$$g_1(t) = bf(\phi(t-\tau))$$
 for $0 \le t \le \tau$.

Then, the solution x of (2.1) with the initial condition that $x(t) = \phi(t)$ for $-\tau \le t \le 0$ satisfies the nonhomogeneous linear differential equation

$$x' = -ax + g_1(t)$$

for $0 \le t \le \tau$. It is easy to find this solution. Let ψ be this solution and let

$$g_2(t) = bf(\psi(t-\tau)) \quad \text{for } \tau \le t \le 2\tau.$$

Then, the solution x of (2.1) with the initial condition that $x(t) = \phi(t)$ for $-\tau \le t \le 0$ satisfies the nonhomogeneous linear differential equation

$$x' = -ax + g_2(t)$$

for $\tau \leq t \leq 2\tau$. By repeating this process, it is possible to obtain the solution x of (2.1) on the whole interval $[0, \infty)$. Equation (2.1) is a hematopoietic model, and the initial function ϕ corresponds to past data. As shown from the above consideration, it is important to know a continuous initial function ϕ . However, it is difficult to obtain such an initial function from the realistic side because it is impossible to continuously measure past data of the density of mature blood cells. For example, it is reported that red blood cells turn into mature cells from immature cells after 7 days of maturity (see [29, Sect. 1]). Let us assume that τ is 7 (days). In order to obtain continuous historical data, healthcare workers will have to measure the number of red blood cells at all the time of one week. Clearly, they cannot engage in such a vast measurement task. It is necessary to simplify the measurement work such as measuring the number of red blood cells at a fixed time every day (this work will be possible enough because the number of measurements is 8 times). In other words, instead of continuous initial functions, only the set

$$\left\{\phi(-7),\phi(-6),\phi(-5),\phi(-4),\phi(-3),\phi(-2),\phi(-1),\phi(0)\right\}$$

of eight initial data will be used to predict the density of mature blood cells. If we think like that, it can be said that the equation

$$x'(t) = -ax(t) + bf(x([t - \tau]))$$
(2.2)

is more appropriate than equation (2.1) as a hematopoietic model. Here, τ is a

natural number and the symbol $[(\cdot)]$ means the greatest integer not exceeding (\cdot) . In equation (2.2), the set of the initial data is

$$\left\{\phi(-\tau), \phi(1-\tau), \dots, \phi(-1), \phi(0)\right\}.$$
 (2.3)

Equation (2.2) becomes the first-order linear differential equation with constant coefficients,

$$x' = -ax + bf(\phi(-\tau)) \quad \text{for } 0 \le t < 1$$

because $[t - \tau] = -\tau$ if $0 \le t < 1$ and $x(-\tau) = \phi(-\tau)$. Hence, we have

$$x(t) = \phi(0)e^{-at} + \frac{b}{a}f(\phi(-\tau))(1 - e^{-at})$$

for $0 \le t < 1$. Let $c = 1 - e^{-a}$ and d = bc/a. Then

$$x(1) \stackrel{\text{def}}{=} \lim_{t \to 1-0} x(t) = (1-c)\phi(0) + df(\phi(-\tau)).$$

Similarly, equation (2.2) becomes

$$x' = -ax + bf(\phi(1-\tau)) \quad \text{for } 1 \le t < 2$$

and we get

$$x(t) = x(1)e^{-a(t-1)} + \frac{b}{a}f(\phi(1-\tau))(1-e^{-a(t-1)})$$

for $1 \le t < 2$. Hence, we have

$$x(2) \stackrel{\text{def}}{=} \lim_{t \to 2-0} x(t) = (1-c)x(1) + df(\phi(1-\tau)).$$

Repeat this calculation, we can obtain the data sets

$$\Big\{x(0), x(1), \dots, x(\tau - 1), x(\tau)\Big\},\\\Big\{x(\tau), x(\tau + 1), \dots, x(2\tau - 1), x(2\tau)\Big\},$$

and so on. Note that $\phi(0) = x(0)$. The following relationship holds between these data:

$$\Delta x(k) \stackrel{\text{def}}{=} x(k+1) - x(k) = -cx(k) + df(x(k-\tau))$$

with $k \in \mathbb{Z}^+ \stackrel{\text{def}}{=} \mathbb{N} \cup \{0\}$. For convenience, this relationship can be rewritten as the difference equation

$$\Delta x(k) = -ax(k) + bf(x(k-\tau)) \tag{2.4}$$

by letting c as a and d as b again. What should be noted here is that the coefficients a and b in equation (2.4) satisfy 0 < a < 1 and b > 0 because of the definitions c and d, respectively.

As mentioned above, using the set (2.3) of the initial data, we can uniquely determine the solution of equation (2.4). All data values are positive because the data imply the number of mature blood cells. Also, we can see that x(k) is also positive for all $k \in \mathbb{N}$ because the solution x of (2.4) satisfies the equality

$$x(k+1) = (1-a)x(k) + bf(x(k-\tau))$$
 for $k \in \mathbb{Z}^+$.

The studies of (2.4) can be refer to [31, 32].

It is unnatural to think that the environment remains constant. The seasons which periodically vary greatly affect the weather, temperature, food supply and sexual activity of organisms. It has been reported that the population density of organisms and the constituents inherent in organisms also change due to changes in various environments surrounding living organisms and behaviors of organisms (see [20]). Of course, blood cells which are important components inherent in organisms periodically influenced by periodic environmental variations due to seasonal changes (see [8, 17, 26]). Unfortunately, models (2.1) and (2.2) have ignored this important fact. The coefficients with actual biological significance should not be assumed to be constants. Based on this discrete perspective, many studies of the modified discrete hematopoiesis model

$$\Delta x(k) = -a(k) x(k) + b(k) f(x(k - \tau(k))), \qquad (2.5)$$

have appeared, for example, refer to [13, 19, 33] and the references cited therein. In equation (2.1), $a: \mathbb{Z} \to (0, 1), b: \mathbb{Z} \to (0, \infty)$ and $\tau: \mathbb{Z} \to \mathbb{Z}^+ \stackrel{\text{def}}{=} \mathbb{N} \cup \{0\}$ are ω -periodic discrete functions with $\omega \in \mathbb{N}$; namely,

$$a(k) = a(k+\omega), \quad b(k) = b(k+\omega) \text{ and } \tau(k) = \tau(k+\omega)$$

for all $k \in \mathbb{Z}$. In this model, periodic environmental changes are taken into account by making coefficients and time lag represented by periodic functions with the same period.

Jiang *et al.* [13] considered equation (2.1) and obtained a sufficient condition for the existence of positive ω -periodic solutions.

Theorem B. Assume that a, b and τ are ω -periodic. If

$$a(k) < b(k) \quad for \ k \in [0, \omega],$$

then equation (2.5) has at least one positive ω -periodic solution.

Blood cells are divided into three types: erythrocyte, leukocyte and thrombocyte. Among them, leukocytes are mainly composed of neutrophils, basophils, eosinophils, lymphocytes, and monocytes. It has confirmed that neutrophils mature in bone marrow in about 2 weeks and are released into the bloodstream after 2 days (see [23]) in clinical studies. Also, basophils differentiate and mature in the bone marrow during 7 days (see [7, 16]). These clinical results suggest that at least two types of leukocytes take different time to enter the bloodstream. Therefore, it is not accurate that assume all types of blood cells mature through the same maturation period. On the other words, a hematopoiesis model should be expressed by multiple production functions.

In this chapter, we take the above factor into account and consider a discrete hematopoiesis model with periodic coefficients and multiple production terms dominated by different delays,

$$\Delta x(k) = -a(k)x(k) + \sum_{i=1}^{m} b_i(k)f(x(k - \tau_i(k))).$$
(H)

Here, *m* is a natural number; $a: \mathbb{Z} \to (0, 1), b_i: \mathbb{Z} \to (0, \infty)$ and $\tau_i: \mathbb{Z} \to \mathbb{Z}^+ (1 \le i \le m)$ are ω -periodic discrete functions; namely,

$$a(k) = a(k+\omega), \quad b_i(k) = b_i(k+\omega) \quad \text{and} \quad \tau_i(k) = \tau_i(k+\omega)$$
 (2.6)

for all $k \in \mathbb{Z}$ and $i = 1, 2, \dots, m$. The function f is defined by $f(u) = u/(1 + u^n)$ for $u \ge 0$ and n > 1.

Remark 2.1. Note that in the Mackey and Glass model (2.1), the production function $f(u) = u/(1 + u^n)$ is defined for n > 0. However, it is monotonically increasing.when $0 < n \le 1$. This means that as blood cells increase, the rate of increase of blood cells also increases. Since it fails to apply the brakes to increase of blood cells, it seems not suitable as a mathematical model describing the hematopoiesis process. Hence, in our main result, we only dealt with the case that n > 1.

Because of the periodicity of τ_i $(1 \leq i \leq m)$, the maximum of them can be determined by

$$\overline{\tau} = \max_{1 \le i \le m} \left\{ \max_{1 \le k \le \omega} \tau_i(k) \right\} \in \mathbb{Z}^+.$$

Let S denote the space of positive discrete functions on $[-\overline{\tau}, 0] \cap \mathbb{Z}$ endowed with the maximum norm

$$||\phi|| = \max_{-\overline{\tau} \le s \le 0} |\phi(s)| \text{ for } \phi \in S.$$

For any $\phi \in S$, since 0 < a(k) < 1 for $k \in \mathbb{Z}$ and $f(u) \ge 0$ for $u \ge 0$, equation (H) has a unique positive solution $x(\cdot; \phi)$ satisfying the initial condition

$$x(k) = \phi(k) > 0 \quad \text{for } k \in [-\overline{\tau}, 0] \cap \mathbb{Z}.$$
(2.7)

Since equation (H) is a biological model, it is natural to assume that the initial function ϕ satisfies $\phi(k) > 0$ for $k \in [-\overline{\tau}, 0] \cap \mathbb{Z}$.

The purpose of this chapter is to give a sufficient condition for the existence of positive ω -periodic solutions of (H). To state our results simply, we denote the maximum value of $b_i(1), b_i(2), \ldots, b_i(\omega)$ by

$$\overline{b}_i = \max_{1 \le k \le \omega} b_i(k) \quad \text{for } 1 \le i \le m.$$

The main result is as follows:

Theorem 2.1. Suppose that (2.6) holds. If there exists a $\gamma > 1$ such that

$$\gamma a(k) < \sum_{i=1}^{m} b_i(k) \quad for \ k = 1, 2, \dots, \omega,$$
 (2.8)

then equation (H) with n > 1 has at least one positive ω -periodic solution located in the region [A, B], where

$$A \le \min\left\{\sqrt[n]{\gamma-1}, \ \frac{\gamma \underline{a}^{n-1} \sum_{i=1}^{m} \overline{b}_i}{\underline{a}^n + \left(\sum_{i=1}^{m} \overline{b}_i\right)^n}\right\} \quad and \quad B = \frac{1}{\underline{a}} \sum_{i=1}^{m} \overline{b}_i,$$

in which $\underline{a} = \min_{1 \le k \le \omega} a(k)$.

Note that the region [A, B] is not empty. In fact, since n > 1, we see that $f(u) = u/(1 + u^n) < 1$ for $u \ge 0$. Hence, it follows that $A \le \gamma f(B) < \gamma$. On the other hand, from (2.8) it turns out that

$$B = \frac{1}{\underline{a}} \sum_{i=1}^{m} \overline{b}_i \ge \frac{1}{a(k)} \sum_{i=1}^{m} \overline{b}_i \ge \frac{1}{a(k)} \sum_{i=1}^{m} b_i(k) > \gamma$$

for some $k \in [1, 2, \ldots, \omega]$.

Remark 2.2. In Theorem 2.1, we assume that the coefficients a, b_i and the time delays τ_i (i = 1, 2, ..., m) have the same period ω . However, this assumption is for the sake of convenience and is not essential. In the case that these periods are different, Theorem 2.1 holds for their least common multiple $\omega \in \mathbb{N}$. If any coefficient or time delay is a constant (that is, if there is no period), then we may regard its period as 1. **Remark 2.3.** Under the assumptions of Theorem 2.1, even if there are two or more positive ω -periodic solutions, they exist in the same range [A, B].

2.2 Parametric delay difference equation

Consider the parametric delay difference equation

$$\Delta x(k) = -\lambda a(k)x(k) + \lambda \sum_{i=1}^{m} \frac{b_i(k)x(k - \tau_i(k))}{1 + x^n(k - \tau_i(k))}$$
(2.9)

for each parameter $\lambda \in (0, 1)$. We give the following result:

Proposition 2.1. Suppose that (2.8) holds. Then every positive ω -periodic solution x of (2.9) with n > 1 satisfies that

$$A < x(k) < B \quad for \ k = 1, 2, \dots, \omega,$$

where A and B are constants given in Theorem 2.1.

Proof. Let x be any positive ω -periodic solution of (2.9) with the initial condition (2.7). For convenience, let

$$\overline{x} = \max_{1 \le k \le \omega} x(k)$$
 and $\underline{x} = \min_{1 \le k \le \omega} x(k)$.

Since b_i $(1 \le i \le m)$ and x are positive ω -periodic, we see that $0 < b_i(k) \le \overline{b}_i$ for all $k \in \mathbb{Z}$ and $\underline{x} \le x(k) \le \overline{x}$ for all $k \in \mathbb{Z}^+$. Equation (2.9) can be rewritten to

$$x(k+1) = (1 - \lambda a(k))x(k) + \lambda \sum_{i=1}^{m} \frac{b_i(k)x(k - \tau_i(k))}{1 + x^n(k - \tau_i(k))}.$$
 (2.10)

Hence, it follows from the periodicities of a, b_i and τ_i $(1 \le i \le m)$ that

$$\overline{x} = \max_{1 \le k \le \omega} \{x(k+1)\}$$
$$\leq \max_{1 \le k \le \omega} \{(1 - \lambda a(k))x(k)\} + \lambda \max_{1 \le k \le \omega} \left\{ \sum_{i=1}^{m} \frac{b_i(k)x(k - \tau_i(k))}{1 + x^n(k - \tau_i(k))} \right\}$$

$$\leq \max_{1 \leq k \leq \omega} \{(1 - \lambda a(k))\} \max_{1 \leq k \leq \omega} \{x(k)\} + \lambda \max_{1 \leq k \leq \omega} \left\{ \sum_{i=1}^{m} \frac{b_i(k)x(k - \tau_i(k))}{1 + x^n(k - \tau_i(k))} \right\}$$

$$\leq (1 - \lambda \underline{a})\overline{x} + \lambda \max_{1 \leq k \leq \omega} \left\{ \sum_{i=1}^{m} \frac{b_i(k)x(k - \tau_i(k))}{1 + x^n(k - \tau_i(k))} \right\},$$

where \underline{a} is a constant given in Theorem 1. Hence, we have

$$\overline{x} \le \frac{1}{\underline{a}} \max_{1 \le k \le \omega} \left\{ \sum_{i=1}^{m} \frac{b_i(k)x(k - \tau_i(k))}{1 + x^n(k - \tau_i(k))} \right\}.$$
(2.11)

Since $0 < \lambda < 1$ and 0 < a(k) < 1 for all $k \in \mathbb{Z}$, we see that $1 - \lambda a(k) > 0$ for $k \in \mathbb{Z}$. Multiply both sides of (2.10) by $\prod_{r=0}^{k} 1/(1 - \lambda a(r))$ to obtain

$$x(k+1)\prod_{r=0}^{k}\frac{1}{1-\lambda a(r)} - x(k)\prod_{r=0}^{k-1}\frac{1}{1-\lambda a(r)} = \lambda\sum_{i=1}^{m}\frac{b_i(k)x(k-\tau_i(k))}{1+x^n(k-\tau_i(k))}\prod_{r=0}^{k}\frac{1}{1-\lambda a(r)}.$$
(2.12)

Let k_1 be a natural number such that

$$\overline{\tau} \le k_1 \le \overline{\tau} + \omega - 1$$
 and $x(k_1) = \underline{x}$.

Summing both sides of (2.12) over k ranging from k_1 to $k_1 + \omega - 1$ and using $x(k_1 + \omega) = x(k_1) = \underline{x}$, we get

$$\underline{x}\prod_{r=0}^{k_1-1}\frac{1}{1-\lambda a(r)}\left(\prod_{r=k_1}^{k_1+\omega-1}\frac{1}{1-\lambda a(r)}-1\right) = \lambda\sum_{s=k_1}^{k_1+\omega-1}\left(\sum_{i=1}^m\frac{b_i(s)x(s-\tau_i(s))}{1+x^n(s-\tau_i(s))}\prod_{r=0}^s\frac{1}{1-\lambda a(r)}\right)$$

Since a is a positive ω -periodic function, we see that

$$\prod_{r=k_1}^{k_1+\omega-1} (1-\lambda a(r)) = \prod_{r=0}^{\omega-1} (1-\lambda a(r)).$$
(2.13)

.

Hence, we have

$$\underline{x} = \frac{\lambda \prod_{r=0}^{k_1 + \omega - 1} (1 - \lambda a(r))}{1 - \prod_{r=k_1}^{k_1 + \omega - 1} (1 - \lambda a(r))} \sum_{s=k_1}^{k_1 + \omega - 1} \left(\sum_{i=1}^m \frac{b_i(s)x(s - \tau_i(s))}{1 + x^n(s - \tau_i(s))} \prod_{r=0}^s \frac{1}{1 - \lambda a(r)} \right)$$

$$= \frac{\lambda \prod_{r=0}^{k_1+\omega-1} (1-\lambda a(r))}{1-\prod_{r=0}^{\omega-1} (1-\lambda a(r))} \sum_{s=k_1}^{k_1+\omega-1} \left(\sum_{i=1}^m \frac{b_i(s)x(s-\tau_i(s))}{1+x^n(s-\tau_i(s))} \prod_{r=0}^s \frac{1}{1-\lambda a(r)} \right)$$

$$= \frac{\lambda}{1-\prod_{r=0}^{\omega-1} (1-\lambda a(r))} \sum_{s=k_1}^{k_1+\omega-1} \left(\sum_{i=1}^m \frac{b_i(s)x(s-\tau_i(s))}{1+x^n(s-\tau_i(s))} \prod_{r=s+1}^{k_1+\omega-1} (1-\lambda a(r)) \right).$$

(2.14)

Note that we have not used the condition that n > 1 so far. Using (2.11) and (2.14), we will estimate the upper bound \overline{x} and the lower bound \underline{x} . Since n > 1, we see that

$$u < u^n < 1 + u^n \quad \text{for } u > 0.$$

Hence, it follows from (2.11) that

$$\overline{x} < \frac{1}{\underline{a}} \max_{1 \le k \le \omega} \left\{ \sum_{i=1}^{m} b_i(k) \right\} \le \frac{1}{\underline{a}} \sum_{i=1}^{m} \overline{b}_i = B.$$

Recall that the function f_n defined by $f_n(u) = u/(1+u^n)$ for $u \ge 0$ is a unimodal function. Since $\underline{x} \le x(k) \le \overline{x}$ for all $k \in \mathbb{Z}^+$, it turns out that

$$\frac{x(s-\tau_i(s))}{1+x^n(s-\tau_i(s))} \ge \min\left\{f_n(\underline{x}), f_n(\overline{x})\right\} \quad \text{for } s \ge \overline{\tau}.$$

Note that $k_1 \geq \overline{\tau}$. Then, by using (2.8), (2.13) and (2.14), we obtain

$$\begin{split} \underline{x} &\geq \frac{\lambda \min\left\{f_{n}(\underline{x}), f_{n}(\overline{x})\right\}}{1 - \prod_{r=0}^{\omega-1}(1 - \lambda a(r))} \sum_{s=k_{1}}^{k_{1}+\omega-1} \left(\sum_{i=1}^{m} b_{i}(s) \prod_{r=s+1}^{k_{1}+\omega-1} (1 - \lambda a(r))\right) \\ &> \frac{\lambda \min\left\{f_{n}(\underline{x}), f_{n}(\overline{x})\right\}}{1 - \prod_{r=0}^{\omega-1}(1 - \lambda a(r))} \sum_{s=k_{1}}^{k_{1}+\omega-1} \left(\gamma a(s) \prod_{r=s+1}^{k_{1}+\omega-1} (1 - \lambda a(r))\right) \\ &= \frac{\gamma \min\left\{f_{n}(\underline{x}), f_{n}(\overline{x})\right\}}{1 - \prod_{r=0}^{\omega-1}(1 - \lambda a(r))} \sum_{s=k_{1}}^{k_{1}+\omega-1} \left(\lambda a(s) \prod_{r=s+1}^{k_{1}+\omega-1} (1 - \lambda a(r))\right) \\ &= \frac{\gamma \min\left\{f_{n}(\underline{x}), f_{n}(\overline{x})\right\}}{1 - \prod_{r=0}^{\omega-1}(1 - \lambda a(r))} \sum_{s=k_{1}}^{k_{1}+\omega-1} \left(\left(1 - (1 - \lambda a(s))\right) \prod_{r=s+1}^{k_{1}+\omega-1} (1 - \lambda a(r))\right) \\ &= \frac{\gamma \min\left\{f_{n}(\underline{x}), f_{n}(\overline{x})\right\}}{1 - \prod_{r=0}^{\omega-1}(1 - \lambda a(r))} \sum_{s=k_{1}}^{k_{1}+\omega-1} \left(\prod_{r=s+1}^{k_{1}+\omega-1} (1 - \lambda a(r)) - \prod_{r=s}^{k_{1}+\omega-1} (1 - \lambda a(r))\right) \end{split}$$

$$= \frac{\gamma \min \left\{ f_n(\underline{x}), f_n(\overline{x}) \right\}}{1 - \prod_{r=0}^{\omega-1} (1 - \lambda a(r))} \left(\prod_{r=k_1+\omega}^{k_1+\omega-1} (1 - \lambda a(r)) - \prod_{r=k_1}^{k_1+\omega-1} (1 - \lambda a(r)) \right).$$

Since $\prod_{r=k_1+\omega}^{k_1+\omega-1}(1-\lambda a(r))$ can be regarded as 1, we can conclude that

$$\underline{x} > \gamma \min \left\{ f_n(\underline{x}), f_n(\overline{x}) \right\}.$$
(2.15)

Here, we divide the argument into two cases to be considered: (i) $f_n(\underline{x}) \leq f_n(\overline{x})$; (ii) $f_n(\underline{x}) > f_n(\overline{x})$.

Case (i): It follows from (2.15) that $\underline{x} > \gamma f_n(\underline{x})$; namely,

$$\underline{x} > \sqrt[n]{\gamma - 1}.$$

Case (ii): The function f_n has the only peak value at $1/\sqrt[n]{n-1}$, and f_n is monotone increasing on $[0, 1/\sqrt[n]{n-1})$ and monotone decreasing on $(1/\sqrt[n]{n-1}, \infty)$. Hence, we see that $\overline{x} > 1/\sqrt[n]{n-1}$. In fact, if $\overline{x} \leq 1/\sqrt[n]{n-1}$, then $f_n(\underline{x}) \leq f_n(\overline{x}) \leq$ $f_n(1/\sqrt[n]{n-1})$. This is a contradiction. Since $\overline{x} > 1/\sqrt[n]{n-1}$, it follows from (2.15) that

$$\underline{x} > \gamma f_n(\overline{x}) > \gamma f_n(B) = \frac{\gamma \underline{a}^{n-1} \sum_{i=1}^m \overline{b}_i}{\underline{a}^n + \left(\sum_{i=1}^m \overline{b}_i\right)^n}.$$

Thus, in both cases, we can estimate that

$$\underline{x} > \min\left\{\sqrt[n]{\gamma - 1}, \ \frac{\gamma \underline{a}^{n-1} \sum_{i=1}^{m} \overline{b}_i}{\underline{a}^n + \left(\sum_{i=1}^{m} \overline{b}_i\right)^n}\right\} \ge A.$$

Thus, every positive ω -periodic solution x of (2.9) satisfies

$$A < \underline{x} \le x(k) \le \overline{x} < B$$

for all $k \in \mathbb{Z}^+$. The proof is now complete.

20

2.3 Proof of main result

We will apply Proposition 2.1 and the continuation theorem introduced in Chapter 1 to prove Theorem 2.1.

Proof. To this end, we define a Banach space X by

$$X = \left\{ x \in C(\mathbb{Z}^+, \mathbb{R}) \colon x(k+\omega) = x(k) \right\}.$$

It is clear that X is endowed with the maximum norm $||x|| = \max_{1 \le k \le \omega} |x(k)|$. Also, we define two mappings L and N by

$$Lx = x(k+1) - x(k)$$

and

$$Nx = -a(k)x(k) + \sum_{i=1}^{m} \frac{b_i(k)x(k - \tau_i(k))}{1 + x^n(k - \tau_i(k))}.$$

If $x \in X$, then

$$Lx(k+\omega) = x(k+\omega+1) - x(k+\omega) = x(k+1) - x(k) = Lx(k)$$

for all $k \in \mathbb{Z}^+$. This means that $Lx \in X$. Let $x_1, x_2 \in X$ and $c_1, c_2 \in \mathbb{R}$. Then

$$L(c_1x_1 + c_2x_2) = (c_1x_1 + c_2x_2)(k+1) - (c_1x_1 + c_2x_2)(k)$$

= $c_1(x_1(k+1) - x_1(k)) + c_2(x_2(k+1) - x_2(k))$
= $c_1Lx_1(k) + c_2Lx_2(k).$

Hence, L is a linear mapping from X to X. Since a, b_i and τ_i $(1 \le i \le m)$ are positive ω -periodic, if $x \in X$, then

$$Nx(k+\omega) = -a(k+\omega)x(k+\omega) + \sum_{i=1}^{m} \frac{b_i(k+\omega)x(k+\omega-\tau_i(k+\omega))}{1+x^n(k+\omega-\tau_i(k+\omega))}$$

$$= -a(k)x(k) + \sum_{i=1}^{m} \frac{b_i(k)x(k+\omega-\tau_i(k))}{1+x^n(k+\omega-\tau_i(k))}$$
$$= -a(k)x(k) + \sum_{i=1}^{m} \frac{b_i(k)x(k-\tau_i(k))}{1+x^n(k-\tau_i(k))} = Nx(k)$$

for all $k \in \mathbb{Z}^+$. Hence, N is a continuous mapping from X to X.

From the definition of L it turns out that

$$\operatorname{Ker} L = \left\{ x \in X \colon x(k) \equiv c \in \mathbb{R} \right\}$$

and

$$\operatorname{Im} L = \left\{ x \in X \colon \sum_{k=1}^{\omega} x(k) = 0 \right\}.$$

In fact, if Lx(k) = 0 for all $k \in \mathbb{Z}^+$, then $x(k+1) \equiv x(k)$. Let $x \in X$. Then

$$\sum_{k=1}^{\omega} Lx(k) = x(\omega+1) - x(1) = 0.$$

It is clear that dim Ker $L = 1 = \text{codim Im } L < +\infty$ and Im L is closed in X. Hence, L is a Fredholm mapping of index zero.

Define $P: X \to X$ by

$$Px = \frac{1}{\omega} \sum_{k=1}^{\omega} x(k),$$

and let Q = P. Then P and Q are continuous projectors. For any $x \in X$,

$$Px(k+1) - Px(k) = \frac{1}{\omega} \sum_{k=1}^{\omega} x(k+1) - \frac{1}{\omega} \sum_{k=1}^{\omega} x(k)$$
$$= \frac{1}{\omega} \sum_{k=2}^{\omega+1} x(k) - \frac{1}{\omega} \sum_{k=1}^{\omega} x(k) = \frac{1}{\omega} (x(\omega+1) - x(1)) = 0$$

for all $k \in \mathbb{Z}^+$. Hence, $\operatorname{Im} P = \operatorname{Ker} L$. It is clear that $x \in \operatorname{Ker} Q \subset X$ if and only if

 $\sum_{k=1}^{\omega} x(k) = 0;$ namely, $x \in \operatorname{Im} L.$ For any $x \in \operatorname{Im} L,$

$$y(k) = x(k) - \frac{1}{\omega} \sum_{k=1}^{\omega} x(k) = x(k)$$

for all $k \in \mathbb{Z}^+$. Hence, $x = y \in \text{Im}(I - Q)$. Conversely, for any $y \in \text{Im}(I - Q)$, there exists an $x \in X$ such that

$$y(k) = x(k) - \frac{1}{\omega} \sum_{k=1}^{\omega} x(k)$$

for all $k \in \mathbb{Z}^+$. Hence, we have

$$\sum_{k=1}^{\omega} y(k) = \sum_{k=1}^{\omega} \left(x(k) - \frac{1}{\omega} \sum_{k=1}^{\omega} x(k) \right) = \sum_{k=1}^{\omega} x(k) - \frac{1}{\omega} \sum_{k=1}^{\omega} x(k) \sum_{k=1}^{\omega} 1$$
$$= \sum_{k=1}^{\omega} x(k) - \sum_{k=1}^{\omega} x(k) = 0.$$

This means that $y \in \text{Im } L$. Thus, we see that Ker Q = Im L = Im(I - Q).

From the relations have shown in the immediately preceding paragraph, the restriction L_P : Dom $L \cap \text{Ker } P \to \text{Im } L$ has the inverse K_P : Im $L \to \text{Dom } L \cap \text{Ker } P$. The inverse K_P is given by

$$K_P x = \sum_{s=0}^{k-1} x(s) - \frac{1}{\omega} \sum_{s=0}^{\omega-1} \sum_{r=0}^{s} x(r)$$

for $x \in \text{Im } L$. In fact, since

$$K_P x(k+\omega) - K_P x(k) = \sum_{s=0}^{k+\omega-1} x(s) - \frac{1}{\omega} \sum_{s=0}^{\omega-1} \sum_{r=0}^{s} x(r) - \sum_{s=0}^{k-1} x(s) + \frac{1}{\omega} \sum_{s=0}^{\omega-1} \sum_{r=0}^{s} x(r)$$
$$= \sum_{s=k}^{k+\omega-1} x(s) = \sum_{s=0}^{\omega-1} x(s) = 0$$

for all $k \in \mathbb{Z}^+$, it follows that $x \in \text{Im } L$ implies $K_P x \in \text{Dom } L$. It also turns out that

$$PK_P x = \frac{1}{\omega} \sum_{k=1}^{\omega} K_P x(k) = \frac{1}{\omega} \sum_{k=1}^{\omega} \left(\sum_{s=0}^{k-1} x(s) - \frac{1}{\omega} \sum_{s=0}^{\omega-1} \sum_{r=0}^{s} x(r) \right)$$
$$= \frac{1}{\omega} \left(\sum_{k=1}^{\omega} \sum_{s=0}^{k-1} x(s) - \frac{\omega}{\omega} \sum_{s=0}^{\omega-1} \sum_{r=0}^{s} x(r) \right) = \frac{1}{\omega} \left(\sum_{k=1}^{\omega} \sum_{s=0}^{k-1} x(s) - \sum_{k=1}^{\omega} \sum_{r=0}^{k-1} x(r) \right) = 0.$$

Hence, $x \in \text{Im } L$ implies $K_P x \in \text{Ker } P$. For any $x \in \text{Im } L$, we have

$$L_P K_P x = K_P x(k+1) - K_P x(k)$$

= $\sum_{s=0}^k x(s) - \frac{1}{\omega} \sum_{s=0}^{\omega-1} \sum_{r=0}^s x(r) - \sum_{s=0}^{k-1} x(s) + \frac{1}{\omega} \sum_{s=0}^{\omega-1} \sum_{r=0}^s x(r)$
= $x(k) = Ix.$

In addition, for any $x \in \text{Dom } L \cap \text{Ker } P$, we have

$$K_P L_P x = K_P (x(k+1) - x(k))$$

= $\sum_{s=0}^{k-1} (x(s+1) - x(s)) - \frac{1}{\omega} \sum_{s=0}^{\omega-1} \sum_{r=0}^{s} (x(r+1) - x(r))$
= $x(k) - x(0) - \frac{1}{\omega} \sum_{s=0}^{\omega-1} (x(s+1) - x(0)) = x(k) - \frac{1}{\omega} \sum_{s=1}^{\omega} x(s).$

Since $x \in \text{Ker } P = \text{Ker } Q = \text{Im } L$, we see that $\sum_{s=1}^{\omega} x(s) = 0$. Hence, $K_P L_P x = x(k) = Ix$. We therefore conclude that $K_P = L_P^{-1}$.

We next show the mapping N defined above is L-compact on $\overline{\Omega}$, where

$$\Omega = \left\{ x \in X \colon A < x(k) < B \right\}.$$

To this end, we will check that

- (a) $QN(\overline{\Omega})$ is bounded,
- (b) $K_P(I-Q)N : \overline{\Omega} \to X$ is compact.

By a straightforward calculation, we obtain

$$QNx = \frac{1}{\omega} \sum_{k=1}^{\omega} \left(-a(k)x(k) + \sum_{i=1}^{m} \frac{b_i(k)x(k-\tau_i(k))}{1+x^n(k-\tau_i(k))} \right)$$

and

$$K_{p}(I-Q)Nx = \sum_{s=0}^{k-1} \left(-a(s)x(s) + \sum_{i=1}^{m} \frac{b_{i}(s)x(s-\tau_{i}(s))}{1+x^{n}(s-\tau_{i}(s))} \right)$$
$$- \left(\frac{k}{\omega} - \frac{\omega+1}{2\omega}\right) \sum_{s=1}^{\omega} \left(-a(s)x(s) + \sum_{i=1}^{m} \frac{b_{i}(s)x(s-\tau_{i}(s))}{1+x^{n}(s-\tau_{i}(s))} \right)$$
$$- \frac{1}{\omega} \sum_{s=0}^{\omega-1} \sum_{r=0}^{s} \left(-a(r)x(r) + \sum_{i=1}^{m} \frac{b_{i}(r)x(r-\tau_{i}(r))}{1+x^{n}(r-\tau_{i}(r))} \right)$$

for $x \in X$.

Since

$$\sum_{k=1}^{\omega} \left(-a(k)x(k) + \sum_{i=1}^{m} \frac{b_i(k)x(k-\tau_i(k))}{1+x^n(k-\tau_i(k))} \right) < \sum_{k=1}^{\omega} \left(\sum_{i=1}^{m} b_i(k) \right) = \omega \sum_{i=1}^{m} \overline{b}_i$$

for $x \in \overline{\Omega}$, the mapping QN is bounded on $\overline{\Omega}$. Hence, the above sentence (a) is true.

To show that the sentence (b) is also true, from the definition of the compactness of mappings, we have only to prove that $K_P(I-Q)N(E)$ is relatively compact for any bounded subset $E \subset \overline{\Omega} \subset X$. As a matter of fact, we can even show that it is compact.

Since E is a subspace of a finite dimensional Banach space X, we see that E is closed. Hence, E is compact. Note that a metric space is compact if and only if it is sequentially compact. Hence, E is sequentially compact; namely, every infinite sequence in E contains a convergent subsequence $\{x_j\}_{j\in\mathbb{N}}$ whose limit x_* belongs to E. Let $y_* = K_P(I-Q)Nx_*$. Since $\lim_{j\to\infty} x_j = x_* \in E$, it turns out that

$$\lim_{j \to \infty} K_p(I-Q)Nx_j = \lim_{j \to \infty} \sum_{s=0}^{k-1} \left(-a(s)x_j(s) \right) + \lim_{j \to \infty} \sum_{s=0}^{k-1} \sum_{i=1}^m \frac{b_i(s)x_j(s-\tau_i(s))}{1+x_j^n(s-\tau_i(s))}$$

$$\begin{aligned} &-\left(\frac{k}{\omega}-\frac{\omega+1}{2\omega}\right)\lim_{j\to\infty}\sum_{s=1}^{\omega}\left(-a(s)x_{j}(s)\right)\\ &-\left(\frac{k}{\omega}-\frac{\omega+1}{2\omega}\right)\lim_{j\to\infty}\sum_{s=1}^{\omega}\sum_{i=1}^{m}\frac{b_{i}(s)x_{j}(s-\tau_{i}(s))}{1+x_{j}^{n}(s-\tau_{i}(s))}\\ &-\frac{1}{\omega}\lim_{j\to\infty}\sum_{s=0}^{\omega-1}\sum_{r=0}^{s}\left(-a(r)x_{j}(r)\right)\\ &-\frac{1}{\omega}\lim_{j\to\infty}\sum_{s=0}^{\omega-1}\sum_{r=0}^{s}\sum_{i=1}^{m}\frac{b_{i}(r)x_{j}(r-\tau_{i}(r))}{1+x_{j}^{n}(r-\tau_{i}(r))}\\ &=\sum_{s=0}^{k-1}\left(-a(s)\lim_{j\to\infty}x_{j}(s)\right)+\sum_{s=0}^{k-1}\sum_{i=1}^{m}\frac{b_{i}(s)\lim_{j\to\infty}x_{j}(s-\tau_{i}(s))}{1+\lim_{j\to\infty}x_{j}^{n}(s-\tau_{i}(s))}\\ &-\left(\frac{k}{\omega}-\frac{\omega+1}{2\omega}\right)\sum_{s=1}^{\omega}\left(-a(s)\lim_{j\to\infty}x_{j}(s)\right)\\ &-\left(\frac{k}{\omega}-\frac{\omega+1}{2\omega}\right)\sum_{s=1}^{\omega}\sum_{i=1}^{m}\frac{b_{i}(s)\lim_{j\to\infty}x_{j}(s-\tau_{i}(s))}{1+\lim_{j\to\infty}x_{j}^{n}(s-\tau_{i}(s))}\\ &-\frac{1}{\omega}\sum_{s=0}^{\omega-1}\sum_{r=0}^{s}\sum_{i=1}^{m}\frac{b_{i}(r)\lim_{j\to\infty}x_{j}(r-\tau_{i}(r))}{1+\lim_{j\to\infty}x_{j}^{n}(r-\tau_{i}(r))}\\ &=K_{p}(I-Q)N\lim_{j\to\infty}x_{j}=K_{p}(I-Q)Nx_{*}=y_{*}.\end{aligned}$$

Hence, $K_p(I-Q)N(E)$ is compact.

Next, we check the first condition of Lemma 1.1 is satisfied. From the definitions of L and N, we see that any ω -periodic solution of (2.6) corresponds one-to-one to a solution of $Lx = \lambda Nx$ with $\lambda \in (0, 1)$. Proposition 2.1 shows that every positive solution of $Lx = \lambda Nx$ stays in the open bounded subset Ω . Let y be an element of $\partial \Omega$. Suppose that y is a solution of $Lx = \lambda Nx$. Of course, $y \in X$. Then, we can find a $k^* \in \{1, 2, \ldots, \omega\}$ so that $y(k^*) = \min_{1 \le k \le \omega} y(k)$. There are three cases to be considered. If $y(k^*) > A$, then y is a positive solution of $Lx = \lambda Nx$. Hence, we see that A < y(k) < B for $k = 1, 2, \ldots, \omega$. It turns out from the fact that there exists a neighborhood of y whose all elements belong to Ω . This contradicts the fact that $y \in \partial \Omega$. If $0 < y(k^*) \le A$, then y is a positive solution of $Lx = \lambda Nx$. However, this contradicts the conclusion of Proposition 2.1. If $y(k^*) \le 0$, then there exists a neighborhood of y whose all elements do not belong to Ω . This also contradicts the fact that $y \in \partial \Omega$. Hence, if $y \in \partial \Omega$, then y is never any solution of $Lx = \lambda Nx$. This means that the first condition of Lemma 1.1 holds.

Finally, we check the second condition of Lemma 1.1 is also satisfied. If $x \in \partial \Omega \cap \text{Ker } L$, then x(k) = A or x(k) = B for all $k \in \mathbb{Z}^+$. Let x_1 and x_2 be sequences satisfying $x_1(k) \equiv A$ and $x_2(k) \equiv B$, respectively. Then, by (2.5) we have

$$QNx_1 = \frac{1}{\omega} \sum_{k=1}^{\omega} \left(-Aa(k) + \frac{A}{1+A^n} \sum_{i=1}^m b_i(k) \right) > \frac{A}{\omega} \left(\frac{\gamma}{1+A^n} - 1 \right) \sum_{k=1}^{\omega} a(k).$$

Since $A \leq \sqrt[n]{\gamma - 1}$, we see that $QNx_1 > 0$. Recall that

$$\overline{b}_i = \max_{1 \le h \le \omega} b_i(k)$$
 and $B = \frac{1}{\underline{a}} \sum_{i=1}^m \overline{b}_i.$

Then we obtain

$$QNx_2 = \frac{1}{\omega} \sum_{k=1}^{\omega} \left(-Ba(k) + \frac{B}{1+B^n} \sum_{i=1}^m b_i(k) \right) \le -\frac{B}{\omega} \sum_{k=1}^{\omega} a(k) + \frac{B}{1+B^n} \sum_{i=1}^m \overline{b}_i$$
$$< -\frac{B}{\omega} \sum_{k=1}^{\omega} a(k) + \sum_{i=1}^m \overline{b}_i \le -\underline{a}B + \underline{a}B = 0.$$

We therefore conclude that $QNx \neq 0$ for each $x \in \partial\Omega \cap \text{Ker } L$. To seek the degree deg $\{QN, \Omega \cap \text{Ker } L, 0\}$, we define a continuous mapping $H \colon \Omega \cap \text{Ker } L \times [0, 1] \to X$ by

$$H(x,\mu) = -\mu\left(Ix - \frac{A+B}{2}\right) + (1-\mu)QNx.$$

It is clear that H connects two continuous mappings QN, $-I + (A + B)/2 : \Omega \cap$ Ker $L \to X$. Recall that the elements of $\partial \Omega \cap$ Ker L are only two sequences x_1 and x_2 satisfying $x_1(k) \equiv A$ and $x_2(k) \equiv B$, respectively. We have

$$H(x_i,\mu) = -\mu\left(Ix_i - \frac{A+B}{2}\right) + (1-\mu)QNx_i = (-1)^i \mu\left(\frac{A-B}{2}\right) + (1-\mu)QNx_i$$

for i = 1, 2 and $\mu \in [0, 1]$. Since A < B and $QNx_2 < 0 < QNx_1$, we see that

 $H(x_2,\mu) < 0 < H(x_1,\mu)$. Hence, $H(x,\mu) \neq 0$ for all $(x,\mu) \in \partial \Omega \cap \text{Ker} L \times [0,1]$, and therefore, H is a homotopic mapping. Since the mappings QN and -I + (A+B)/2are homotopy equivalent, it turns out that

$$\deg\left\{QN,\,\Omega\cap\operatorname{Ker} L,\,0\right\} = \deg\left\{-I + \frac{A+B}{2},\,\Omega\cap\operatorname{Ker} L,\,0\right\} = 1 \neq 0.$$

Hence, the second condition of Lemma 1.1 holds.

Since all assumptions of Lemma 1.1 are satisfied, the equation Lx = Nx has at least one solution lying in $X \cap \overline{\Omega}$. In other words, equation (H) has at least one positive ω -periodic solution located in the region [A, B]. The proof is now complete.

2.4 Examples

In this section, we give two examples to illustrate Theorem 2.1. One is a mathematical example, we can find a positive ω -periodic solution by using hand calculations. The other one is a practical example related to the red blood cells. In this example, by use of the actual measurement data of red blood cells number obtained in clinical examination, we can know that a positive ω -periodic solution exists in the region determined by the actual data. We now introduce the first example.

Example 2.1. Consider the equation

$$\Delta x(k) = -a(k)x(k) + \frac{b_1(k)x(k-\tau_1(k))}{1+x^2(k-\tau_1(k))} + \frac{b_2(k)x(k-\tau_2(k))}{1+x^2(k-\tau_2(k))},$$
(2.16)

where

$$a(k) = \begin{cases} 1/2 & \text{if } k = 0, \\ 5/6 & \text{if } k = 1, \\ 1/4 & \text{if } k = 2, \\ 1/5 & \text{if } k = 3, \end{cases}$$

$$b_{1}(k) = \begin{cases} 3/2 & \text{if } k = 0, \\ 1/2 & \text{if } k = 1, \\ 2 & \text{if } k = 2, \\ 1/4 & \text{if } k = 3, \end{cases} \qquad b_{2}(k) = \begin{cases} 1 & \text{if } k = 0, \\ 7/6 & \text{if } k = 1, \\ 5/8 & \text{if } k = 2, \\ 3/4 & \text{if } k = 3, \end{cases}$$
$$\tau_{1}(k) = 6 + 2\cos\left(\frac{\pi}{2}k\right) = \begin{cases} 8 & \text{if } k = 0, \\ 6 & \text{if } k = 1, \\ 4 & \text{if } k = 2, \\ 6 & \text{if } k = 3, \end{cases} \qquad \tau_{2}(k) = 5 + 3\sin\left(\frac{\pi}{2}k\right) = \begin{cases} 5 & \text{if } k = 0, \\ 8 & \text{if } k = 1, \\ 5 & \text{if } k = 2, \\ 2 & \text{if } k = 3, \end{cases}$$

and a, b_i , and τ_i are 4-periodic for i = 1, 2. Then equation (2.16) has at least one positive 4-periodic solution.

It is clear that 0 < a(k) < 1, $b_i(k) > 0$ and $\tau_i(k) > 0$ for $k \in \mathbb{Z}$ and i = 1, 2. Let

$$\gamma = \frac{1 + \min_{1 \le k \le 4} \left\{ \frac{b_1(k) + b_2(k)}{a(k)} \right\}}{2} = \frac{3}{2} > 1.$$

Then it is easy to check that condition (2.8) is satisfied. Hence, Theorem 2.1 shows that equation (2.16) has at least one positive 4-periodic solution.

Theorem 2.1 ensures that we can evaluate the existence range of the positive ω -periodic solutions of (2.16). In this example, since m = n = 2, $\gamma = 3/2$,

$$\underline{a} = \min_{1 \le k \le \omega} a(k) = 1/5, \quad \overline{b}_1 = \max_{1 \le k \le \omega} b_1(k) = 2 \quad \text{and} \quad \overline{b}_2 = \max_{1 \le k \le \omega} b_2(k) = \frac{7}{6}$$

we can calculate that

$$\sqrt{\gamma - 1} = \frac{1}{\sqrt{2}}, \quad \sum_{i=1}^{m} \overline{b}_i / \underline{a} = \frac{19}{6} \quad \text{and} \quad \frac{\gamma \underline{a}^{n-1} \sum_{i=1}^{m} \overline{b}_i}{\underline{a}^n + \left(\sum_{i=1}^{m} \overline{b}_i\right)^n} = \frac{45}{511}.$$

Hence, from Theorem 2.1 we see that positive 4-periodic solutions locate in the region

$$[A,B] = \left[\frac{45}{511}, \frac{95}{6}\right].$$

Choosing a set of initial points $\phi(-\overline{\tau})$, $\phi(-\overline{\tau}+1)$,..., $\phi(0)$, where

$$\overline{\tau} = \max_{1 \le i \le 2} \left\{ \max_{1 \le k \le 4} \tau_i(k) \right\} = 8.$$

We can find a positive 4-periodic solution by using hand calculations. Let

$$\phi(k) = \begin{cases} 1/2 & \text{if } k = -8, \\ 1/2 & \text{if } k = -7, \\ * & \text{if } k = -6, \\ 1/2 & \text{if } k = -5, \end{cases} \text{ and } \phi(k) = \begin{cases} 2 & \text{if } k = -4, \\ 2 & \text{if } k = -3, \\ 1 & \text{if } k = -2, \\ 2 & \text{if } k = -1, \\ 2 & \text{if } k = 0, \end{cases}$$

where * can be any positive real number. Note that the initial points $\phi(k)$ (-8 $\leq k \leq 0$) have no periodicity. Then we have

$$\begin{aligned} x(1) &= \left(1 - a(0)\right) x(0) + \frac{b_1(0)x(0 - \tau_1(0))}{1 + x^2(0 - \tau_1(0))} + \frac{b_2(0)x(0 - \tau_2(0))}{1 + x^2(0 - \tau_2(0))} \\ &= \left(1 - \frac{1}{2}\right) \times 2 + \frac{3}{2} \times \frac{x(-8)}{1 + x^2(-8)} + 1 \times \frac{x(-5)}{1 + x^2(-5)} = 2, \end{aligned}$$

$$x(2) = (1 - a(1))x(1) + \frac{b_1(1)x(1 - \tau_1(1))}{1 + x^2(1 - \tau_1(1))} + \frac{b_2(1)x(1 - \tau_2(1))}{1 + x^2(1 - \tau_2(1))}$$
$$= (1 - \frac{5}{6}) \times 2 + \frac{1}{2} \times \frac{x(-5)}{1 + x^2(-5)} + \frac{7}{6} \times \frac{x(-7)}{1 + x^2(-7)} = 1,$$

$$x(3) = (1 - a(2))x(2) + \frac{b_1(2)x(2 - \tau_1(2))}{1 + x^2(2 - \tau_1(2))} + \frac{b_2(2)x(2 - \tau_2(2))}{1 + x^2(2 - \tau_2(2))}$$
$$= (1 - \frac{1}{4}) \times 1 + 2 \times \frac{x(-2)}{1 + x^2(-2)} + \frac{5}{8} \times \frac{x(-3)}{1 + x^2(-3)} = 2,$$

$$x(4) = (1 - a(3))x(3) + \frac{b_1(3)x(3 - \tau_1(3))}{1 + x^2(3 - \tau_1(3))} + \frac{b_2(3)x(3 - \tau_2(3))}{1 + x^2(3 - \tau_2(3))}$$
$$= (1 - \frac{1}{5}) \times 2 + \frac{1}{4} \times \frac{x(-3)}{1 + x^2(-3)} + \frac{3}{4} \times \frac{x(1)}{1 + x^2(1)} = 2,$$

$$x(5) = (1 - a(4))x(4) + \frac{b_1(4)x(4 - \tau_1(4))}{1 + x^2(4 - \tau_1(4))} + \frac{b_2(4)x(4 - \tau_2(4))}{1 + x^2(4 - \tau_2(4))}$$
$$= (1 - \frac{1}{2}) \times 2 + \frac{3}{2} \times \frac{x(-4)}{1 + x^2(-4)} + 1 \times \frac{x(-1)}{1 + x^2(-1)} = 2,$$

$$\begin{aligned} x(6) &= \left(1 - a(5)\right)x(5) + \frac{b_1(5)x(5 - \tau_1(5))}{1 + x^2(5 - \tau_1(5))} + \frac{b_2(5)x(5 - \tau_2(5))}{1 + x^2(5 - \tau_2(5))} \\ &= \left(1 - \frac{5}{6}\right) \times 2 + \frac{1}{2} \times \frac{x(-1)}{1 + x^2(-1)} + \frac{7}{6} \times \frac{x(-3)}{1 + x^2(-3)} = 1, \end{aligned}$$

$$\begin{aligned} x(7) &= \left(1 - a(6)\right)x(6) + \frac{b_1(6)x(6 - \tau_1(6))}{1 + x^2(6 - \tau_1(6))} + \frac{b_2(6)x(6 - \tau_2(6))}{1 + x^2(6 - \tau_2(6))} \\ &= \left(1 - \frac{1}{4}\right) \times 1 + 2 \times \frac{x(2)}{1 + x^2(2)} + \frac{5}{8} \times \frac{x(1)}{1 + x^2(1)} = 2, \end{aligned}$$

$$\begin{aligned} x(8) &= \left(1 - a(7)\right)x(7) + \frac{b_1(7)x(7 - \tau_1(7))}{1 + x^2(7 - \tau_1(7))} + \frac{b_2(7)x(7 - \tau_2(7))}{1 + x^2(7 - \tau_2(7))} \\ &= \left(1 - \frac{1}{5}\right) \times 2 + \frac{1}{4} \times \frac{x(1)}{1 + x^2(1)} + \frac{3}{4} \times \frac{x(5)}{1 + x^2(5)} = 2, \end{aligned}$$

and so on (see Figure 2.1). Certainly, the solution x is positive and 4-periodic satisfying

$$A = \frac{45}{511} < 1 \le x(k) \le 2 < \frac{95}{6} = B$$

for all $k \in \mathbb{Z}^+$.

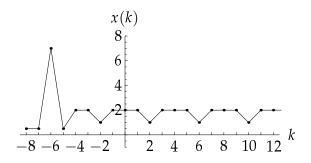


Figure 2.1: A graph of the solution of (2.16)

In Example 2.1, for the given positive numbers m, n, the coefficients a, b_i and the time delays τ_i (i = 1, 2, ..., m), we estimated the existence range [A, B] of the

positive periodic solutions of (H). Conversely, for the given value A and B, we can choose the positive numbers m, n, the coefficients a, b_i and the time delays τ_i so that the positive periodic solutions of (H) exist in the range [A, B]. We will explain this situation below.

It is reported that the number of red blood cells per microliter is different depending on sex and race, even for healthy humans. The lower and upper limits of the measured value are slightly different depending on health agencies. For example, according to the guidelines for clinical examination (JSLM2012) by Japanese Society of Laboratory Medicine, the standard value of red blood cells is 4.1×10^6 to 5.3×10^6 per $1\mu\ell$ for adult males, 3.8×10^6 to 4.8×10^6 per $1\mu\ell$ for adult females. Let A be the lower limit and let B be the upper limit. In the case of Japanese people, even if A and B are regarded as 3.6×10^6 and 6.0×10^6 per $1\mu\ell$ respectively, there would be no big difference from the reality. Of course, it is also possible to change the values A and B.

It is known that red blood cells start a immature cells in the bone marrow and after about 7 days of maturation they are released into the bloodstream (see [29, Sect. 1]). For this reason, we assume that time lag is 7 days; namely, $\tau_i(k) = 7$ for i = 1, 2, ..., m and $k = 1, 2, ..., \omega$. To simplify hand calculations, we set m = 2 and $\omega = 7$.

Example 2.2. Let $A = 3.6 \times 10^6$ and $B = 6.0 \times 10^6$. If

$$a(k) = \begin{cases} 0.60 & \text{if } k = 0, \\ 0.66 & \text{if } k = 1, \\ 0.60 & \text{if } k = 2, \\ 0.72 & \text{if } k = 3, \\ 0.66 & \text{if } k = 4, \\ 0.60 & \text{if } k = 5, \\ 0.66 & \text{if } k = 6, \end{cases}$$
(2.17)

$$b_{1}(k) = \begin{cases} 0.8 \times 10^{6} & \text{if } k = 0, \\ 0.5 \times 10^{6} & \text{if } k = 1, \\ 0.6 \times 10^{6} & \text{if } k = 2, \\ 0.8 \times 10^{6} & \text{if } k = 3, \\ 0.7 \times 10^{6} & \text{if } k = 4, \\ 0.2 \times 10^{6} & \text{if } k = 5, \\ 0.6 \times 10^{6} & \text{if } k = 6, \end{cases} \qquad b_{2}(k) = \begin{cases} 2.2 \times 10^{6} & \text{if } k = 0, \\ 2.8 \times 10^{6} & \text{if } k = 2, \\ 2.8 \times 10^{6} & \text{if } k = 3, \\ 2.6 \times 10^{6} & \text{if } k = 4, \\ 2.8 \times 10^{6} & \text{if } k = 4, \\ 2.8 \times 10^{6} & \text{if } k = 4, \\ 2.8 \times 10^{6} & \text{if } k = 5, \\ 2.7 \times 10^{6} & \text{if } k = 6, \end{cases}$$
(2.18)

and $a(k) = a(k+7), b_1(k) = b_1(k+7), b_2(k) = b_2(k+7)$ for $k \in \mathbb{Z}$. Then the equation

$$\Delta x(k) = -a(k)x(k) + \frac{b_1(k)x(k-7)}{1+x^{1.02}(k-7)} + \frac{b_2(k)x(k-7)}{1+x^{1.02}(k-7)}$$
(2.19)

has at least one positive 7-periodic solution x satisfying

$$A \le x(k) \le B$$
 for $k \in \mathbb{Z}^+$.

In the case that n > 1, the production function f_n given by

$$f_n(u) = \frac{u}{1+u^n} \quad \text{for } u \ge 0$$

has the maximum value

$$\left(\frac{(n-1)^{n-1}}{n^n}\right)^{1/n}$$

at $u^* = \sqrt[n]{1/(n-1)}$. As *n* approaches 1, the maximum value $f_n(u^*)$ increases and converges to 1, and the value u^* diverges to ∞ . Hence, we can find n > 1 so that $f_n(B) > A/B$, because A/B < 1. In the case that $A = 3.6 \times 10^6$ and $B = 6.0 \times 10^6$, we can choose *n* as 1.02. In fact,

$$f_{1.02}(6.0 \times 10^6) = \frac{6.0 \times 10^6}{1 + (6.0 \times 10^6)^{1.02}} = 0.7318 \dots > 0.6 = \frac{A}{B}.$$

Next, we choose a γ satisfying

$$\gamma \ge \max\left\{\frac{A}{f_n(B)}, A^n + 1\right\}.$$

Since n = 1.02, $A = 3.6 \times 10^6$ and $B = 6.0 \times 10^6$, we see that $A/f_n(B) = 4,918,872\cdots$ and $A^n + 1 = 4,868,875\cdots$. Hence, we can choose γ as 4.95×10^6 .

It is clear that a, b_1 and b_2 are 7-periodic discrete functions satisfying $0 < a(k) < 1, b_1(k) > 0$ and $b_2(k) > 0$ for $k \in \mathbb{Z}$. Since $\underline{a} = 0.60, \overline{b}_1 = 0.8 \times 10^6$ and $\overline{b}_2 = 2.8 \times 10^6$, it turns out that

$$B = 6.0 \times 10^6 = \frac{1}{0.6} (0.8 \times 10^6 + 2.8 \times 10^6) = \frac{1}{\underline{a}} (\overline{b}_1 + \overline{b}_2).$$

From (2.17) and (2.18), we see that condition (2.8) holds for $\gamma = 4.95$, m = 2 and $\omega = 7$. Hence, Theorem 2.1 ensures that equation (2.19) has at least one positive 7-periodic solution located in the region [A, B] under the assumptions (2.17) and (2.18).

2.5 The case that $0 < n \le 1$

As is said in Section 2.1, equation (H) is not suitable as a mathematical model describing the hematopoiesis process when $0 < n \leq 1$. However, from pure mathematical side, it is worth considering the case that $0 < n \leq 1$. We have the following result.

Theorem 2.2. Suppose that (2.6) and (2.8) hold. Then equation (H) with $0 < n \le 1$ has at least one positive ω -periodic solution located in the region [C, D], where

$$C = \sqrt[n]{\gamma - 1}$$
 and $D = \sqrt[n]{\frac{\omega \sum_{i=1}^{m} b_i^*}{\underline{a}} - 1},$

in which γ and \underline{a} are constants given in Theorem 2.1 and $b_i^* = \left(\sum_{k=1}^{\omega} b_i(k)\right) / \omega$ for $1 \leq i \leq m$.

By using continuation theorem, we can show that Theorem 2.2 holds in the same way as the proof of Theorem 2.1. To apply continuation theorem to the proof of Theorem 2.2, it is only necessary to show the following proposition (leave the details to the reader).

Proposition 2.2. Suppose that (2.8) holds. Then every positive ω -periodic solution x of (2.9) with $0 < n \le 1$ satisfies

$$C < x(k) < D \quad for \quad k = 1, 2, \dots, \omega,$$

where C and D are constants given in Theorem 2.2.

Proof. As in the proof of Proposition 2.1, we can show that the inequalities (2.11) and (2.14) hold. Since $0 < n \le 1$, the function f_n defined by $f_n(u) = u/(1+u^n)$ is increasing for $u \ge 0$. Hence, it follows from (2.11) that

$$\overline{x} \leq \frac{1}{\underline{a}} \max_{1 \leq k \leq \omega} \left\{ \sum_{i=1}^{m} b_i(k) f(x(k - \tau_i(k))) \right\}$$
$$\leq \frac{f(\overline{x})}{\underline{a}} \max_{1 \leq k \leq \omega} \left\{ \sum_{i=1}^{m} b_i(k) \right\} \leq \frac{f(\overline{x})}{\underline{a}} \sum_{i=1}^{m} \overline{b}_i$$
$$< \frac{\omega f(\overline{x})}{\underline{a}} \sum_{i=1}^{m} b_i^*.$$

Arranging this inequality, we obtain

$$\overline{x} < \sqrt[n]{\frac{\omega \sum_{i=1}^{m} b_i^*}{\underline{a}} - 1} = D.$$

From (2.8) and (2.14) it turns out that

$$\underline{x} = \frac{\lambda}{1 - \prod_{r=0}^{\omega-1} (1 - \lambda a(r))} \sum_{s=k_1}^{k_1 + \omega - 1} \left(\sum_{i=1}^m b_i(s) f_n(x(s - \tau_i(s))) \prod_{r=s+1}^{k_1 + \omega - 1} (1 - \lambda a(r)) \right)$$
$$\geq \frac{\lambda f_n(\underline{x})}{1 - \prod_{r=0}^{\omega-1} (1 - \lambda a(r))} \sum_{s=k_1}^{k_1 + \omega - 1} \left(\sum_{i=1}^m b_i(s) \prod_{r=s+1}^{k_1 + \omega - 1} (1 - \lambda a(r)) \right)$$

$$> \frac{\gamma f_n(\underline{x})}{1 - \prod\limits_{r=0}^{\omega-1} (1 - \lambda a(r))} \sum_{s=k_1}^{k_1 + \omega - 1} \left(\lambda a(s) \prod_{r=s+1}^{k_1 + \omega - 1} (1 - \lambda a(r)) \right)$$
$$> \frac{\gamma f_n(\underline{x})}{1 - \prod\limits_{r=0}^{\omega-1} (1 - \lambda a(r))} \left(1 - \prod\limits_{r=0}^{\omega-1} (1 - \lambda a(r)) \right) = \gamma f_n(\underline{x}).$$

Hence, we can estimate that

$$\underline{x} > \sqrt[n]{\gamma - 1} = C.$$

We therefore conclude that

$$C < \underline{x} \le x(k) < \overline{x} < D$$

for all $k \in \mathbb{Z}^+$. This completes the proof of Proposition 2.2.

Chapter 3

Global asymptotic stability of a unique positive ω -periodic solution

3.1 Main result

For continuous hematopoiesis models with unimodal function, we can find a few research results on the global asymptotic stability of a positive ω -periodic solution. For example, see [25, 28]. Though it is not a research result on the global attractivity of a positive ω -periodic solution of discrete hematopoiesis models, there are research results of a unique positive equilibrium point (see [27, 31, 32]). However, there is no research on the global asymptotic stability of a unique positive ω -periodic solution of discrete hematopoiesis models with unimodal function untill now. In this chapter, we deal with this problem.

In chapter 2, we considered the discrete hematopoiesis model

$$\Delta x(k) = -a(k)x(k) + \sum_{i=1}^{m} b_i(k)f(x(k - \tau_i(k)))$$
(H)

with $m \in \mathbb{N}$. Here $a : \mathbb{Z} \to (0, 1), b_i : \mathbb{Z} \to (0, \infty)$ and $\tau_i : \mathbb{Z} \to \mathbb{Z}^+ (1 \le i \le m)$ are ω -periodic discrete functions satisfying periodic relation (2.6). The function fis defined by $f(u) = u/(1+u^n)$ for $u \ge 0$ and n > 1. The existence of positive ω periodic solutions of (H) has been obtained. We will make an attempt continuously on model (H) in this chapter. We intend to explore the global asymptotic stability of a unique positive ω -periodic solution of (H) base on the existence result Theorem 2.1.

Recall that function f is defined by $f(u) = u/(1+u^n)$ for $u \ge 0$. Since

$$f'(u) = \frac{1 - (n-1)u^n}{(1+u^n)^2},$$

the function f has the only one peak value at $1/\sqrt[n]{n-1}$. For simplicity, let

$$n_* = \frac{1}{\sqrt[n]{n-1}}$$
 and $\overline{f} = f(n_*) = \sqrt[n]{\frac{(n-1)^{(n-1)}}{n^n}} < 1.$

Let us define constants as follows:

$$C = \max_{A \le u \le B} |f'(u)|$$
 and $C_{\varepsilon} = \max_{A - \varepsilon \le u \le B} |f'(u)|$

for any $\varepsilon > 0$, where A and B are positive numbers given in Theorem 2.1. Since f'(u) is continuous on $[0, \infty)$, we see that $C_{\varepsilon} \to C$ as $\varepsilon \to 0$. Hence, the following lemma holds.

Lemma 3.1. If

$$BC < 1, \tag{3.1}$$

then there exists an $\varepsilon_0 > 0$ such that $B C_{\varepsilon} < 1$ for any $\varepsilon \in (0, \varepsilon_0]$.

We are now ready to describe our main result.

Theorem 3.1. Suppose that (2.8) and (3.1) hold. Then equation (H) with n > 1 has exactly one positive ω -periodic solution located in the region [A, B], which is globally asymptotically stable.

3.2 Upper and lower limit values on positive solutions

To complete the proof of global asymptotic stability of a unique positive ω periodic solution of (H), we need some information on the bound estimate of all positive solutions of (1.1), which are not necessarily periodic. Recall that the positive solution of (H) with initial condition (2.7) for any $\phi \in S$ is denoted by $x(\cdot; \phi)$. To know the fluctuation range of $x(k; \phi)$ for $k \in \mathbb{Z}^+$ sufficiently large, we examine the limit superior and limit inferior of $x(\cdot; \phi)$. From now on, we write $x(k; \phi)$ as x(k)for simplicity if necessary.

Equation (H) can be rewritten to

$$x(k+1) - (1 - a(k))x(k) = \sum_{i=1}^{m} b_i(k)f(x(k - \tau_i(k))).$$
(3.2)

Multiplying both sides of (3.2) by $\prod_{r=0}^{k} 1/(1-a(r))$ to obtain

$$x(k+1)\prod_{r=0}^{k}\frac{1}{1-a(r)} - x(k)\prod_{r=0}^{k-1}\frac{1}{1-a(r)} = \sum_{i=1}^{m}b_i(k)f(x(k-\tau_i(k)))\prod_{r=0}^{k}\frac{1}{1-a(r)}.$$
(3.3)

We here regard $\prod_{r=0}^{-1} 1/(1-a(r))$ as 1.

Lemma 3.2. For any $\phi \in S$, the positive solution $x(\cdot; \phi)$ satisfies

$$\limsup_{k \to \infty} x(k;\phi) \le \overline{f}B.$$

Proof. Summing both sides of (3.3) from 0 to k - 1, we get

$$x(k)\prod_{r=0}^{k-1}\frac{1}{1-a(r)} - x(0) = \sum_{s=0}^{k-1}\left(\sum_{i=1}^{m}b_i(s)f(x(s-\tau_i(s)))\prod_{r=0}^{s}\frac{1}{1-a(r)}\right).$$

This implies that

$$x(k) = x(0) \prod_{r=0}^{k-1} (1 - a(r)) + \sum_{s=0}^{k-1} \left(\sum_{i=1}^{m} b_i(s) f(x(s - \tau_i(s))) \prod_{r=s+1}^{k-1} (1 - a(r)) \right).$$
(3.4)

Note that $\underline{a} \leq a(k) < 1$ and $0 < b_i(k) \leq \overline{b}_i$ $(1 \leq i \leq m)$ for all $k \in \mathbb{Z}$, and that function f has the maximum \overline{f} . It follows from (3.4) that

$$\begin{aligned} x(k) &\leq x(0) \prod_{r=0}^{k-1} (1-a(r)) + \overline{f} \sum_{s=0}^{k-1} \left(\sum_{i=1}^{m} b_i(s) \prod_{r=s+1}^{k-1} (1-a(r)) \right) \\ &\leq x(0) \prod_{r=0}^{k-1} (1-\underline{a}) + \overline{f} \sum_{i=1}^{m} \overline{b}_i \sum_{s=0}^{k-1} \left(\prod_{r=s+1}^{k-1} (1-\underline{a}) \right) \\ &= x(0)(1-\underline{a})^k + \frac{\overline{f} \sum_{i=1}^{m} \overline{b}_i}{\underline{a}} \left(1 - (1-\underline{a})^k \right) \\ &= \left(x(0) - \frac{\overline{f} \sum_{i=1}^{m} \overline{b}_i}{\underline{a}} \right) (1-\underline{a})^k + \frac{\overline{f} \sum_{i=1}^{m} \overline{b}_i}{\underline{a}}. \end{aligned}$$

Since $(1 - \underline{a})^k$ converges to 0 as $k \to \infty$, we see that $\limsup_{k\to\infty} x(k) \leq \overline{f}B$. **Lemma 3.3.** Assume (2.8). Then, for any $\phi \in S$, the positive solution $x(\cdot; \phi)$ satisfies

$$\liminf_{k \to \infty} x(k;\phi) \ge A.$$

Proof. We first show that

$$\liminf_{k \to \infty} x(k) > 0.$$

By way of contradiction, suppose that $\liminf_{k\to\infty} x(k) = 0$. Then there exists a divergent sequence $\{k_j\}_{j\in\mathbb{N}}$ such that

$$\lim_{j \to \infty} x(k_j + 1) = 0 \tag{3.5}$$

and $x(k_j + 1) \le x(q)$ for $q = 0, 1, \ldots, k_j$. From (3.2) it follows that

$$x(k_j + 1) - (1 - a(k_j))x(k_j) = \sum_{i=1}^m b_i(k_j)f(x(k_j - \tau_i(k_j))).$$

Since $x(k_j + 1) \leq x(k_j)$, we see that

$$a(k_j)x(k_j+1) \ge \sum_{i=1}^m b_i(k_j)f(x(k_j-\tau_i(k_j))).$$
(3.6)

Let $\overline{a} = \max_{1 \le k \le \omega} a(k)$ and $\underline{b}_i = \min_{1 \le k \le \omega} b_i(k)$ for each $i = 1, 2, \dots, m$. Then we

have

$$\overline{a} x(k_j+1) \ge \underline{b}_1 f(x(k_j - \tau_1(k_j))) \ge 0.$$

From (3.5) it turns out that $\lim_{j\to\infty} f(x(k_j - \tau_1(k_j))) = 0$. Recall that $f(u) = u/(1+u^n)$ for $u \ge 0$. By Lemma 3.2, we see that $x(k_j - \tau_1(k_j))$ cannot diverge to infinity as $j \to \infty$. Hence, it has to converge to zero as $j \to \infty$. Similarly, we obtain

$$\lim_{j \to \infty} x(k_j - \tau_i(k_j)) = 0 \quad \text{for each } i = 1, 2, \dots, m.$$
 (3.7)

Let us consider the sequence $\{a(k_j)\}$. Since the coefficient a is a discrete function with ω -period, each $a(k_j)$ coincides with any one of $a(1), a(2), \ldots, a(\omega)$. Hence, there exist a subsequence $\{k_j^1\} \subset \{k_j\}$ and a number a^* such that $a(k_j^1) = a^*$ for all $j \in \mathbb{N}$, where a^* is one of $a(1), a(2), \ldots, a(\omega)$. Next, consider the sequence $\{b_1(k_j^1)\}$. Since the coefficient b_1 is also a discrete function with ω -period, each $b_1(k_j^1)$ coincides with any one of $b_1(1), b_1(2), \ldots, b_1(\omega)$. Hence, there exist a subsequence $\{k_j^2\} \subset \{k_j^1\}$ and a number b_1^* such that $b_1(k_j^2) = b_1^*$ for all $j \in \mathbb{N}$, where b_1^* is one of $b_1(1), b_1(2), \ldots, b_1(\omega)$. Of course, $a(k_j^2) = a^*$. Similarly, there exist subsequences $\{k_j^2\} \supset \{k_j^3\} \supset \cdots \supset \{k_j^m\} \supset \{k_j^{m+1}\}$ and numbers $b_2^*, b_3^*, \ldots, b_m^*$ such that $b_2(k_j^3) =$ $b_2^*, b_3(k_j^4) = b_3^*, \ldots, b_m(k_j^{m+1}) = b_m^*$. For simplicity, we write $\{k_j^{m+1}\}$ as $\{\ell_j\}_{j \in \mathbb{N}}$.

$$a(\ell_j) = a^*$$
 and $b_i(\ell_j) = b_i^*$ for each $i = 1, 2, \dots, m.$ (3.8)

Since the coefficients a and b_i (i = 1, 2, ..., m) are ω -period discrete functions and we assume (2.8), we see that

$$\gamma a^* < \sum_{i=1}^m b_i^*.$$
 (3.9)

From (3.6) it follows that

$$a(\ell_j) \ge \sum_{i=1}^m b_i(\ell_j) \frac{f(x(\ell_j - \tau_i(\ell_j)))}{x(\ell_j + 1)} = \sum_{i=1}^m \frac{b_i(\ell_j)}{1 + x^n(\ell_j - \tau_i(\ell_j))} \frac{x(\ell_j - \tau_i(\ell_j))}{x(\ell_j + 1)}.$$

Taking into account that $x(\ell_j + 1) \leq x(\ell_j - \tau_i(\ell_j))$, we get the inequality

$$a(\ell_j) \ge \sum_{i=1}^m \frac{b_i(\ell_j)}{1 + x^n(\ell_j - \tau_i(\ell_j))}$$

Hence, using (3.7)–(3.9), we obtain

$$a^* \ge \sum_{i=1}^m b_i^* > \gamma a^*.$$

This contradicts $\gamma > 1$. Thus, we can conclude that $\liminf_{k\to\infty} x(k) > 0$.

Let $D = \liminf_{k \to \infty} x(k) > 0$. Then it turns out from Lemma 3.2 that

$$D = \liminf_{k \to \infty} x(k) \le \limsup_{k \to \infty} x(k) \le \overline{f}B < B.$$
(3.10)

We next show that $D \ge \min \{ \sqrt[n]{\gamma - 1}, \gamma f(B) \} = A$. It is clear that $D \ge \gamma f(D)$ implies $D \ge \sqrt[n]{\gamma - 1}$. We will prove that $D < \gamma f(D)$ implies $D \ge \gamma f(B)$. We proceed our argument by dividing into two cases: (i) $f(D) \le f(B)$ and (ii) f(D) >f(B). Recall that the function f has the only one peak value at n_* ; namely, it is strictly increasing on $[0, n_*)$ and strictly decreasing on $[n_*, \infty)$. Note that $n_* < B$ in the case (i) and $D < n_*$ in the case (ii). Since f is a strictly increasing function on $[0, n_*)$, it has the inverse function on this interval. Let f^{-1} be the inverse function.

Case (i) We choose

$$c = \frac{\gamma f(D) - D}{2\gamma} > 0.$$

Then we have

$$\gamma(f(D) - c) = \frac{\gamma f(D) + D}{2} > \frac{D + D}{2} = D.$$
 (3.11)

This means that $0 < f(D) - c < f(D) \le f(B)$. Taking into account of (3.10), we can choose a $K_1 \in \mathbb{N}$ so that

$$f^{-1}(f(D) - c) < x(k) < B \text{ for } k \ge K_1 - \overline{\tau}.$$

Hence, we have

$$f(x(k - \tau_i(k))) > f(D) - c \text{ for } k \ge K_1 \text{ and } i = 1, 2, \dots, m.$$
 (3.12)

Summing both sides of (3.3) from K_1 to k - 1, we get

$$x(k) = x(K_1) \prod_{r=K_1}^{k-1} (1 - a(r)) + \sum_{s=K_1}^{k-1} \left(\sum_{i=1}^m b_i(s) f(x(s - \tau_i(s))) \prod_{r=s+1}^{k-1} (1 - a(r)) \right).$$

From (2.8), (3.12) and the definitions of \overline{a} and \underline{a} , we see that

$$\begin{aligned} x(k) > x(K_1)(1-\overline{a})^{k-K_1} + \left(f(D)-c\right) \sum_{s=K_1}^{k-1} \left(\sum_{i=1}^m b_i(s) \prod_{r=s+1}^{k-1} (1-a(r))\right) \\ > x(K_1)(1-\overline{a})^{k-K_1} + \gamma \left(f(D)-c\right) \sum_{s=K_1}^{k-1} \left(a(s) \prod_{r=s+1}^{k-1} (1-a(r))\right) \\ = x(K_1)(1-\overline{a})^{k-K_1} + \gamma \left(f(D)-c\right) \sum_{s=K_1}^{k-1} \left(\left(1-(1-a(s))\right) \prod_{r=s+1}^{k-1} (1-a(r))\right) \\ = x(K_1)(1-\overline{a})^{k-K_1} + \gamma \left(f(D)-c\right) \sum_{s=K_1}^{k-1} \left(\prod_{r=s+1}^{k-1} (1-a(r)) - \prod_{r=s}^{k-1} (1-a(r))\right) \\ = x(K_1)(1-\overline{a})^{k-K_1} + \gamma \left(f(D)-c\right) \left(1 - \prod_{r=K_1}^{k-1} (1-a(r))\right) \\ \ge x(K_1)(1-\overline{a})^{k-K_1} + \gamma \left(f(D)-c\right) \left(1 - \prod_{r=K_1}^{k-1} (1-a(r))\right) \\ = x(K_1)(1-\overline{a})^{k-K_1} + \gamma \left(f(D)-c\right) \left(1 - \prod_{r=K_1}^{k-1} (1-a(r))\right) \end{aligned}$$

for $k \ge K_1$. Since $0 < \underline{a} \le \overline{a} < 1$, we obtain

$$D = \liminf_{k \to \infty} x(k) \ge \gamma \left(f(D) - c \right).$$

However, this contradicts (3.11). Thus, Case (i) does not occur.

Case (ii) There are two subcases to be considered:

(a) $n_* < D$

(b)
$$n_* \ge D$$
.

Subcase (a) Let $d = (D - n_*)/2 > 0$. Then it is clear that $n_* < D - d < D < B$. Hence, we see that f(D - d) > f(D) > f(B). From (3.10), we see that there exists a $K_2 \in \mathbb{N}$ such that

$$D - d < x(k) < B$$
 for $k \ge K_2 - \overline{\tau}$.

Hence, we have

$$f(x(k - \tau_i(k))) > f(B)$$
 for $k \ge K_2$ and $i = 1, 2, \dots, m$.

Using this inequality instead of (3.12), we can obtain

$$D \ge \gamma f(B)$$

as in the proof of the case of Case (i). This is a desired evaluation. Subcase (b) Let e = (f(D) - f(B))/2 > 0. Then it is clear that f(D) > f(D) - e > f(B). From (3.10), we see that there exists a $K_3 \in \mathbb{N}$ such that

$$f^{-1}(f(D) - e)) < x(k) < B \text{ for } k \ge K_3 - \overline{\tau}.$$

Hence, we have

$$f(x(k - \tau_i(k))) > f(B)$$
 for $k \ge K_3$ and $i = 1, 2, \dots, m$.

This inequality gives the same conclusion as subcase (a).

We therefore conclude that

$$\liminf_{k \to \infty} x(k) = D \ge \min\left\{\sqrt[n]{\gamma - 1}, \ \gamma f(B)\right\} = A.$$

Thus, the proof of Lemma 3.3 is complete.

3.3 Proof of main result

In this section, we will prove Theorem 3.1 by Lemmas 3.1-3.3.

Proof. Note that the condition (2.8) guarantees that there is at least one positive ω -periodic solution of (H). Let $x_*(\cdot; \psi)$ be such a positive ω -periodic solution, where ψ belongs to S and satisfies the initial condition $x_*(s; \psi) = \psi(s) > 0$ for $s \in [-\overline{\tau}, 0] \cap \mathbb{Z}$. For simplicity, we denote $x_*(k) = x_*(k; \psi)$ for $k \geq -\overline{\tau}$. We will evaluate the difference between the positive ω -periodic solution $x_*(k)$ and any positive solution x(k) of (H). Let the initial function of the positive solution x(k) be $\phi \in S$. Then it follows from (3.2) that

$$x(k) - x_*(k) = (1 - a(k - 1)) (x(k - 1) - x_*(k - 1)) + \sum_{i=1}^m b_i(k - 1) (f(x(k - 1 - \tau_i(k - 1))) - f(x_*(k - 1 - \tau_i(k - 1)))))$$

for $k \in \mathbb{N}$. Hence, by the mean-value theorem, we have

$$|x(k) - x_{*}(k)|$$

$$\leq (1 - \underline{a}) |x(k-1) - x_{*}(k-1)|$$

$$+ \sum_{i=1}^{m} \overline{b}_{i} |f(x(k-1 - \tau_{i}(k-1))) - f(x_{*}(k-1 - \tau_{i}(k-1)))|$$

$$= (1 - \underline{a}) |x(k-1) - x_{*}(k-1)|$$

$$+ \sum_{i=1}^{m} \overline{b}_{i} |f'(\eta_{ik})| |x(k-1 - \tau_{i}(k-1)) - x_{*}(k-1 - \tau_{i}(k-1))|, \qquad (3.13)$$

where η_{ik} is a value between $x(k-1-\tau_i(k-1))$ and $x_*(k-1-\tau_i(k-1))$ for $i=1,2,\ldots,m$ and $k\in\mathbb{N}$.

Since

$$f'(u) = \frac{1 - (n - 1)u^n}{(1 + u^n)^2}$$

and

$$f''(u) = \frac{n u^n ((n-1)u^n - (n+1))}{(1+u^n)^3}$$

for $u \ge 0$, we see that the derivative f' has the properties as follows:

- 1. f'(0) = 1 and $f'(n_*) = 0$,
- 2. f' is decreasing on $\left[0, \sqrt[n]{(n+1)/(n-1)}\right)$ and increasing on $\left[\sqrt[n]{(n+1)/(n-1)}, \infty\right)$,
- 3. $f'(u) \nearrow 0$ as $u \to \infty$.

For simplicity, let $n^* = \sqrt[n]{(n+1)/(n-1)}$. From the above properties, it turns out that f' takes the minimum value

$$-\frac{(n-1)^2}{4n}$$

at $u = n^*$. Since n is a number greater than 1, we see that

$$|f'(u)| \le M \quad \text{for } u \ge 0,$$

where

$$M = \begin{cases} \frac{(n-1)^2}{4n} & \text{if } n \ge 3 + 2\sqrt{2}, \\ 1 & \text{if } 1 < n < 3 + 2\sqrt{2}. \end{cases}$$

Note that M depends on n, but it is a constant that is not less than 1 (see Figures 3.1 and 3.2).

From (3.13) it follows that

$$|x(k) - x_*(k)| \le (1 - \underline{a}) |x(k-1) - x_*(k-1)| + M \sum_{i=1}^m \overline{b}_i |x(k-1 - \tau_i(k-1)) - x_*(k-1 - \tau_i(k-1))|$$
(3.14)

for $k \in \mathbb{N}$. Needless to say, the following inequality holds:

$$|x(k) - x_*(k)| \le \max_{-\overline{\tau} \le s \le 0} |x(s) - x_*(s)| = ||\phi - \psi|| \quad \text{for } k = -\overline{\tau}, -\overline{\tau} + 1, \dots, 0.$$
(3.15)

From (3.14) and (3.15), we see that

$$|x(1) - x_{*}(1)| \leq (1 - \underline{a}) |x(0) - x_{*}(0)| + M \sum_{i=1}^{m} \overline{b}_{i} |x(-\tau_{i}(0)) - x_{*}(-\tau_{i}(0))| \leq (1 - \underline{a}) ||\phi - \psi|| + M \sum_{i=1}^{m} \overline{b}_{i} ||\phi - \psi|| = \left(1 - \underline{a} + M \sum_{i=1}^{m} \overline{b}_{i}\right) ||\phi - \psi||.$$
(3.16)

As stated immediately after Theorem 2.1, assumption (2.8) implies that $B > \gamma > 1$. Since $\underline{a} > 0$ and $M \ge 1$, we see that

$$1 - \underline{a} + M \sum_{i=1}^{m} \overline{b}_i \ge 1 - \underline{a} + \sum_{i=1}^{m} \overline{b}_i = 1 + (B - 1) \underline{a} > 1.$$
 (3.17)

From (3.14) it follows that

$$|x(2) - x_*(2)| \le (1 - \underline{a}) |x(1) - x_*(1)| + M \sum_{i=1}^m \overline{b}_i |x(1 - \tau_i(1)) - x_*(1 - \tau_i(1))|.$$
(3.18)

If $\tau_i(1) \in \mathbb{N}$ for some i = 1, 2, ..., m, then by (3.15) we have

$$|x(1 - \tau_i(1)) - x_*(1 - \tau_i(1))| \le ||\phi - \psi||.$$

If $\tau_i(1) = 0$ for some $i = 1, 2, \ldots, m$, then by (3.16) we have

$$|x(1 - \tau_i(1)) - x_*(1 - \tau_i(1))| \le \left(1 - \underline{a} + M \sum_{i=1}^m \overline{b}_i\right) ||\phi - \psi||.$$

Hence, it turns out from (3.17) and (3.18) that

$$|x(2) - x_*(2)| \le (1 - \underline{a}) \left(1 - \underline{a} + M \sum_{i=1}^m \overline{b}_i \right) ||\phi - \psi||$$
$$+ M \sum_{i=1}^m \overline{b}_i \left(1 - \underline{a} + M \sum_{i=1}^m \overline{b}_i \right) ||\phi - \psi||$$
$$= \left(1 - \underline{a} + M \sum_{i=1}^m \overline{b}_i \right)^2 ||\phi - \psi||.$$

Mathematical induction leads the inequality

$$|x(k) - x_*(k)| \le \left(1 - \underline{a} + M \sum_{i=1}^m \overline{b}_i\right)^k ||\phi - \psi|| \quad \text{for } k \in \mathbb{N}.$$
(3.19)

By Lemmas 3.2 and 3.3, there exists a $K_4 \in \mathbb{N}$ with $K_4 \geq \overline{\tau}$ such that

$$A - \varepsilon_0 < x(k) < B \quad \text{for } k \ge K_4 - 1 - \overline{\tau}, \tag{3.20}$$

where ε_0 is a positive constant given in Lemma 3.1. Let

$$\beta = \left(1 - \underline{a} + M \sum_{i=1}^{m} \overline{b}_i\right)^{K_4 - 1}.$$

Then it follows from (3.17) that β is a constant larger than 1. Hence, by (3.15) and (3.19), we can evaluate that

$$|x(k) - x_*(k)| \le \beta ||\phi - \psi||$$
 for $k = -\overline{\tau}, -\overline{\tau} + 1, \dots, K_4 - 1.$ (3.21)

Note that

$$k-1-\tau_i(k-1) \ge k-1-\overline{\tau} \ge K_4-1-\overline{\tau} \quad \text{for } k \ge K_4.$$

Hence, it turns out from (3.20) that

$$A - \varepsilon_0 < x(k - 1 - \tau_i(k - 1)) < B \quad \text{for } k \ge K_4.$$

On the other hand, Theorem 2.1 guarantees that

$$A \le x(k-1-\tau_i(k-1)) \le B$$
 for $k \in \mathbb{N}$.

Since η_{ik} is between $x(k-1-\tau_i(k-1))$ and $x_*(k-1-\tau_i(k-1))$ for $i=1,2,\ldots,m$ and $k \in \mathbb{N}$, we see that $A-\varepsilon_0 \leq \eta_{ik} \leq B$ for $i=1,2,\ldots,m$ and $k \geq K_4+1$. Hence, we obtain

$$|f'(\eta_{ik})| \leq C_{\varepsilon_0}$$
 for $i = 1, 2, \dots, m$ and $k \geq K_4$.

From this inequality and (3.13), we see that

$$|x(k) - x_*(k)| = (1 - \underline{a}) |x(k-1) - x_*(k-1)| + C_{\varepsilon_0} \sum_{i=1}^m \overline{b}_i |x(k-1 - \tau_i(k-1)) - x_*(k-1 - \tau_i(k-1))| \quad (3.22)$$

for $k \geq K_4$.

Using (3.21) and (3.22), we obtain

$$|x(K_4) - x_*(K_4)| = (1 - \underline{a}) |x(K_4 - 1) - x_*(K_4 - 1)| + C_{\varepsilon_0} \sum_{i=1}^m \overline{b}_i |x(K_4 - 1 - \tau_i(K_4 - 1)) - x_*(K_4 - 1 - \tau_i(K_4 - 1))| \leq (1 - \underline{a}) \beta ||\phi - \psi|| + \underline{a} B C_{\varepsilon_0} \beta ||\phi - \psi|| \leq \left(1 - \underline{a} (1 - B C_{\varepsilon_0})\right) \beta ||\phi - \psi||.$$

Recall that $0 < \underline{a} = \min_{1 \le k \le \omega} a(k) < 1$. From Lemma 3.1 and the assumption (3.1), we see that

$$0 < 1 - \underline{a} \left(1 - B C_{\varepsilon_0} \right) < 1. \tag{3.23}$$

Hence, we get

$$|x(K_{4}+1) - x_{*}(K_{4}+1)| = (1 - \underline{a}) |x(K_{4}) - x_{*}(K_{4})| + C_{\varepsilon_{0}} \sum_{i=1}^{m} \overline{b}_{i} |x(K_{4} - \tau_{i}(K_{4})) - x_{*}(K_{4} - \tau_{i}(K_{4}))| \leq (1 - \underline{a}) \Big(1 - \underline{a} (1 - B C_{\varepsilon_{0}}) \Big) \beta ||\phi - \psi|| + \underline{a} B C_{\varepsilon_{0}} \beta ||\phi - \psi|| \leq \Big(1 - \underline{a} (1 - B C_{\varepsilon_{0}}) \Big) \beta ||\phi - \psi||.$$

Similarly, we have

$$|x(k) - x_*(k)| \le \left(1 - \underline{a} \left(1 - B C_{\varepsilon_0}\right)\right) \beta ||\phi - \psi|| \quad \text{for } k = K_4, K_4 + 1, \dots, K_4 + \overline{\tau}.$$
(3.24)

Using (3.21), (3.22) and (3.24), we obtain

$$|x(K_4 + \overline{\tau} + 1) - x_*(K_4 + \overline{\tau} + 1)| \leq (1 - \underline{a}) \left(1 - \underline{a} (1 - B C_{\varepsilon_0}) \right) \beta ||\phi - \psi||$$
$$+ \underline{a} B C_{\varepsilon_0} \left(1 - \underline{a} (1 - B C_{\varepsilon_0}) \right) \beta ||\phi - \psi||$$
$$\leq \left(1 - \underline{a} (1 - B C_{\varepsilon_0}) \right)^2 \beta ||\phi - \psi||.$$

Similarly, we have

$$|x(k) - x_*(k)| \le \left(1 - \underline{a} \left(1 - B C_{\varepsilon_0}\right)\right)^2 \beta ||\phi - \psi||$$

for $k = K_4 + \overline{\tau} + 1, K_4 + \overline{\tau} + 2, \dots, K_4 + 2\overline{\tau} + 1$. Repeating the same calculation process, we can derive the evaluation formula

$$|x(k) - x_*(k)| \le \left(1 - \underline{a} \left(1 - B C_{\varepsilon_0}\right)\right)^{\mu} \beta ||\phi - \psi||$$

for $k = K_4 + (\mu - 1)(\overline{\tau} + 1), K_4 + (\mu - 1)(\overline{\tau} + 1) + 1, \dots, K_4 + \mu \overline{\tau} + \mu - 1$, where $\mu \in \mathbb{N}$. Note that if k diverges to infinity, then μ also diverges to infinity. From (3.11) it follows that

$$|x(k) - x_*(k)| \le \beta ||\phi - \psi||$$
 for $k \in \mathbb{N}$

and

$$|x(k) - x_*(k)| \to 0 \text{ as } k \to \infty.$$

Hence, from the former we see that the positive period solution $x_*(\cdot; \psi)$ is stable, and from the latter we see that it is globally attractive.

3.4 On the condition of Theorem 3.1

Let us examine when condition (3.1) will be satisfied. Needless to say, the value $C = \max_{A \le u \le B} |f'(u)| \text{ changes depending on the numbers}$

$$A = \min\left\{\sqrt[n]{\gamma - 1}, \ \gamma f(B)\right\} \text{ and } B = \frac{1}{\underline{a}} \sum_{i=1}^{m} \overline{b}_i.$$

The properties of the derivative f' of the production function f were already described in Section 3.3. In particular, we have to take into account of the maximum value 1 and the minimum value

$$-\frac{(n-1)^2}{4\,n}$$

of f'.

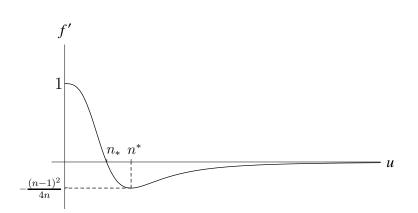


Figure 3.1: This curve is a graph of the derivative f' of the production function f in the case that n is less than $3 + 2\sqrt{2}$. The graph intersects the *u*-axis at $u = n_*$, and takes the minimum value less than 1 at $u = n^*$.

If $1 < n < 3 + 2\sqrt{2}$, then $(n-1)^2/(4n) < 1$ (see Figure 3.1). From the properties of f', six classifications are required. We see that

$$C = \begin{cases} f'(A) & \text{if } A < B \le n_*, \\\\ \max \left\{ f'(A), \ -f'(B) \right\} & \text{if } A \le n_* < B < n^*, \\\\ \max \left\{ f'(A), \ (n-1)^2/(4n) \right\} & \text{if } A \le n_* < n^* \le B, \\\\ -f'(B) & \text{if } n_* < A < B < n^*, \\\\ (n-1)^2/(4n) & \text{if } n_* < A < n^* \le B, \\\\ -f'(A) & \text{if } n^* \le A < B. \end{cases}$$

In either case, the value C is less than 1. Hence, though $B > \gamma > 1$, there is a possibility that condition (3.1) holds.

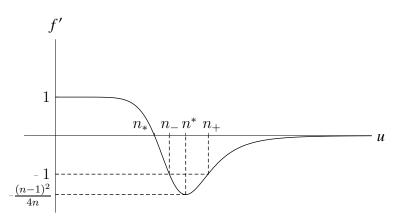


Figure 3.2: This curve is a graph of the derivative f' of the production function f in the case that n is larger than $3+2\sqrt{2}$. The graph intersects the *u*-axis at $u = n_*$, and takes the minimum value larger than 1 at $u = n^*$. The value of the derivative f' becomes -1 at $u = n_-$ and at $u = n_+$.

If $n \ge 3 + 2\sqrt{2}$, then $(n-1)^2/(4n) > 1$ (see Figure 3.2). Let

$$n_{-} = \sqrt[n]{\frac{n-3-\sqrt{n^2-6n+1}}{2}}$$
 and $n_{+} = \sqrt[n]{\frac{n-3+\sqrt{n^2-6n+1}}{2}}$

Then $f'(n_{-}) = f'(n_{+}) = -1$ and

$$-1 < f'(u) \le 1 \quad \text{for } 0 \le u < n_{-},$$

$$-\frac{(n-1)^{2}}{4n} < f'(u) < -1 \quad \text{for } n_{-} < u < n_{+},$$

$$-1 < f'(u) < 0 \quad \text{for } u > n_{+}.$$

Using these inequalities, we see that

$$C = \begin{cases} f'(A) & \text{if } A < B \le n_*, \\ \max \left\{ f'(A), -f'(B) \right\} & \text{if } A \le n_* < B < n_-, \\ -f'(B) & \text{if } A \le n_* < n_- \le B < n^*, \\ (n-1)^2/(4n) & \text{if } A \le n_* < n^* \le B, \\ -f'(B) & \text{if } n_* < A < B < n_-, \\ -f'(B) & \text{if } n_* < A < n_- \le B < n^*, \\ (n-1)^2/(4n) & \text{if } n_* < A < n^* \le B, \\ -f'(A) & \text{if } n_* < A < n^* \le B, \end{cases}$$

In three cases that $A < B \le n_*$, $A \le n_* < B < n_-$ and $n_* < A < B < n_-$, the value C is less than 1, but otherwise it becomes greater than or equals to 1. Hence, only the three cases have the possibility that the condition (1.5) holds. In other cases, condition (1.5) does not hold because neither B nor C are less than 1.

3.5 Examples

Example 3.1. To illustrate Theorem 3.1, we consider the difference equation

$$\Delta x(k) = -a(k)x(k) + \frac{b_1(k)x(k-\tau_1(k))}{1+x^2(k-\tau_1(k))} + \frac{b_2(k)x(k-\tau_2(k))}{1+x^2(k-\tau_2(k))},$$
(3.25)

where

$$a(k) = \begin{cases} 1/2 & \text{if } k = 0, \\ 8/15 & \text{if } k = 1, \\ 8/13 & \text{if } k = 2, \\ 1/2 & \text{if } k = 3, \end{cases}$$

$$b_{1}(k) = \begin{cases} 5/8 & \text{if } k = 0, \\ 4/5 & \text{if } k = 1, \\ 1 & \text{if } k = 2, \\ 7/8 & \text{if } k = 3, \end{cases} \qquad b_{2}(k) = \begin{cases} 1 & \text{if } k = 0, \\ 14/15 & \text{if } k = 1, \\ 1 & \text{if } k = 2, \\ 3/4 & \text{if } k = 3, \end{cases}$$
$$\tau_{1}(k) = \begin{cases} 4 & \text{if } k = 0, \\ 4 & \text{if } k = 1, \\ 3 & \text{if } k = 2, \\ 4 & \text{if } k = 3, \end{cases} \qquad \tau_{2}(k) = \begin{cases} 3 & \text{if } k = 0, \\ 4 & \text{if } k = 1, \\ 3 & \text{if } k = 2, \\ 4 & \text{if } k = 3, \end{cases}$$

and a(k) = a(k+4), $b_i(k) = b_i(k+4)$, $\tau_i(k) = \tau_i(k+4)$ for $k \in \mathbb{Z}$ and i = 1, 2. We will confirm that equation (3.25) can be applied to Theorem 3.1.

First note that m = n = 2 and the production function f is given by

$$f(u) = \frac{u}{1+u^2} \quad \text{for } u \ge 0.$$

Since the coefficients a, b_1, b_2 and the time delays τ_1, τ_2 are 4-period discrete functions, the period ω is 4. These discrete functions satisfy

$$0 < a(k) < 1$$
, $b_1(k) > 0$, $b_2(k) > 0$, $\tau_1(k) > 0$ and $\tau_2(k) > 0$

for $k \in \mathbb{N}$. Let $\gamma = 3 > 1$. Then the inequality

$$\gamma a(k) < b_1(k) + b_2(k)$$

holds for k = 1, 2, 3, 4. Hence, condition (2.5) is satisfied. Since

$$\underline{a} = \min_{1 \le k \le \omega} a(k) = 1/2, \quad \overline{b}_1 = \max_{1 \le k \le \omega} b_1(k) = 1 \text{ and } \overline{b}_2 = \max_{1 \le k \le \omega} b_2(k) = 1,$$

we see that

$$B = \frac{1}{\underline{a}} \left(\overline{b}_1 + \overline{b}_2 \right) = \frac{1+1}{1/2} = 4, \quad \sqrt{\gamma - 1} = \sqrt{2} \quad \text{and} \quad \gamma f(B) = 3 \times \frac{4}{1+4^2} = \frac{12}{17},$$

and therefore,

$$A = \min\left\{\sqrt{\gamma - 1}, \ \gamma f(B)\right\} = \frac{12}{17}.$$

Since

$$n_* = \frac{1}{\sqrt{n-1}} = 1$$
 and $n^* = \sqrt{\frac{n+1}{n-1}} = \sqrt{3}.$

we see that

$$A = \frac{12}{17} < 1 = n_* < n^* = \sqrt{3} < 4 = B.$$

As we have examined in Section 3.4, in this case,

$$C = \max\left\{f'(A), \, \frac{(n-1)^2}{4n}\right\} = \max\left\{\frac{1 - (12/17)^2}{(1 + (12/17)^2)^2}, \, \frac{1}{8}\right\} < 0.23.$$

Hence, we obtain

$$BC < 4 \times 0.23 = 0.92 < 1;$$

namely, condition (3.1).

Thus, we can apply Theorem 3.1 to this example and conclude that equation (3.25) has exactly one positive 4-periodic solution which is globally asymptotically stable. The periodic solution is in the region [12/17, 4]. Indeed, we can use hand

calculations to find the positive periodic solution. Note that

$$\overline{\tau} = \max_{1 \le i \le 2} \left\{ \max_{1 \le k \le 4} \tau_i(k) \right\} = 4.$$

As a set of initial points $\psi(-\overline{\tau}), \psi(-\overline{\tau}+1), \dots, \psi(0)$, we choose

$$\psi(k) = \begin{cases} 2/3 & \text{if } k = -4, \\ 2/3 & \text{if } k = -3, \\ * & \text{if } k = -2, \\ 3/2 & \text{if } k = -1, \\ 3/2 & \text{if } k = 0, \end{cases}$$
(3.26)

where * indicates any positive real number. Then we can calculate as follows:

$$\begin{aligned} x(1) &= \left(1 - a(0)\right) x(0) + \frac{b_1(0)x(0 - \tau_1(0))}{1 + x^2(0 - \tau_1(0))} + \frac{b_2(0)x(0 - \tau_2(0))}{1 + x^2(0 - \tau_2(0))} \\ &= \left(1 - \frac{1}{2}\right) \times \frac{3}{2} + \frac{5}{8} \times \frac{x(0 - 4)}{1 + x^2(0 - 4)} + 1 \times \frac{x(0 - 3)}{1 + x^2(0 - 3)} \\ &= \frac{1}{2} \times \frac{3}{2} + \frac{5}{8} \times \frac{2/3}{1 + 4/9} + 1 \times \frac{2/3}{1 + 4/9} = \frac{3}{2}, \end{aligned}$$

$$\begin{aligned} x(2) &= \left(1 - a(1)\right) x(1) + \frac{b_1(1)x(1 - \tau_1(1))}{1 + x^2(1 - \tau_1(1))} + \frac{b_2(1)x(1 - \tau_2(1))}{1 + x^2(1 - \tau_2(1))} \\ &= \left(1 - \frac{8}{15}\right) \times \frac{3}{2} + \frac{4}{5} \times \frac{x(1 - 4)}{1 + x^2(1 - 4)} + \frac{14}{15} \times \frac{x(1 - 4)}{1 + x^2(1 - 4)} \\ &= \frac{7}{15} \times \frac{3}{2} + \frac{4}{5} \times \frac{2/3}{1 + 4/9} + \frac{14}{15} \times \frac{2/3}{1 + 4/9} = \frac{3}{2}, \end{aligned}$$

$$\begin{aligned} x(3) &= \left(1 - a(2)\right)x(2) + \frac{b_1(2)x(2 - \tau_1(2))}{1 + x^2(2 - \tau_1(2))} + \frac{b_2(2)x(2 - \tau_2(2))}{1 + x^2(2 - \tau_2(2))} \\ &= \left(1 - \frac{8}{13}\right) \times \frac{3}{2} + 1 \times \frac{x(2 - 3)}{1 + x^2(2 - 3)} + 1 \times \frac{x(2 - 3)}{1 + x^2(2 - 3)} \\ &= \frac{5}{13} \times \frac{3}{2} + 1 \times \frac{3/2}{1 + 9/4} + 1 \times \frac{3/2}{1 + 9/4} = \frac{3}{2}, \end{aligned}$$

$$\begin{aligned} x(4) &= \left(1 - a(3)\right)x(3) + \frac{b_1(3)x(3 - \tau_1(3))}{1 + x^2(3 - \tau_1(3))} + \frac{b_2(3)x(3 - \tau_2(3))}{1 + x^2(3 - \tau_2(3))} \\ &= \left(1 - \frac{1}{2}\right) \times \frac{3}{2} + \frac{7}{8} \times \frac{x(3 - 4)}{1 + x^2(3 - 4)} + \frac{3}{4} \times \frac{x(3 - 4)}{1 + x^2(3 - 4)} \\ &= \frac{1}{2} \times \frac{3}{2} + \frac{7}{8} \times \frac{3/2}{1 + 9/4} + \frac{3}{4} \times \frac{3/2}{1 + 9/4} = \frac{3}{2}, \end{aligned}$$

$$\begin{aligned} x(5) &= \left(1 - a(4)\right) x(4) + \frac{b_1(4)x(4 - \tau_1(4))}{1 + x^2(4 - \tau_1(4))} + \frac{b_2(4)x(4 - \tau_2(4))}{1 + x^2(4 - \tau_2(4))} \\ &= \left(1 - \frac{1}{2}\right) \times \frac{3}{2} + \frac{5}{8} \times \frac{x(4 - 4)}{1 + x^2(4 - 4)} + 1 \times \frac{x(4 - 3)}{1 + x^2(4 - 3)} \\ &= \frac{1}{2} \times \frac{3}{2} + \frac{5}{8} \times \frac{3/2}{1 + 9/4} + 1 \times \frac{3/2}{1 + 9/4} = \frac{3}{2}, \end{aligned}$$

$$\begin{aligned} x(6) &= \left(1 - a(5)\right)x(5) + \frac{b_1(5)x(5 - \tau_1(5))}{1 + x^2(5 - \tau_1(5))} + \frac{b_2(5)x(5 - \tau_2(5))}{1 + x^2(5 - \tau_2(5))} \\ &= \left(1 - \frac{8}{15}\right) \times \frac{3}{2} + \frac{4}{5} \times \frac{x(5 - 4)}{1 + x^2(5 - 4)} + \frac{14}{15} \times \frac{x(5 - 4)}{1 + x^2(5 - 4)} \\ &= \frac{7}{15} \times \frac{3}{2} + \frac{4}{5} \times \frac{3/2}{1 + 9/4} + \frac{14}{15} \times \frac{3/2}{1 + 9/4} = \frac{3}{2}, \end{aligned}$$

$$\begin{aligned} x(7) &= \left(1 - a(6)\right)x(6) + \frac{b_1(6)x(6 - \tau_1(6))}{1 + x^2(6 - \tau_1(6))} + \frac{b_2(6)x(6 - \tau_2(6))}{1 + x^2(6 - \tau_2(6))} \\ &= \left(1 - \frac{8}{13}\right) \times \frac{3}{2} + 1 \times \frac{x(6 - 3)}{1 + x^2(6 - 3)} + 1 \times \frac{x(6 - 3)}{1 + x^2(6 - 3)} \\ &= \frac{5}{13} \times \frac{3}{2} + 1 \times \frac{3/2}{1 + 9/4} + 1 \times \frac{3/2}{1 + 9/4} = \frac{3}{2}, \end{aligned}$$

$$\begin{aligned} x(8) &= \left(1 - a(7)\right)x(7) + \frac{b_1(7)x(7 - \tau_1(7))}{1 + x^2(7 - \tau_1(7))} + \frac{b_2(7)x(7 - \tau_2(7))}{1 + x^2(7 - \tau_2(7))} \\ &= \left(1 - \frac{1}{2}\right) \times \frac{3}{2} + \frac{7}{8} \times \frac{x(7 - 4)}{1 + x^2(7 - 4)} + \frac{3}{4} \times \frac{x(7 - 4)}{1 + x^2(7 - 4)} \\ &= \frac{1}{2} \times \frac{3}{2} + \frac{7}{8} \times \frac{3/2}{1 + 9/4} + \frac{3}{4} \times \frac{3/2}{1 + 9/4} = \frac{3}{2}, \end{aligned}$$

and so on. The value x(k) of this solution is the constant 3/2 for $k \in \mathbb{N}$. Hence, we may say that this solution is only one positive 4-period solution $x_*(\cdot; \psi)$ of (3.25)

(see Figure 3.3).

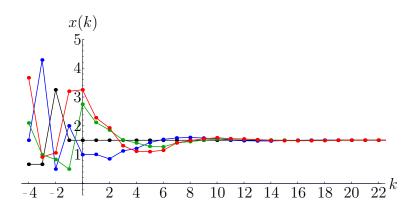


Figure 3.3: These line graphs are trajectories of four solutions of (3.25).

In Figure 3.3, we draw the trajectories of only one periodic solution $x_*(\cdot; \psi)$ and other three solutions $x(\cdot; \phi)$ of (3.25). The periodic solution satisfies the initial condition (3.26), where * = 13/4. The initial conditions of the other solutions $x(\cdot; \phi)$ are

$$\phi(k) = \begin{cases} 2/3 & \text{if } k = -4, \\ 30/7 & \text{if } k = -3, \\ 1/2 & \text{if } k = -2, \\ 2 & \text{if } k = -1, \\ 1 & \text{if } k = 0, \end{cases} \begin{cases} 21/10 & \text{if } k = -4, \\ 1/3 & \text{if } k = -3, \\ 5/6 & \text{if } k = -2, \\ 1/2 & \text{if } k = -2, \\ 1/2 & \text{if } k = -1, \\ 11/4 & \text{if } k = 0, \end{cases} \begin{cases} 11/3 & \text{if } k = -4, \\ 11/12 & \text{if } k = -3, \\ 17/16 & \text{if } k = -2, \\ 16/5 & \text{if } k = -1, \\ 13/4 & \text{if } k = 0, \end{cases}$$

respectively. As can be seen from Figure 3.3, the three solutions $x(\cdot; \phi)$ other than the periodic solution approaches 3/2 while becoming larger or smaller than 3/2. In other words, the three solutions $x(\cdot; \phi)$ gradually approach the periodic solution $x_*(\cdot; \psi)$. Similarly, for any $\phi \in S$, the solution $x(\cdot; \phi)$ of (3.25) approaches the periodic solution $x_*(\cdot; \psi)$; namely, the periodic solution $x_*(\cdot; \psi)$ is globally asymptotically stable.

Example 3.2. In Chapter 2, the practical Example 2.2 based on the actual measurement value of red blood cells is considered. The difference equation is presented

by

$$\Delta x(k) = -a(k)x(k) + \frac{b_1(k)x(k-7)}{1+x^{1.02}(k-7)} + \frac{b_2(k)x(k-7)}{1+x^{1.02}(k-7)},$$
(3.27)

where

$$(k) = \begin{cases} 0.60 & \text{if } k = 0, \\ 0.66 & \text{if } k = 1, \\ 0.60 & \text{if } k = 2, \\ 0.72 & \text{if } k = 3, \\ 0.66 & \text{if } k = 4, \\ 0.60 & \text{if } k = 5, \\ 0.66 & \text{if } k = 6, \end{cases}$$

a

$$b_{1}(k) = \begin{cases} 0.8 \times 10^{6} & \text{if } k = 0, \\ 0.5 \times 10^{6} & \text{if } k = 1, \\ 0.6 \times 10^{6} & \text{if } k = 2, \\ 0.8 \times 10^{6} & \text{if } k = 3, \\ 0.7 \times 10^{6} & \text{if } k = 4, \\ 0.2 \times 10^{6} & \text{if } k = 5, \\ 0.6 \times 10^{6} & \text{if } k = 6, \end{cases} \qquad b_{2}(k) = \begin{cases} 2.2 \times 10^{6} & \text{if } k = 0, \\ 2.8 \times 10^{6} & \text{if } k = 1, \\ 2.4 \times 10^{6} & \text{if } k = 2, \\ 2.8 \times 10^{6} & \text{if } k = 3, \\ 2.6 \times 10^{6} & \text{if } k = 4, \\ 2.8 \times 10^{6} & \text{if } k = 4, \\ 2.8 \times 10^{6} & \text{if } k = 4, \\ 2.8 \times 10^{6} & \text{if } k = 5, \\ 2.7 \times 10^{6} & \text{if } k = 6, \end{cases}$$

and a(k) = a(k+7), $b_1(k) = b_1(k+7)$, $b_2(k) = b_2(k+7)$ for $k \in \mathbb{Z}$. In this example, $m = 2, n = 1.02, \underline{a} = 0.6, \overline{b}_1 = 0.8 \times 10^6$ and $\overline{b}_2 = 2.8 \times 10^6$. The reason that the maximum time delay is equal to 7 is that it takes about 7 days for immature cells to mature into red blood cells within the bone marrow and be released into the blood stream.

Let $\gamma = 4.91887265 \times 10^6$. Then it is easy to check that

$$\gamma a(k) < b_1(k) + b_2(k) \text{ for } k = 1, 2, \dots, 7,$$

that is, condition (2.8) holds. Hence, Theorem 2.1 obtained in Chapter 2 guarantees

that there exists at least one positive 7-periodic solution of (3.27) located within the region [A, B], where

$$B = \frac{1}{\underline{a}} \left(\overline{b}_1 + \overline{b}_2 \right) = \frac{1}{0.6} \left(0.8 \times 10^6 + 2.8 \times 10^6 \right) = 6.0 \times 10^6$$

and

$$A = \min\left\{ \frac{1.02}{\sqrt{\gamma - 1}}, \ \gamma f(B) \right\}$$

= $\min\left\{ \frac{1.02}{\sqrt{4.91887265 \times 10^6 - 1}}, \ 4.91887265 \times 10^6 \times \frac{6.0 \times 10^6}{1 + (6.0 \times 10^6)^{1.02}} \right\}$
= 3.6×10^6 .

By using Theorem 3.1, we can show that the positive 7-periodic solution of (3.25) guaranteed by Theorem 2.1 is unique and the unique periodic solution is globally asymptotically stable. Indeed, since

$$n_* = \sqrt[1.02]{\frac{1}{1.02 - 1}} = 46.30808...$$
 and $n^* = \sqrt[1.02]{\frac{1.02 + 1}{1.02 - 1}} = 92.26159...,$

we see that

$$n_* < n^* < 93 < A < B.$$

Hence, as we have shown in Section 3.4,

$$C = -f'(A) = \frac{0.02 \times (3.6 \times 10^6)^{1.02} - 1}{\left(1 + (3.6 \times 10^6)^{1.02}\right)^2} < 4.2 \times 10^{-9},$$

and therefore,

$$BC < 6.0 \times 10^6 \times 4.2 \times 10^{-9} = 0.0252 << 1.$$

Thus, condition (3.1) is satisfied.

Chapter 4

Global attractivity of a unique positive ω -periodic solution

4.1 Main result

In Chapter 3, we considered the discrete hematopoiesis model

$$\Delta x(k) = -a(k)x(k) + \sum_{i=1}^{m} b_i(k)f(x(k - \tau_i(k)))$$
(H)

with $m \in \mathbb{N}$. Here $a : \mathbb{Z} \to (0, 1), b_i : \mathbb{Z} \to (0, \infty)$ and $\tau_i : \mathbb{Z} \to \mathbb{Z}^+ (1 \le i \le m)$ are ω -periodic discrete functions satisfying periodic relation (2.6). The function fis defined by

$$f(u) = \frac{u}{1+u^n} \quad \text{for } u \ge 0 \text{ and } n > 1.$$

It is obvious that f takes the maximum value $\overline{f} = \sqrt[n]{(n-1)^{n-1}/n^n}$ smaller than 1 when $u = 1/\sqrt[n]{n-1}$. Moreover, the derivative f' satisfies

$$|f'| \le \max\left\{1, \frac{(n-1)^2}{4n}\right\}.$$

Hence, for a given n > 1, the derivative of the production function f is bounded.

We obtained the global asymptotic stability of a unique positive ω -periodic solution of hematopoiesis model (H) through the method of mathematical analysis. In this chapter, we investigate the global attractivity of a unique positive ω -periodic solution of hematopoiesis model (*H*) by a different approach. The Schauder fixed point theorem will be applied.

Theorem 4.1. Suppose that (2.8) holds. Then equation (H) has only one positive ω -periodic solution that is globally attractive.

Remark 4.1. Note that assumptions (2.8) is the condition that guarantee the existence of positive ω -periodic solutions of (*H*). The main result Theorem 4.1 shows that as long as positive ω -periodic solutions exist (maybe only one exists), then all positive periodic solutions are globally attractive.

4.2 Basic fact

Before going the main topic, we will explain that for any positive initial condition (2.7), the solution of (H) is bounded. We have

$$x(k+1) - (1 - a(k))x(k) = \sum_{i=1}^{m} b_i(k)f(x(k - \tau_i(k))).$$

Multiplying both sides of this relationship by $\prod_{r=0}^{k} 1/(1-a(r))$, we get

$$x(k+1)\prod_{r=0}^{k}\frac{1}{1-a(r)}-x(k)\prod_{r=0}^{k-1}\frac{1}{1-a(r)}=\sum_{i=1}^{m}b_{i}(k)f(x(k-\tau_{i}(k)))\prod_{r=0}^{k}\frac{1}{1-a(r)}.$$

Note that $\prod_{r=0}^{-1} 1/(1 - a(r)) = 1$. Sum both sides of this evaluation over k from 0 to k - 1 to obtain

$$x(k)\prod_{r=0}^{k-1}\frac{1}{1-a(r)} - x(0) = \sum_{s=0}^{k-1} \left(\sum_{i=1}^{m} b_i(s)f(x(s-\tau_i(s)))\prod_{r=0}^{s}\frac{1}{1-a(r)}\right).$$

Recall that \overline{f} is the maximum value of the production function f, and a and b_i are ω -periodic discrete functions with the minimum value \underline{a} and the maximum value \overline{b}_i , respectively. From the above equality, we see that

$$\begin{aligned} x(k) &= x(0) \prod_{r=0}^{k-1} (1-a(r)) + \sum_{s=0}^{k-1} \left(\sum_{i=1}^{m} b_i(s) f\left(x(s-\tau_i(s))\right) \prod_{r=s+1}^{k-1} (1-a(r)) \right) \\ &\leq x(0) \prod_{r=0}^{k-1} (1-\underline{a}) + \overline{f} \sum_{i=1}^{m} \overline{b}_i \sum_{s=0}^{k-1} \left(\prod_{r=s+1}^{k-1} (1-a(r)) \right) \\ &\leq x(0) (1-\underline{a})^k + \overline{f} \sum_{i=1}^{m} \overline{b}_i \left((1-\underline{a})^{k-1} + (1-\underline{a})^{k-2} + \dots + (1-\underline{a}) + 1 \right) \\ &= x(0) (1-\underline{a})^k + \overline{f} \sum_{i=1}^{m} \overline{b}_i \frac{1-(1-\underline{a})^k}{\underline{a}} \\ &= \left(x(0) - \frac{\overline{f} \sum_{i=1}^{m} \overline{b}_i}{\underline{a}} \right) (1-\underline{a})^k + \frac{\overline{f} \sum_{i=1}^{m} \overline{b}_i}{\underline{a}} < \max \left\{ x(0), \ \frac{\overline{f} \sum_{i=1}^{m} \overline{b}_i}{\underline{a}} \right\} \end{aligned}$$

for $k \in \mathbb{N}$. Hence, the solution x of (H) with the initial condition (2.7) is bounded. In other words, the solution set for equation (H) consists of bounded discrete functions.

We choose one arbitrarily from the positive ω -periodic solutions whose existence is guaranteed from Theorem 2.1 and name it $x_*(\cdot; \psi)$. Let Ω be a space of bounded discrete functions defined on $[-\overline{\tau}, \infty) \cap \mathbb{Z}$. It is well known that Ω is a Banach space endowed with the norm

$$|||z||| \stackrel{\text{def}}{=} \sup_{k \in [-\overline{\tau}, \infty) \cap \mathbb{Z}} |z(k)| \quad \text{for } z \in \Omega.$$

In fact, we can show that every Cauchy sequence in Ω is convergent. Let $\{z_p\}_{p\in\mathbb{N}}$ be a Cauchy sequence in Ω . For every $\varepsilon > 0$, there exists $\zeta > 0$ such that $|||z_p - z_q||| < \varepsilon$ for $p, q > \zeta$. Hence,

$$|z_p(k) - z_q(k)| \le |||z_p - z_q||| < \varepsilon \text{ for } k \in [-\overline{\tau}, \infty] \cap \mathbb{Z} \text{ and } p, q > \zeta.$$

This means that for each $k \in [-\overline{\tau}, \infty] \cap \mathbb{Z}$, the sequence of real numbers $\{z_p(k)\}_{u \in \mathbb{N}}$ is a Cauchy sequence in the filed \mathbb{R} of real numbers. Since \mathbb{R} is complete, sequence $\{z_p(k)\}_{p \in \mathbb{N}}$ is convergent for each $k \in [-\overline{\tau}, \infty) \cap \mathbb{Z}$. Denote the limit of $\{z_p(k)\}_{u \in \mathbb{N}}$ by $z_{\infty}(k)$ for each $k \in [-\overline{\tau}, \infty) \cap \mathbb{Z}$, then we obtain a function $z_{\infty}(k)$ defined on $[-\overline{\tau}, \infty) \cap \mathbb{Z}$. We now prove the function z_{∞} is the limit of $\{z_p\}_{u \in \mathbb{N}}$. For each $k \in [-\overline{\tau}, \infty] \cap \mathbb{Z}$ and $p, q > \zeta$, we have

$$|z_p(k) - z_{\infty}(k)| = \lim_{q \to \infty} |z_p(k) - z_q(k)| < \varepsilon.$$

Hence,

$$|||z_p - z_{\infty}||| = \sup_{k \ge -\overline{\tau}} |z_p(k) - z_{\infty}(k)| < \varepsilon \quad \text{for } p > \zeta.$$

This leads to z_{∞} is the limit of $\{z_p\}_{u\in\mathbb{N}}$. Since Cauchy sequence $\{z_p\}_{p\in\mathbb{N}}$ in normed space Ω is bounded, the limit z_{∞} is a bounded discrete function on $[-\overline{\tau}, \infty) \cap \mathbb{Z}$. Therefore, we see that $z_{\infty} \in \Omega$. In conclusion, the Cauchy sequence $\{z_p\}_{p\in\mathbb{N}}$ in Ω is convergent in Ω .

Denote by U a subset of Ω in which all the elements z satisfy the following conditions:

(a) there exists an M > 0 such that $|||z||| \le M$;

(b)
$$z(k) \ge -x_*(k;\psi)$$
 for $k \in [-\overline{\tau},\infty) \cap \mathbb{Z}$;

(c) for any $\varepsilon > 0$, there exists a $K(\varepsilon) \in \mathbb{N}$ independent of z such that $|z(k)| < \varepsilon$ for $k \in [K, \infty) \cap \mathbb{N}$.

From condition (c), it is obvious that z satisfies $\lim_{k\to\infty} z(k) = 0$.

We will show U is closed. Let $\{z_j\}_{j\in\mathbb{N}}$ be a convergent function sequence in U and let z_{∞} be the limit function of the sequence $\{z_j\}$. Then it follows from condition (a) that

$$|z_j(k)| \le M$$
 for all $k \in [-\overline{\tau}, \infty) \cap \mathbb{Z}$ and all $j \in \mathbb{N}$. (4.1)

Suppose that $|||z_{\infty}||| = \sup_{k \in [-\bar{\tau},\infty) \cap \mathbb{Z}} |z_{\infty}(k)| > M$. Then there exists a $k_1 \in [-\bar{\tau},\infty) \cap \mathbb{Z}$ such that $|z_{\infty}(k_1)| = \lim_{j\to\infty} |z_j(k_1)| > M$. Hence, there exists a $J_1 \in \mathbb{N}$ such that $|z_j(k_1)| > M$ for all $j \geq J_1$. This contradicts (3.1). Thus, z_{∞} satisfies condition (a). From condition (b), we see that

$$z_j(k) \ge -x_*(k;\psi)$$
 for all $k \in [-\overline{\tau},\infty) \cap \mathbb{Z}$ and all $j \in \mathbb{N}$. (4.2)

Suppose that there exists a $k_2 \in [-\overline{\tau}, \infty) \cap \mathbb{Z}$ such that $z_{\infty}(k_2) = \lim_{j \to \infty} z_j(k_2) < -x_*(k; \psi)$. Then there exists a $J_2 \in \mathbb{N}$ such that $z_j(k_2) < -x_*(k; \psi)$ for all $j \ge J_2$. This contradicts (4.2). Thus, z_{∞} satisfies condition (b). From condition (c), we see that

for any
$$\varepsilon > 0$$
, there exists a $K(\varepsilon) \in \mathbb{N}$ such that
 $|z_j(k)| < \varepsilon$ for all $k \in [K, \infty) \cap \mathbb{N}$ and all $j \in \mathbb{N}$.
$$(4.3)$$

Suppose that z_{∞} dose not satisfy condition (c). Then there exist an $\eta_0 > 0$ and a sequence $\{k_n\}$ with $k_n \in [-\overline{\tau}, \infty) \cap \mathbb{Z}$ and $k_n \to \infty$ as $n \to \infty$ such that $|z_{\infty}(k_n)| = \lim_{j\to\infty} |z_j(k_n)| \ge \eta_0$. Hence, we find a sequence $\{j_n\}$ with $j_n \in \mathbb{N}$ such that $|z_j(k_n)| \ge \eta_0$ for $j \ge j_n$. Since ε is arbitrary, we can choose η_0 as ε in (4.3). However, this is a contradiction. Thus, z_{∞} satisfies condition (c). Hence, we can conclude that z_{∞} belongs to U and U is a closed subset of Ω .

We next show U is convex. To verify this, we choose two elements \hat{z} and \tilde{z} of U arbitrarily. Let $\lambda \in [0, 1]$. From conditions (a) and (c) it follows that

$$|||\lambda \hat{z} + (1-\lambda)\tilde{z}||| = \lambda |||\hat{z}||| + (1-\lambda)|||\tilde{z}||| \le \lambda M + (1-\lambda)M = M$$

and

$$\left(\lambda \hat{z} + (1-\lambda)\tilde{z}\right)(k) \ge -\lambda x_*(k;\psi) - (1-\lambda)x_*(k;\psi) = -x_*(k;\psi) \quad \text{for } k \in [-\overline{\tau},\infty) \cap \mathbb{Z},$$

respectively. From condition (c) it follows that for any $\varepsilon > 0$, there exists a $K(\varepsilon) \in \mathbb{N}$ such that $|\hat{z} < \varepsilon$ and $|\tilde{z} < \varepsilon$ for all $k \in [K, \infty) \cap \mathbb{N}$. Hence, we have

$$|\lambda \hat{z} + (1-\lambda)\tilde{z}(k)| \le \lambda |z(k)| + |(1-\lambda)\tilde{z}(k)| < \lambda \varepsilon + (1-\lambda)\varepsilon = \varepsilon$$

for all $k \in [K, \infty) \cap \mathbb{N}$. Thus, $\lambda \hat{z} + (1 - \lambda) \tilde{z} \in U$. This means that U is a convex subset of Ω .

4.3 Equivalence transformation

Assume that $x(\cdot; \phi)$ is any positive solution of (H), where $\phi \in S$ is the initial function. We pay our attention to the difference between any positive solution $x(\cdot; \phi)$ of (H) and a specific positive ω -period solution $x_*(\cdot; \psi)$ of (H). For simplicity, we write $y(k) = x(k; \phi) - x_*(k; \psi)$ for $k \in [-\overline{\tau}, \infty) \cap \mathbb{Z}$. Define

$$g(w(\cdot)) = f\left(w(\cdot) + x_*(\cdot;\psi)\right) - f\left(x_*(\cdot;\psi)\right).$$

Then we have

$$\Delta y(k) = \Delta x(k;\phi) - \Delta x_*(k;\psi) = -a(k)y(k) + \sum_{i=1}^m b_i(k)g(y(k-\tau_i(k)))$$
(4.4)

for $k \in \mathbb{Z}^+$. It is clear that equation (4.4) has the zero solution, which corresponds to the periodic solution $x_*(\cdot; \psi)$ of (*H*). The global attractivity of the positive ω periodic solution $x_*(\cdot; \psi)$ of (*H*) is equivalent to that of the zero solution of (4.4). Hence, to prove the positive ω -periodic solution $x_*(\cdot; \psi)$ of (*H*) is globally attractive, we have only to show that the zero solution of (4.4) is globally attractive, that is, for any $\phi \in S$,

$$\lim_{k \to \infty} y(k) = 0.$$

4.4 Proof of main result

As explained in the previous section, in order to complete the proof of Theorem 4.1, we only need to prove that y(k) approaches to 0 as $k \to \infty$. We will apply the Schauder fixed point theorem to achieve it.

Proof. For arbitrarily fixed $\phi \in S$ and a given $\psi \in S$, let

$$\varphi(s) = \phi(s) - \psi(s)$$
 for $s = -\overline{\tau}, 1 - \overline{\tau}, \dots, -1, 0.$

By using the same way as in Section 4.2, we can obtain

$$y(k) = \varphi(0) \prod_{r=0}^{k-1} (1 - a(r)) + \sum_{s=0}^{k-1} \left(\sum_{i=1}^{m} b_i(s) g(y(s - \tau_i(s))) \prod_{r=s+1}^{k-1} (1 - a(r)) \right)$$

for $k \in \mathbb{N}$. Considering this evaluation, we define a mapping T on U as follows:

$$Tz(k) = \begin{cases} \varphi(k) & \text{for } k = -\overline{\tau}, 1 - \overline{\tau}, \dots, -1, 0, \\ \varphi(0) \prod_{r=0}^{k-1} (1 - a(r)) + \sum_{s=0}^{k-1} \left(\sum_{i=1}^{m} b_i(s) g(z(s - \tau_i(s))) \prod_{r=s+1}^{k-1} (1 - a(r)) \right) & \text{for } k \in \mathbb{N}. \end{cases}$$

If there is a fixed point z^* of the mapping T, then it is a unique solution y of (4.1) with the initial condition $y(s) = \varphi(s)$ for $s = -\overline{\tau}, 1 - \overline{\tau}, \ldots, -1, 0$. Of course, $z^* \in U$. Hence, it follows from condition (c) of the subset $U \subset \Omega$ that $\lim_{k\to\infty} z^*(k) = 0$, and therefore, y(k) approaches zero as $k \to \infty$. This is our desired conclusion. Therefore, in order to complete the proof, we need to find a fixed point in U.

We will show the existence of a fixed point using the Schauder fixed point theorem. To this end, we have to verify the following three points:

- (i) T is a mapping from U to U;
- (ii) T is continuous;
- (iii) TU is relatively compact.

Proof of point (i): It is sufficient to show that Tz satisfies conditions (a)–(c) in Section 4.2 for each fixed $z \in U$. Let $\widetilde{M} = ||\varphi|| + 2B$, where

$$B = \frac{1}{\underline{a}} \sum_{i=1}^{m} \overline{b}_i > 0.$$

It is clear that $|Tz(k)| = |\varphi(k)| \le ||\varphi|| < \widetilde{M}$ for $k = -\overline{\tau}, 1 - \overline{\tau}, \dots, -1, 0$. Note that

$$\left|g(z(\cdot))\right| \le \left|f(z(\cdot) + x_*(\cdot;\psi))\right| + \left|f(x_*(\cdot;\psi))\right| \le 2\overline{f} < 2.$$

$$(4.5)$$

We have

$$\begin{split} |Tz(k)| &\leq |\varphi(0)| \prod_{r=0}^{k-1} (1-a(r)) + \sum_{s=0}^{k-1} \left(\sum_{i=1}^m b_i(s) \left| g \left(z(s-\tau_i(s)) \right) \right| \prod_{r=s+1}^{k-1} (1-a(r)) \right) \\ &< |\varphi(0)| + 2 \sum_{s=0}^{k-1} \left(\sum_{i=1}^m b_i(s) \prod_{r=s+1}^{k-1} (1-a(r)) \right) \leq |\varphi(0)| + 2 \sum_{i=1}^m \overline{b}_i \sum_{s=0}^{k-1} \prod_{r=s+1}^{k-1} (1-\underline{a}) \\ &= |\varphi(0)| + 2 \sum_{i=1}^m \overline{b}_i \sum_{s=0}^{k-1} (1-\underline{a})^{k-s-1} = |\varphi(0)| + 2 \sum_{i=1}^m \overline{b}_i \frac{1-(1-\underline{a})^k}{\underline{a}} \\ &< ||\varphi|| + 2B = \widetilde{M} \end{split}$$

for $k \in \mathbb{N}$. Hence, we see that $Tz \in \Omega$ and

$$|||Tz||| = \sup_{k \in [-\overline{\tau},\infty) \cap \mathbb{Z}} |Tz(k)| \le \widetilde{M},$$

and therefore, Tz satisfies condition (a).

From the definition of the mapping T and the fact that $\phi \in S$, we see that $Tz(k) = \varphi(k) = \phi(k) - \psi(k) > -\psi(k) = -x_*(k;\psi)$ for $k = -\overline{\tau}, 1 - \overline{\tau}, \dots, -1, 0$. We have

$$x_*(k;\psi) = \psi(0) \prod_{r=0}^{k-1} (1-a(r)) + \sum_{s=0}^{k-1} \left(\sum_{i=1}^m b_i(s) f\left(x_*(s-\tau_i(s);\psi)\right) \prod_{r=s+1}^{k-1} (1-a(r)) \right)$$

for $k \in \mathbb{N}$. Taking into account that

$$g(z(\cdot)) = f\left(z(\cdot) + x_*(\cdot;\psi)\right) - f\left(x_*(\cdot;\psi)\right) \ge -f\left(x_*(\cdot;\psi)\right),$$

we obtain

$$Tz(k) = \varphi(0) \prod_{r=0}^{k-1} (1 - a(r)) + \sum_{s=0}^{k-1} \left(\sum_{i=1}^{m} b_i(s) g(z(s - \tau_i(s))) \prod_{r=s+1}^{k-1} (1 - a(r)) \right)$$

> $-\psi(0) \prod_{r=0}^{k-1} (1 - a(r)) - \sum_{s=0}^{k-1} \left(\sum_{i=1}^{m} b_i(s) f(x_*(s - \tau_i(s); \psi)) \prod_{r=s+1}^{k-1} (1 - a(r)) \right)$
= $-x_*(k; \psi)$

for $k \in \mathbb{N}$. Hence, Tz satisfies condition (b).

The element z of U satisfies condition (c). Hence, for any $\varepsilon > 0$, let

$$K_1(\varepsilon) = K\left(\frac{\varepsilon}{2B\max\left\{1, (n-1)^2/(4n)\right\}}\right) + \overline{\tau}, \tag{4.6}$$

where n is a fixed parameter of the production function f. Then we have

$$|z(k)| < \frac{\varepsilon}{2B \max\left\{1, (n-1)^2/(4n)\right\}} \quad \text{for } k \in [K_1 - \overline{\tau}, \infty) \cap \mathbb{N},$$

By this inequality and the mean value theorem, we have

$$|g(z(s - \tau_i(s)))| = |f(z(s - \tau_i(s)) + x_*(s - \tau_i(s); \psi)) - f(x_*(s - \tau_i(s); \psi))|$$

$$\leq \max\left\{1, \frac{(n-1)^2}{4n}\right\} |z(s - \tau_i(s))| < \frac{\varepsilon}{2B}$$
(4.7)

for $s \in [K_1, \infty) \cap \mathbb{N}$. We can choose a $K_2(\varepsilon) \in \mathbb{N}$ with $K_2 > K_1$ so that

$$\prod_{r=K_1}^{K_2-1} (1-a(r))) < \frac{\varepsilon}{2(|\varphi(0)|+2B)}$$
(4.8)

because 0 < a(k) < 1 for $k \in \mathbb{N}$. Using (4.5), (4.4) and (4.8), we obtain

$$\begin{aligned} |Tz(k)| \\ \leq |\varphi(0)| \prod_{r=0}^{k-1} (1-a(r)) + \sum_{s=0}^{k-1} \left(\sum_{i=1}^{m} b_i(s) |g(z(s-\tau_i(s)))| \prod_{r=s+1}^{k-1} (1-a(r)) \right) \\ = |\varphi(0)| \prod_{r=0}^{k-1} (1-a(r)) + \sum_{s=0}^{K_1-1} \left(\sum_{i=1}^{m} b_i(s) |g(z(s-\tau_i(s)))| \prod_{r=s+1}^{k-1} (1-a(r)) \right) \prod_{r=K_1}^{k-1} (1-a(r)) \\ + \sum_{s=K_1}^{k-1} \left(\sum_{i=1}^{m} b_i(s) |g(z(s-\tau_i(s)))| \prod_{r=s+1}^{k-1} (1-a(r)) \right) \\ \leq |\varphi(0)| \prod_{r=0}^{k-1} (1-a(r)) + 2 \sum_{i=1}^{m} \overline{b}_i \sum_{s=0}^{K_1-1} (1-\underline{a})^{K_1-s-1} \prod_{r=K_1}^{k-1} (1-a(r)) \\ + \sum_{i=1}^{m} \overline{b}_i \sum_{s=K_1}^{k-1} |g(z(s-\tau_i(s)))| (1-\underline{a})^{k-s-1} \end{aligned}$$

$$<|\varphi(0)| \prod_{r=0}^{k-1} (1-a(r)) + 2B \prod_{r=K_1}^{k-1} (1-a(r)) + B \frac{\varepsilon}{2B}$$
$$< (|\varphi(0)| + 2B) \prod_{r=K_1}^{K_2-1} (1-a(r)) + \frac{\varepsilon}{2} < \frac{\varepsilon}{2} + \frac{\varepsilon}{2} = \varepsilon$$

for $k \in [K_2, \infty) \cap \mathbb{N}$. This means that Tz satisfies condition (c).

Proof of point (ii): For any $\varepsilon > 0$, let

$$\delta(\varepsilon) = \frac{\varepsilon}{B \max\left\{1, (n-1)^2/(4n)\right\}}.$$

We arbitrarily choose two elements \hat{z} and \tilde{z} of U that satisfy $|||\hat{z} - \tilde{z}||| < \delta$. It is clear that $T\hat{z}(k) = \varphi(k) = T\tilde{z}(k)$ for $k = -\overline{\tau}, 1 - \overline{\tau}, \dots, -1, 0$. Hence, we see that

$$|||T\hat{z} - T\tilde{z}||| = \sup_{k \in \mathbb{N}} |T\hat{z}(k) - T\tilde{z}(k)|.$$

Using the mean value theorem, we obtain

$$\begin{aligned} |T\hat{z}(k) - T\tilde{z}(k)| \\ &= \left| \sum_{s=0}^{k-1} \left(\sum_{i=1}^{m} b_i(s) \left(g(\hat{z}(s - \tau_i(s))) - g(\tilde{z}(s - \tau_i(s))) \right) \prod_{r=s+1}^{k-1} (1 - a(r)) \right) \right| \\ &= \left| \sum_{s=0}^{k-1} \left(\sum_{i=1}^{m} b_i(s) \left(f(\hat{z}(s - \tau_i(s)) + x_*(s - \tau_i(s); \psi)) - f(\tilde{z}(s - \tau_i(s)) + x_*(s - \tau_i(s); \psi)) \right) \prod_{r=s+1}^{k-1} (1 - a(r)) \right) \right| \\ &\leq \sum_{s=0}^{k-1} \left(\sum_{i=1}^{m} b_i(s) \left| f(\hat{z}(s - \tau_i(s)) + x_*(s - \tau_i(s); \psi)) - f(\tilde{z}(s - \tau_i(s)) + x_*(s - \tau_i(s); \psi)) \right| \prod_{r=s+1}^{k-1} (1 - a(r)) \right) \right| \\ &\leq \max\left\{ 1, \frac{(n-1)^2}{4n} \right\} \sum_{s=0}^{k-1} \left(\sum_{i=1}^{m} b_i(s) \left| \hat{z}(s - \tau_i(s)) - \tilde{z}(s - \tau_i(s)) \right| (1 - a)^{k-s-1} \right) \end{aligned}$$

for $k \in \mathbb{N}$. It holds that

$$\left|\hat{z}(s-\tau_i(s)) - \tilde{z}(s-\tau_i(s))\right| < \delta \text{ for } s \in \mathbb{Z}^+$$

because $|||\hat{z} - \tilde{z}||| < \delta$. Hence, we have

$$\begin{aligned} |T\hat{z}(k) - T\tilde{z}(k)| &< \max\left\{1, \ \frac{(n-1)^2}{4n}\right\}\delta\sum_{i=1}^m \overline{b}_i\sum_{s=0}^{k-1}(1-\underline{a})^{k-s-1} \\ &< B\max\left\{1, \ \frac{(n-1)^2}{4n}\right\}\delta < \varepsilon \end{aligned}$$

for $k \in \mathbb{N}$. This means that T is continuous.

Proof of point (iii): We only need to show that any sequence in TU has a convergent subsequence in Ω . Let $\{z_j\}_{j\in\mathbb{N}}$ be any sequence in U. By using the diagonal method, we will find a convergent subsequence of $\{Tz_j\}$ in Ω .

Let $i \in \{1, 2, ..., m\}$ be fixed arbitrarily. It follows from $z_j \in U$ that $|z_j(0 - \tau_i(0))| \leq M$ for all $j \in \mathbb{N}$, that is, $\{z_j(0 - \tau_i(0))\}$ is a bounded sequence. By the Bolzano-Weierstrass theorem, it has at least one convergent subsequence. Let $\{z_{j,0}\}$ be a subsequence of $\{z_j\}$ such that $\{z_{j,0}(0 - \tau_i(0))\}$ converges. Of course, since $z_{j,0} \in U$, it holds that $|z_{j,0}(1 - \tau_i(1))| \leq M$ for all $j \in \mathbb{N}$. Hence, $\{z_{j,0}(1 - \tau_i(1))\}$ is also bounded and it has a convergent subsequence $\{z_{j,1}(1 - \tau_i(1))\}$. Note that $\{z_{j,1}\}$ is a subsequence of $\{z_{j,0}\}$. Repeating the same process, we can find a set of subsequences $\{z_{j,\ell}\}$ with $\ell \in \mathbb{Z}^+$ so that

$$\{z_j\} \supset \{z_{j,0}\} \supset \{z_{j,1}\} \supset \{z_{j,2}\} \supset \cdots \cdots$$

and $\{z_{j,\ell}(\ell - \tau_i(\ell))\}$ converges.

For any $\ell \in \mathbb{N}$, we take the *j*-th element $z_{j,j}$ out from the subsequence $\{z_{j,\ell}\}$ and denote $\{w_j\}_{j\in\mathbb{N}}$ the new sequence consisting of them. From how to make the sequence $\{w_j\}$, we see that for each $k \in \mathbb{Z}^+$, $\{w_j(k - \tau_i(k))\}$ convergence a limit as $j \to \infty$. Hence, for any $\varepsilon > 0$ and any $k \in \mathbb{Z}^+$, there exists an $J_i(\varepsilon, k) \in \mathbb{N}$ with $i = 1, 2, \ldots, m$ such that if p and q are integers greater than J_i , then

$$|w_p(k - \tau_i(k)) - w_q(k - \tau_i(k))| < \frac{\varepsilon}{B \max\{1, (n-1)^2/(4n)\}}.$$
(4.9)

We show that $J_i(\varepsilon, k)$ is bounded with respect to k. Note that $w_p \in U$ and $w_q \in U$.

From condition (c) of U, we see that there exists a $K(\varepsilon) \in \mathbb{N}$ such that

$$|w_p(k - \tau_i(k))| < \frac{\varepsilon}{2B \max\{1, (n-1)^2/(4n)\}}$$

and

$$|w_q(k - \tau_i(k))| < \frac{\varepsilon}{2B \max\{1, (n-1)^2/(4n)\}}$$

for $k \in [K_1, \infty) \cap \mathbb{N}$, where K_1 is a constant defined by (4.6) that depends only on ε . Note that K_1 dose not depend on p or q. We have

$$|w_p(k - \tau_i(k)) - w_q(k - \tau_i(k))| \le |w_p(k - \tau_i(k))| + |w_q(k - \tau_i(k))| < \frac{\varepsilon}{B \max\{1, (n-1)^2/(4n)\}}$$

for $k \in [K_1, \infty) \cap \mathbb{N}$. Hence, when k is greater than or equal to $K_1(\varepsilon)$, the equality (4.9) holds provided that $p \ge J_i(\varepsilon, K_1)$ and $q \ge J_i(\varepsilon, K_1)$. This means that $J_i(\varepsilon, k)$ can be regarded as $J_i(\varepsilon, K_1)$ for all $k \in [K_1, \infty) \cap \mathbb{N}$. Thus, we concluded that

$$\max_{k\in\mathbb{Z}^+} J_i(\varepsilon,k) = \max J_i(\varepsilon,0), J_i(\varepsilon,1\ldots,J_i(\varepsilon,K_1);$$

namely, $J_i(\varepsilon, k)$ is bounded with respect to k. In other words, $\max_{k \in \mathbb{Z}^+} J_i(\varepsilon, k)$ is determined only by $i \in 1, 2, ..., m$ and $\varepsilon > 0$. Hence, we an represent $\max_{k \in \mathbb{Z}^+} J_i(\varepsilon, k)$ as $J_i(\varepsilon)$.

Let
$$J^*(\varepsilon) = \max_{J_1(\varepsilon), J_2(\varepsilon), \dots, J_m(\varepsilon)}$$
. Then, for $i \in \{1, 2, \dots, m\}$, $p \ge J^*$ and $q \ge J^*$,

$$\sup_{k\in\mathbb{Z}^+} |w_p(k-\tau_i(k)) - w_q(k-\tau_i(k))| < \frac{\varepsilon}{B\max\{1, (n-1)^2/(4n)\}}.$$
(4.10)

It is clear that $Tw_p(k) = \varphi(k) = Tw_q(k)$ for $k = -\overline{\tau}, 1 - \overline{\tau}, \dots, -1, 0$. It follows from (4.8) that

$$|Tw_p(k) - Tw_q(k)| = \left| \sum_{s=0}^{k-1} \left(\sum_{i=1}^m b_i(s) \left(g(w_p(s - \tau_i(s))) - g(w_q(s - \tau_i(s))) \right) \prod_{r=s+1}^{k-1} (1 - a(r)) \right) \right|$$

$$\leq \sum_{s=0}^{k-1} \left(\sum_{i=1}^{m} b_i(s) \left| g \left(w_p(s - \tau_i(s)) \right) - g \left(w_q(s - \tau_i(s)) \right) \right| \prod_{r=s+1}^{k-1} (1 - a(r)) \right)$$

$$\leq \max \left\{ 1, \frac{(n-1)^2}{4n} \right\} \sum_{s=0}^{k-1} \left(\sum_{i=1}^{m} b_i(s) \left| w_p(s - \tau_i(s)) - w_q(s - \tau_i(s)) \right| (1 - \underline{a})^{k-s-1} \right)$$

$$\leq \max \left\{ 1, \frac{(n-1)^2}{4n} \right\} \sup_{k \in \mathbb{Z}^+} \left| w_p(k - \tau_i(k)) - w_q(k - \tau_i(k)) \right| \sum_{i=1}^{m} \overline{b}_i \sum_{s=0}^{k-1} (1 - \underline{a})^{k-s-1}$$

$$< \max \left\{ 1, \frac{(n-1)^2}{4n} \right\} \frac{\varepsilon}{B \max\{1, (n-1)^2/(4n)\}} B = \varepsilon$$

for $k \in \mathbb{N}$. Hence, we can conclude that

$$|||Tw_p - Tw_q||| = \sup_{k \in [-\overline{\tau}, \infty) \cap \mathbb{Z}} |Tw_p(k) - Tz_q(k)| < \varepsilon \quad \text{for } p \ge J^* \text{ and } q \ge J^*.$$

From this inequality, we see that $\{Tw_j\}$ is a Cauchy sequence. As mentioned in Section 4.3, since Ω is a Banach space, $\{Tw_j\}$ is a convergent subsequence of $\{Tz_j\}$ in Ω . Thus, TU is relatively compact.

The points (i)-(iii) were confirmed as shown above. Thanks to the Schauder fixed point theorem, equation (H) has only one positive ω -periodic solution and the positive ω -periodic solution is globally attractive. The proof is complete.

References

- R.P. Agarwal, M. Bohner, S.R. Grace, D. O'Regan, Discrete Oscillation Theory, New York, USA, 2005.
- [2] R.P. Agarwal, S. Arshad, D. O' Regan, V. Lupulescu, A Schauder fixed point theorem in semilinear spaces and applications, Fixed Point Theory Appl. 306 (2013), 13pp.
- [3] L. Berezansky, E. Braverman, L. Idels, Mackey-Glass model of hematopoiesis with non-monotone feedback: stability, oscillation and control, Appl. Math. Comput. 219 (2013) 6268–6283. MR3018470
- [4] J.G. Betts, P. Desaix, E. Johnson, et al., Anatomy & Physiology, OpenStax, Rice University, Houston, 2017.
- [5] T.A. Burton, Stability by Fixed Point Theory for Functional Differential Equations, Dover Publications, Inc., Mineola, New York, 2006.
- [6] T.A. Burton, Bo Zhang, A Schauder-type fixed point theorem, J. Math. Anal. Appl. 417 (2014), 552–558.
- [7] M.C. Dinauer, P.E. Newburger, N. Borregaard, Phagocyte system and disorders of granulopoiesis and granulocyte function, in *Nathan and Oski's Hematology* and Oncology of Infancy and Childhood (eds. S.H. Orkin, D.E. Fisher, D. Ginsburg, A. Thomas, S.E. Lux, D.G. Nathan), 8th Edition, Chap. 22, pp. 773– 847.e29, Elsevier, Philadelphia, 2015.

- [8] P. Fortin, M.C. Mackey, Periodic chronic myelogenous leukemia: Spectral analysis of blood cell counts and aetiological implications, British Journal of Haematology, 104 (1999) 336–345.
- R.E. Gaines, J.L. Mawhin, Coincidence degree, and nonlinear differential equations, Lecture Notes in Mathematics 568, Springer-Verlag, Berlin-New York, 1977. MR0637067 (58 #30551)
- K. Gopalsamy, M.R.S. Kulenović, G. Ladas, Oscillations and global attractivity in models of hematopoiesis, J. Dynam. Differential Equations 2 (1990) 117–132. MR1050639 (91k:92013)
- [11] K. Gopalsamy, S.I. Trofinchuk, N.R. Bantsur, A note on global attractivity in models of hematopoiesis, Ukrainian Math. J. 50 (1998) 3–12. MR1669243 (2000e:92009)
- [12] I. Györi, G. Ladas, Oscillation Theory of Delay Differential Equations with Applications, Oxford Mathematical Monographs, The Clarendon Press, Oxford University Press, New York, 1991. MR1168471 (93m:34109)
- [13] D. Jiang, D. O'Regan, R.P. Agarwal, Optimal existence theory for single and multiple positive periodic solutions to functional difference equations, Appl. Math. Comput. 161 (2005) 441–462. MR2112417 (2005h:39013)
- [14] A. Khastan, J.J. Nieto, R. Rodr'guez-L'opez, Schauder fixed-point theorem in semilinear spaces and its application to fractional differential equations with uncertainty, Fixed Point Theory Appl. 21(2014), 14pp.
- [15] H. Kiskinov, A. Zahariev, S. Zlatev, Permanence of the positive solutions of the generalized hematopoiesis Mackey-Glass model, C. R. Acad. Bulgare Sci. 67 (2014) 745–752. MR3242161
- S.S. Long, Laboratory manifestations of infectious diseases, in *Principles and Practice of Pediatric Infectious Diseases* (eds. S.S. Long, L.K. Pickering, C.G. Prober), 4th Edition, pp. 1400–1412, Elsevier, Edinburgh, 2012.

- [17] S. Lynch, Analysis of a blood cell population model, Internat. J. Bifur. Chaos Appl. Sci. Engrg. 15 (2005) 2311–2316.
- [18] M.C. Mackey, L. Glass, Oscillation and chaos in physiological control system, Science, New Series. 197 (1977) 287–289.
- [19] M. Mohamed, O. Omar, Positive periodic solutions of singular first order functional difference equation, Int. J. Math. Anal. (Ruse) 6 (2012) 2665–2675. MR2975093
- [20] A.J. Nicholson, The balance of animal population, J. Animal Ecology 2 (1933) 132–178.
- [21] S. Padhi, J.R. Graef, P.D.N. Srinivasu, Periodic Solutions of First-Order Functional Differential Equations in Population Dynamics, Springer, New Delhi, 2014. MR3243763
- [22] J. Peypouquet, Convex Optimization in Normed Spaces: Theory, Methods and Examples, Springer, Chile, 2014.
- [23] D. Roos, Neutrophils, in *Encyclopedia of Immunology* (eds. P.J. Delves, I.M. Roitt), 2nd Edition, pp. 1854–1858, Academic Press, New York, 1998.
- [24] G. Rost, On the global attractivity controversy for a delay model of hematopoiesis, Appl. Math. Comput. 190 (2007) 846-850. MR2338758 (2008g:34195)
- [25] S.H. Saker, Oscillation and global attractivity in hematopoiesis model with periodic coefficients, Appl. Math. Comput. 142 (2003) 477–494. MR1979447 (2004c:34204)
- [26] K. Satué, J.C. Gardón, A. Muñoz, Influence of the month of the year in the hematological profile in carthusian broodmares, Hematol. Leuk. 1:6 (2013) pp. 1–6.

- [27] L.-Y. Wang, D.-C. Zhang, B. Shi, X.-Y. Zeng, Oscillation and global asymptotic stability of a discrete hematopoiesis model, J. Appl. Math. Comput. 28 (2008) 1–14.
- [28] P.-X. Weng, Global attractivity of periodic solution in a model of hematopoiesis, Comput. Math. Appl. 44 (2002) 1019–1030.
- [29] L. Wijayasiri, K. McCombe, The Primary FRCA Structured Oral Exam Guide1, 2nd Edition, Taylor & Francis Group, Boca Raton, 2016.
- [30] X.-M. Wu, J.-W. Li, H.-Q. Zhou, A necessary and sufficient condition for the existence of positive periodic solutions of a model of hematopoiesis, Comput. Math. Appl. 54 (2007) 840–849. MR2348268 (2008e:34104)
- [31] M. Xu, B. Shi, D.-C. Zhang, Global behaviour of a discrete haematopoiesis model, Indian J. Pure Appl. Math. 35 (2004) 273–283. MR2046494 (2004k:39050)
- [32] M. Xu, S. Xu, Global behavior of a discrete hematopoiesis model with several delays, Appl. Math. Comput. 217 (2010) 441–449. MR2672605
- [33] Z. Zeng, Existence of positive periodic solutions for a class of nonautonomous difference equations, Electron. J. Differential Equations 2006, No. 3, 18 pp. MR2198916. (2006h:39021)