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A Neutral Equation Arising from Compartmental Systems with Pipes

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We consider compartmental models for the mathematical description of many biological processes in which the material transport between compartments takes a nonnegligible length of time and each compartment produces or swallows materials. The proposed mathematical model is a neutral functional differential equation. We describe some of the global dynamics of the solutions to the linear model equation.

KEY WORDS: Neutral equations; compartmental systems; asymptotic behavior.

1. MODEL EQUATIONS

In theoretical epidemiology, physiology, and population dynamics, compartmental models are frequently used to describe the evolution of systems which can be divided into separate compartments, marking the pathways of material flow between compartments and the possible outflow into and inflow from the environment of the system. Usually the time required for the material flow between compartments cannot be neglected. A model for such system can be visualized as one in which compartments are connected by (imaginary) pipes which material passes through in definite time. Because of the time lags caused by pipes, the model equations for such systems are differential equations with retarded arguments, as opposed to the classical case where model equations are ordinary differential equations. For details, we refer to Jacquez (1972), Anderson (1983), Györi (1986), and the references therein. A concrete example is the radiocardiogram

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based on the model pictured in Fig. 1, where the two compartments correspond to the left and right ventricles of the heart, and the pipes between them represent the pulmonary and systematic circulation. Pipes coming out from and returning into the same compartment may represent shunts and the coronary circulation. See Győri (1982) and Kanyar *et al.* (1981) for details.

In order to make it easier to refer to, we denote by $C_1, \ldots, C_n$ the compartments of a compartmental system, by $x_i(t)$ the amount of the material in compartment C_i at time t, and by C_0 the environment of the compartmental system. We make the following assumptions.

(H1) The change of the amount of material of any compartment C_i, $1 \leqslant i \leqslant n$, in any interval of time equals the difference between the total influx into and the total outflux from C_i in the same time interval.

(H2) The inflow rate of material from the environment C_0 into the compartment C_i at time t is given by the input function $I_i(t)$, $i = 1, \ldots, n$.

(H3) At time $t \geqslant 0$, the rate of material outflow from C_i in the direction of C_j is given by the so-called transport function $g_{ji}(t, x_i(t))$, $j = 0, 1, \ldots, n$ and $i = 1, \ldots, n$.

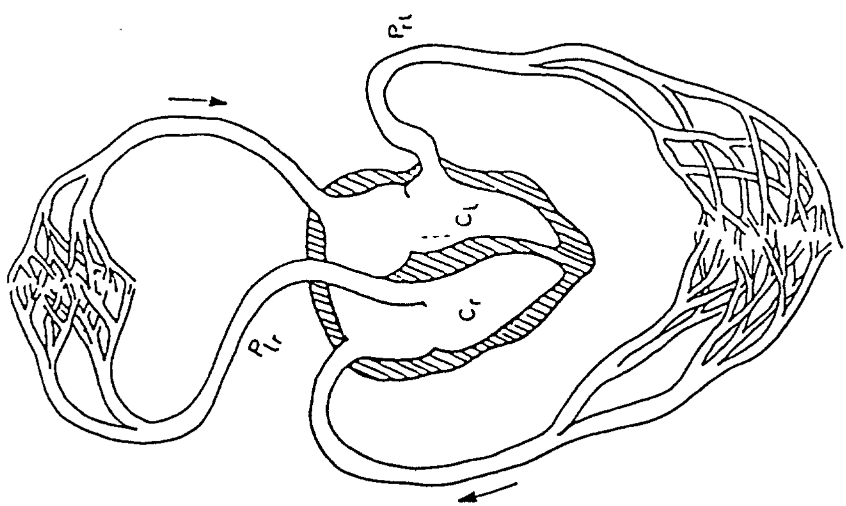

Fig. 1. A pipe-compartmental model of blood circulation.

(H4) Material flows from compartment C_j into compartment C_i through a pipe P_{ij} having a transit time distribution function $F_{ij}(t, s)$, $i=1,\dots, n$, $j=0, 1,\dots, n$, $t \geqslant 0$, $s \geqslant 0$, where a function F: $[0, \infty) \times [0, \infty) \to [0, \infty)$ is called the transit time distribution function of a pipe P, if

(a) $F(t, 0)=0$, $t \geqslant 0$;

(b) for any fixed $t \geqslant 0$, $F(t, s)$ as a function of s is monotone nondecreasing and continuous from the left;

(c) $\lim_{s \to +\infty} F(t, s)=F(t, \infty)=1$, $t \geqslant 0$;

(d) for any fixed $u \geqslant 0$ the function $F(t, t-u)$ is monotone nondecreasing in the variable t, that is,

$$F(t_1, t_1-u) \geqslant F(t_2, t_2-u), \qquad u \geqslant 0, \qquad t_1 > t_2 \geqslant 0$$

(e) the amount of material leaving pipe P until time t is given by $\int_0^\infty \int_{-\infty}^{t-s} h(u)\, du\, d_s F(t, s)$, where $h(t)$ is the rate of inflow into the pipe P for $-\infty < t < +\infty$.

Under these assumptions, one can easily image the situation where material flow between compartments takes place through pipes of definite lengths with definite positive transit time distribution. The schematic picture of such a system is shown in Fig. 2.

The model equation is then

$$\begin{aligned} x_i(t)-x_i(\bar{t}) = &-\sum_{j=0}^{n} \int_{\bar{t}}^{t} g_{ji}(u, x_i(u))\, du \\ &+\sum_{j=1}^{n} \int_0^\infty \int_{-\infty}^{t-s} g_{ij}(u, x_j(u))\, du\, d_s F_{ij}(t, s) \\ &-\sum_{j=1}^{n} \int_0^\infty \int_{-\infty}^{\bar{t}-s} g_{ij}(u, x_j(u))\, du\, d_s F_{ij}(\bar{t}, s) + \int_{\bar{t}}^{t} I_i(t)\, dt \end{aligned}$$

for all $t \geqslant \bar{t} \geqslant 0$. Setting $\bar{t}=0$ and

$$x_i(t)=\varphi_i(t) \qquad \text{for} \quad t \leqslant 0, \quad i=1,\dots, n$$

we obtain the following model equation:

$$\begin{aligned} x_i(t) = C_i(\varphi) &+ \sum_{j=1}^{n} \int_0^\infty \int_{-\infty}^{t-s} g_{ij}(u, x_j(u))\, du\, d_s F_{ij}(t, s) \\ &- \sum_{j=0}^{n} \int_0^t g_{ji}(u, x_i(u))\, du + \int_0^t I_i(t)\, dt \end{aligned}$$

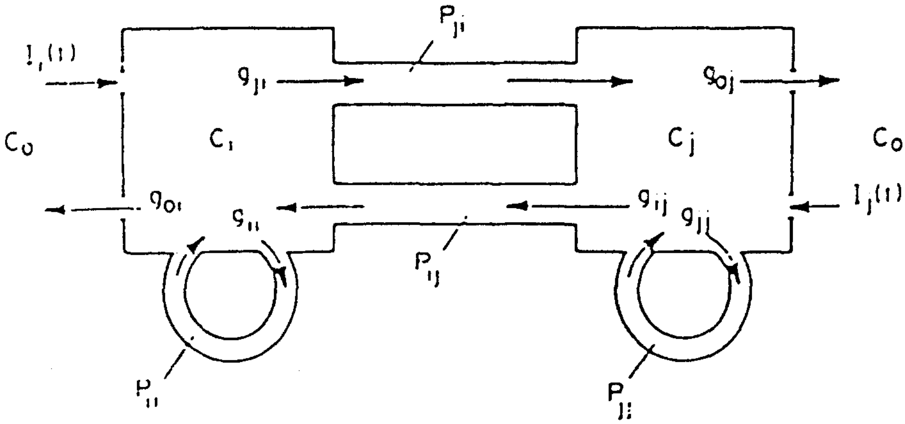

Fig. 2. Schematic of the ith and jth compartments in a compartmental system with pipes.

where

$$C_i(\varphi) = \varphi_i(0) - \sum_{j=1}^{n} \int_0^{\infty} \int_{-\infty}^{-s} g_{ij}(u, \varphi_j(u))\, du\, d_s F_{ij}(0, s)$$

For simplicity, we consider a special case where

$$F_{ij}(t, s) = F_{ij}(s), \qquad t \geqslant 0, \qquad s \geqslant 0, \qquad i = 1,..., n, \qquad j = 0, 1,..., n$$

where $F_{ij}(s)$ is monotone nondecreasing and continuous from the left with $F_{ij}(0) = 0$ and $F_{ij}(\infty) = 1$. In this case, the model equation becomes

$$\begin{aligned} x_i(t) = C_i(\varphi) &- \sum_{j=0}^{n} \int_0^t g_{ji}(u, x_i(u))\, du \\ &+ \sum_{j=1}^{n} \int_0^{\infty} \int_{-\infty}^{t-s} g_{ij}(u, x_j(u))\, du\, dF_{ij}(s) + \int_0^t I_i(u)\, du \qquad (1.1) \end{aligned}$$

for $t \geqslant 0$, $i = 1,..., n$. We now make the following assumption, which is the major difference between our model equation and those investigated by Araki-Mori (1979), Bellman (1970, 1971), Brown and Godfrey (1979), Györi and Eller (1981), Györi (1982, 1986), Lewis and Anderson (1980), Mazanov (1976), and Ohta (1981).

(H5) Each compartment is "active" in the sense that at the moment t some material is produced or swallowed by each compartment.

We can interpret this flow of material as a part of the net inflow rate $I_i(t)$ of material from the environment into the compartment C_i, and hence we assume that $I_i(u)$ satisfies

$$\int_0^t I_i(u)\,du = \int_{-\infty}^t S_i(u, x_i(u))\,dG_i(t-u) + \int_0^t h_i(u)\,du \tag{1.2}$$

where S_i: $[0, \infty) \times [0, \infty) \to (-\infty, +\infty)$, G_i: $[0, \infty) \to (-\infty, +\infty)$, and h_i: $[0, \infty) \to (-\infty, +\infty)$ are given continuous functions. Substituting (1.2) into (1.1) and taking derivatives, we obtain the following neutral functional differential equation:

$$\frac{d}{dt}\left[x_i(t) - \int_0^\infty S_i(t-u, x_i(t-u))\,dG_i(u)\right]$$
$$= -\sum_{j=0}^{n} g_{ji}(t, x_i(t)) + \sum_{j=1}^{n} \int_0^\infty g_{ij}(t-s, x_j(t-s))\,dF_{ij}(s) + h_i(t) \tag{1.3}$$

for all $t \geqslant 0$.

If S_i is identically zero, Eq. (1.3) is reduced to a retarded integro-differential equation which has been widely investigated in the literature [see Györi and Eller (1981), Györi (1982, 1986), and references therein for details]. In this situation, the compartments are "passive," which means that they do not produce and swallow material, and therefore the law of the mass conservation holds true.

In the case where S_i is not identically zero, $\int_{-\infty}^t S_i(u, x_i(u))\,dG_i(t-u)$ represents the net amouont of material produced ($S_i > 0$) or swallowed ($S_i < 0$) by the compartment C_i during the time interval $[0, t]$. Such a system can be visualized as one in which there exists a pipe T_i setting out off and returning to the compartment C_i which the produced or swallowed material passes through. In such a situation, G_i can be regarded as the transit time distribution function for the pipe T_i, and thus G_i is monotone nondecreasing and continuous from the left with $G_i(0) = 0$ and $G_i(\infty) = 1$, where $i = 1,..., n$.

The major purpose of this paper is to propose the model equation (1.3) for "active" compartmental systems and to make a start at the study of the qualitative analysis of such a model equation.

2. QUALITATIVE ANALYSIS OF LINEAR MODELS

In this section, we describe some qualitative properties of solutions to linear model equations. Of major interest is the stability and asymptotic stability problem. This problem has significance from the viewpoint of theory and application. In application, due to the self-regulating feature, a biological system endeavors to get to an equilibrium state which appears, in the model equation, as the model equation possesses an equilibrium point and the solution tends to such an equilibrium point as $t \to \infty$. Theoretically, if the equilibrium state of the system is asymptotically stable, then the knowledge of the equilibrium state and the numerical solution on a finite interval allows one to make an inference for the infinite interval.

We make the following assumption in our model equation (1.3):

(H6) $g_{ij}(t, x_j) = a_{ij} x_j$ and $S_i(t, x_i) = b_i x_i$, where a_{ij}, b_i are constants, and $a_{ij} \geqslant 0$, $i = 1,..., n$, $j = 0, 1,..., n$.

Let

$$\lambda_i = \sum_{j=0}^{n} a_{ji}$$

$$r_{ij}(s) = a_{ij} F_{ij}(s)$$

$$u_i(s) = b_i G_i(s) \qquad \text{for} \qquad 1 \leqslant i, j \leqslant n \qquad \text{and} \qquad s \geqslant 0$$

Then we have

(i) $r_{ij}(s)$, $1 \leqslant i, j \leqslant n$, are monotone nondecreasing functions on $[0, \infty)$ with $r_{ij}(0) = 0$, $r_{ij}(\infty) < \infty$.

With respect to $u_i(s)$, we assume that

(H7) $u_i(s)$, $1 \leqslant i \leqslant n$, are monotone nondecreasing functions on $[0, \infty)$ with $u_i(0) = 0$, $u_i(\infty) < 1$.

We further assume the following continuity conditions:

(H8) for any continuous function $x: R \to R$, the functions $\int_0^{+\infty} x(t-s)\, du_i(s)$ and $\int_0^{+\infty} x(t-s)\, dr_{ij}(s)$, $i, j = 1,..., n$, are continuous for all $t \in [0, \infty)$; and

(H9) $h_i(t)$, $1 \leqslant i \leqslant n$, are continuous functions on $[0, \infty)$.

Under the above assumptions, Eq. (1.3) can be written as

$$\frac{d}{dt}\left[x_i(t) - \int_0^{+\infty} x_i(t-s)\, du_i(s)\right]$$
$$= -\lambda_i x_i(t) + \int_0^{+\infty} \sum_{j=1}^{n} x_j(t-s)\, dr_{ij}(s) + h_i(t) \tag{2.1}$$

According to Wu (1986, 1987) and Wang and Wu (1985), for any $\varphi=(\varphi_1,..., \varphi_n)$, $\varphi_i \in BC((-\infty, 0], R)$, the set of bounded continuous functions on $(-\infty, 0]$, there exists a unique function $x=(x_1,..., x_n)$: $(-\infty, +\infty) \to R^n$ such that $x_i(t) = \varphi_i(t)$ for $t \leqslant 0$, $x_i(t)-\int_0^\infty x_i(t-s)\, du_i(s)$ is differentiable on $[0, \infty)$ and (2.1) holds for all $t \geqslant 0$. Throughout this section, we assume that solutions of Eq. (2.1) satisfy the following property: $x_i(t) \geqslant 0$ and $x_i(t)-\int_0^\infty x_i(t-s)\, du_i(s) \geqslant 0$ for $t \geqslant 0$ and $i=1,..., n$, provided that $\varphi_i(s) \geqslant 0$ for all $s \leqslant 0$ and $\varphi_i(0)-\int_0^\infty \varphi_i(-s)\, du_i(s) \geqslant 0$ for $i=1,..., n$. In the next section, we investigate this property.

Our first result describes the stability and boundedness of solutions.

Theorem 2.1. *If there exist positive constants $a_1,..., a_n$ such that*

$$\lambda_i-\sum_{j=1}^{n} \frac{|\bar{r}_{ij}|(\infty)}{1-u_j(\infty)} \frac{a_i}{a_j} \geqslant 0 \tag{2.2}$$

where

$$|\bar{r}_{ij}|(\infty)=\begin{cases} r_{ij}(\infty), & 1 \leqslant i \neq j \leqslant n \\ \int_0^\infty d\,|r_{ii}(s)-\lambda_i u_i(s)|, & 1 \leqslant i=j \leqslant n \end{cases}$$

then we have the following conclusions:

(i) if $h_i(t)=0$ for $i=1,..., n$ and $t \geqslant 0$, then the zero solution of Eq. (2.1) is stable; and

(ii) if $\int_0^\infty |h_i(t)| < +\infty$, then all solutions of Eq. (2.1) are bounded.

Proof. Let

$$V(t)=\max_{1 \leqslant i \leqslant n} \left\{a_i \left[x_i(t)-\int_0^\infty x_i(t-s)\, du_i(s)\right]\right\}$$

and

$$W(t)=\max\{V(t), \max_{1 \leqslant j \leqslant n} a_j(1-u_j(\infty))\, \|\varphi_j\|\}$$

where

$$\|\varphi_i\|=\sup_{s \leqslant 0} |\varphi_i(s)|$$

If at moment $t>0$, we have $W(s) \leqslant W(t)$ for $s \in [0, t]$, then only two cases may occur.

Case 1. $W(t) = \max_{1 \leqslant j \leqslant n} a_j(1-u_j(\infty)) \|\varphi_j\|$ and

$$\max_{1 \leqslant j \leqslant n} \{a_j(1-u_j(\infty)) \|\varphi_j\|\} > V(t)$$

In this case, by the continuity of V, we have $W(\tau) = \max_{1 \leqslant j \leqslant n}\{a_j(1-u_j(\infty)) \|\varphi_j\|\}$ for $\tau \geqslant t$ and close to t. Therefore $\dot{W}^+(t)=0$, where

$$\dot{W}^+(t) = \overline{\lim_{t \to t^+}} \frac{W(\tau)-W(t)}{\tau - t}$$

Case 2. $W(t) = V(t) \geqslant \max_{1 \leqslant i \leqslant n}(1-u_i(\infty))\, a_i \|\varphi_i\|$.

According to the definition of $\dot{W}^+(t)$, we can find a sequence $\{t_k\}$ such that $t_k \to 0^+$ as $k \to \infty$ and

$$\dot{W}^+(t) = \lim_{k \to \infty} \frac{W(t+t_k)-W(t)}{t_k}$$

If there exist infinitely many t_k such that

$$W(t+t_k) = \max_{1 \leqslant j \leqslant n} (1-u_j(\infty))\, a_j \|\varphi_j\|$$

then

$$\dot{W}^+(t) = \lim_{k \to \infty} \frac{\max_{1 \leqslant j \leqslant n}(1-u_j(\infty))\, a_j \|\varphi_j\| - W(t)}{t_k}$$

Noting that $W(t) = V(t) \geqslant \max_{1 \leqslant j \leqslant n}(1-u_j(\infty))\, a_j \|\varphi_j\|$, we obtain $\dot{W}^+(t) \leqslant 0$.

If there are infinitely many t_k such that $W(t+t_k) = V(t+t_k) \neq \max_{1 \leqslant j \leqslant n}[1-u_j(\infty)]\, a_j \|\varphi_j\|$, then we have

$$\dot{W}^+(t) = \lim_{k \to \infty} \frac{V(t+t_k)-V(t)}{t_k}$$

Let $J = \{j;\ 1 \leqslant j \leqslant n,\ a_j[x_j(t) - \int_0^\infty x_j(t-s)\, du_j(s)] = V(t)\}$. Then J is a finite set, and thus we can find an integer $m \in J$ and a subsequence of $\{t_k\}$ (denoted by $\{t_k\}$ for simplicity) so that

$$\begin{aligned}
\dot{W}^+(t) &= \lim_{k \to \infty} \frac{a_m[x_m(t+t_k) - \int_0^{+\infty} x_m(t+t_k-s)\, du_m(s)] - V(t)}{t_k} \\
&\leqslant \frac{d}{dt}\left\{a_m\left[x_m(t) - \int_0^{+\infty} x_m(t-s)\, du_m(s)\right]\right\} \\
&\leqslant a_m\left\{-\lambda_m\left[x_m(t) - \int_0^{\infty} x_m(t-s)\, du_m(s)\right]\right. \\
&\quad \left. + \sum_{j=1}^{n} \int_0^{+\infty} x_j(t-s)\, d|\bar{r}_{mj}|(s) + h_m(t)\right\} \\
&= a_m\left[-\frac{\lambda_m}{a_m} V(t) + \sum_{j=1}^{n} \int_0^{+\infty} x_j(t-s)\, d|\bar{r}_{mj}|(s) + h_m(t)\right]
\end{aligned}$$

On the other hand,

$$W(s) = \max\{V(s), \max_{1 \leqslant j \leqslant n} a_j(1-u_j(\infty))\|\varphi_j\|\} \leqslant W(t) = V(t)$$

for $s \in [0, t]$ implies that

$$a_j\left[x_j(s) - \int_{-\infty}^{s} x_j(s-u)\, du_j(u)\right] \leqslant V(t) \qquad \text{for} \quad 0 \leqslant s \leqslant t$$

Therefore if these exists $\tau \in [0, t]$ such that $x_j(\tau) = \sup_{-\infty < s \leqslant t} x_j(s)$, then

$$x_j(\tau) \leqslant \int_0^{+\infty} x_j(\tau - s)\, du_j(s) + \frac{V(t)}{a_j}$$

which implies that

$$x_j(\tau) \leqslant \frac{1}{1-u_j(\infty)} \cdot \frac{V(t)}{a_j}$$

Moreover, if there exists no $\tau \in [0, t]$ such that $x_j(\tau) = \sup_{-\infty < s \leqslant t} x_j(s)$, then obviously

$$x_j(s) \leqslant \|\varphi_j\| \leqslant \frac{V(t)}{a_j(1-u_j(\infty))} \qquad \text{for} \quad s \leqslant t$$

In summary, we have

$$\sup_{-\infty < s \leqslant t} x_j(s) \leqslant \frac{V(t)}{a_j(1-u_j(\infty))}$$

and hence

$$\sum_{j=1}^{n} \int_0^{\infty} x_j(t-s)\, d|\bar{r}_{mj}|\,(s) \leqslant \sum_{j=1}^{n} \frac{|\bar{r}_{mj}|\,(\infty)}{a_j(1-u_j(\infty))} V(t)$$

Therefore

$$\dot{W}^+(t) = -\left[\lambda_m - \sum_{j=1}^{n} \frac{a_m |\bar{r}_{mj}|\,(\infty)}{a_j(1-u_j(\infty))}\right] V(t) + a_m h_m(t) \leqslant a_m h_m(t)$$

So, in both case 1 and case 2, we have shown that if at the moment $t > 0$, $W(s) \leqslant W(t)$ is satisfied for $s \in [0, t]$, then $\dot{W}^+(t) \leqslant \max_{1 \leqslant m \leqslant n} a_m |h_m(t)|$. Therefore, by the well-known comparison principle in the theory of functional differential equations (cf. Lakshmikantham and Leela, 1969), we obtain that

$$W(t) \leqslant W(0) + \max_{1 \leqslant m \leqslant n} a_m \int_0^t |h_m(t)|\, dt, \qquad t \geqslant 0$$

This implies that

$$V(t) \leqslant W(0) + \max_{1 \leqslant m \leqslant n} a_m \int_0^t |h_m(s)|\, ds, \qquad t \geqslant 0$$

and hence

$$|x_i(t)| \leqslant \frac{1}{1-u_i(\infty)} \cdot \frac{1}{a_i}\left[W(0) + \max_{1 \leqslant m \leqslant n} a_m \int_0^t |h_m(s)|\, ds\right] + \|\varphi_i\|, \qquad t \geqslant 0$$

Therefore our conclusions follow from the inequality

$$W(0) \leqslant \max\left\{\max_{1 \leqslant i \leqslant n} a_i\left[\varphi_i(0) - \int_0^{\infty} \varphi_i(-s)\, du_i(s)\right], \max_{1 \leqslant i \leqslant n} a_i[1-u_i(\infty)]\, \|\varphi_i\|\right\}$$

The proof is complete.

Theorem 2.2. *Suppose that*

(i) $\lambda_i - \Sigma_{j=1}^{n} r_{ji}(0) = \beta_i \geqslant 0$, $1 \leqslant i \leqslant n$,

(ii) $|h_i| \in L^1[0, \infty)$, *and*

(iii) $\int_0^{+\infty} s dr_{ij}(s) < +\infty$ *for* $i, j = 1, \ldots, n$.

Then we have the following conclusions:

(a) *all solutions of Eq. (2.1) are bounded;*

(b) *if $\beta_i > 0$ for $i = 1,..., n$, then $\int_0^\infty |x_i(t)|\, dt < +\infty$ for $1 \leqslant i \leqslant n$; and*

(c) *if $h_i(t) \equiv 0$ for $1 \leqslant i \leqslant n$ and $t \geqslant 0$, and $\beta_i > 0$ for $1 \leqslant i \leqslant n$, then $x_i(t) \to 0$ as $t \to \infty$ for all $i = 1,..., n$.*

Proof. Integrating Eq. (2.1), we get

$$x_i(t) - \int_0^\infty x_i(t-s)\, du_i(s) = \varphi_i(0) - \int_0^\infty \varphi_i(-s)\, du_i(s) - \lambda_i \int_0^t x_i(s)\, ds + \int_0^t \int_0^{+\infty} \sum_{j=1}^n x_j(u-s)\, dr_{ij}(s)\, du + \int_0^t h_i(s)\, ds$$

Noticing that

$$\begin{aligned}
&\int_0^t \int_0^\infty x_j(u-s)\, dr_{ij}(s)\, du \\
&= \int_0^t \int_0^u x_j(u-s)\, dr_{ij}(s)\, du + \int_0^t \int_u^\infty x_j(u-s)\, dr_{ij}(s)\, du \\
&= \int_0^t \int_0^u x_j(u-s)\, dr_{ij}(s)\, du + \int_0^t \int_u^\infty \varphi_j(u-s)\, dr_{ij}(s)\, du \\
&= \int_0^t \int_s^t x_j(u-s)\, du\, dr_{ij}(s) + \int_0^t \int_u^\infty \varphi_j(u-s)\, dr_{ij}(s)\, du \\
&= \int_0^t \int_0^t x_j(v)\, dv\, dr_{ij}(s) - \int_0^t \int_{t-s}^t x_j(v)\, dv\, dr_{ij}(s) \\
&\quad + \int_0^t \int_u^\infty \varphi_j(u-s)\, dr_{ij}(s)\, du
\end{aligned}$$

We obtain

$$\begin{aligned}
&x_i(t) - \int_0^\infty x_i(t-s)\, du_i(s) + \lambda_i \int_0^t x_i(s)\, ds - \sum_{j=1}^n \int_0^t x_j(v)\, dvr_{ij}(t) \\
&= \varphi_i(0) - \int_0^\infty \varphi_i(-s)\, du_i(s) + \int_0^t h_i(s)\, ds \\
&\quad + \sum_{j=1}^n \int_0^t \int_u^\infty \varphi_j(u-s)\, dr_{ij}(s)\, du - \sum_{j=1}^n \int_0^t \int_{t-s}^t x_j(v)\, dv\, dr_{ij}(s) \qquad (2.3)
\end{aligned}$$

from which it follows that

$$\sum_{i=1}^{n}\left[x_i(t)-\int_0^\infty x_i(t-s)\,du_i(s)\right]+\sum_{i=1}^{n}\int_0^t\left[\lambda_i-\sum_{j=1}^{n}r_{ji}(v)\right]x_i(v)\,dv$$

$$\leqslant\sum_{i=1}^{n}\left[\varphi_i(0)-\int_0^\infty\varphi_i(-s)\,du_i(s)\right]+\sum_{i=1}^{n}\int_0^t h_i(s)\,ds$$

$$+\sum_{i=1}^{n}\sum_{j=1}^{n}\int_0^t\int_u^\infty\varphi_j(u-s)\,dr_{ij}(s)\,du \tag{2.4}$$

On the other hand,

$$\int_0^t\int_u^\infty\varphi_j(u-s)\,dr_{ij}(s)\,du=\int_0^t\int_0^s\varphi_j(u-s)\,du\,dr_{ij}(s)$$

$$+\int_t^\infty\int_0^t\varphi_j(u-s)\,du\,dr_{ij}(s)$$

$$\leqslant\int_0^t sdr_{ij}(s)\,\|\varphi_j\|+\int_t^\infty tdr_{ij}(s)\,\|\varphi_j\|$$

$$\leqslant\int_0^\infty sdr_{ij}(s)\,\|\varphi_j\| \tag{2.5}$$

and

$$x_i(t)-\int_0^\infty x_i(t-s)\,du_i(s)\,ds\geqslant 0\qquad\text{for}\quad t\geqslant 0,\ i=1,\ldots,n$$

Then from inequality (2.4), it follows that

$$\sum_{i=1}^{n}\left[x_i(t)-\int_0^\infty x_i(t-s)\,du_i(s)\right]\leqslant M(\varphi)\qquad\text{for}\quad t\geqslant 0 \tag{2.6}$$

where

$$M(\varphi)=\sum_{i=1}^{n}\left[\varphi_i(0)-\int_0^\infty\varphi_i(-s)\,du_i(s)\right]+\sum_{i=1}^{n}\int_0^t h_i(s)\,ds$$

$$+\sum_{i=1}^{n}\sum_{j=1}^{n}\int_0^\infty sdr_{ij}(s)\,\|\varphi_j\|$$

Equation (2.6) implies that

$$x_i(t)\leqslant\frac{M(\varphi)}{1-u_i(\infty)}+\|\varphi_i\|\qquad\text{for all}\quad t\geqslant 0$$

and thus (a) is proved.

If $\beta_i > 0$, from inequality (2.4) it follows that

$$\sum_{i=1}^{n} \beta_i \int_0^t x_i(v)\, dv \leqslant M(\varphi)$$

Therefore, since $x_i(t) \geqslant 0$ for all t, we have

$$\int_0^\infty x_i(v)\, dv \leqslant \frac{1}{\beta_i} M(\varphi)$$

which implies (b).

To prove (c), we consider the integral $\int_0^\infty \int_0^\infty x_j(t-s)\, dt\, dr_{ij}(s)$. By interchanging the order of integration, we have

$$\begin{aligned}
&\int_0^\infty \int_0^\infty x_j(t-s)\, dt\, dr_{ij}(s) \\
&\quad = \int_0^\infty \int_0^t x_j(t-s)\, dr_{ij}(s)\, dt + \int_0^\infty \int_t^\infty \varphi_j(t-s)\, dr_{ij}(s)\, dt \\
&\quad = \int_0^\infty \int_s^\infty x_j(t-s)\, dt\, dr_{ij}(s) + \int_0^\infty \int_t^\infty \varphi_j(t-s)\, dr_{ij}(s)\, dt \\
&\quad \leqslant r_{ij}(\infty) \int_0^\infty x_j(v)\, dv + \int_0^\infty s dr_{ij}(s)\, \|\varphi_j\|
\end{aligned}$$

and thus

$$\begin{aligned}
-\lambda_i \int_0^\infty x_i(t)\, dt &\leqslant \int_0^\infty \frac{d}{dt}\left[x_i(t) - \int_0^\infty x_i(t-s)\, du_i(s)\right] dt \\
&= -\int_0^\infty \lambda_i x_i(t)\, dt + \int_0^\infty \int_0^\infty \sum_{j=1}^{n} x_j(t-s)\, dr_{ij}(s)\, dt \\
&\leqslant -\lambda_i \int_0^\infty x_i(t)\, dt + \sum_{j=1}^{n} r_{ij}(\infty) \int_0^\infty x_j(v)\, dv \\
&\qquad + \sum_{j=1}^{n} \int_0^\infty s dr_{ij}(s)\, \|\varphi_j\|
\end{aligned}$$

which implies that

$$\frac{d}{dt}\left[x_i(t) - \int_0^\infty x_i(t-s)\, du_i(s)\right] \in L^1[0, \infty)$$

and thus

$$\lim_{t \to \infty} \left[x_i(t) - \int_0^\infty x_i(t-s)\, du_i(s) \right] = C_i < \infty$$

exists. Consider now the difference

$$y_i(t) = x_i(t) - \frac{C}{1 - u_i(\infty)}$$

Evidently, $\lim_{t \to \infty} [y_i(t) - \int_0^\infty y_i(t-s)\, du_i(s)] = 0$. Let

$$y_i(t) - \int_0^\infty y_i(t-s)\, du_i(s) = h(t)$$

For any $\varepsilon > 0$, choose $T > 0$ sufficiently large so that

$$|h(t)| + \left| \int_T^\infty y_i(t-s)\, du_i(s) \right| < \varepsilon \qquad \text{for all} \quad t \geqslant T$$

Therefore, for all $t \geqslant T$, we have

$$|y_i(t)| \leqslant \left| \int_0^T y_i(t-s)\, du_i(s) \right| + \varepsilon$$

$$\leqslant u_i(\infty) \sup_{t-T \leqslant s \leqslant t} |y_i(s)| + \varepsilon$$

Choose $t_n \in I_n = [nT, (n+1)T]$ so that

$$|y_i(t_n)| = \max_{t \in I_n} |y_i(t)|$$

then

$$|y_i(t_n)| \leqslant \varepsilon + u_i(\infty)\, |y_i(t_{n-1})|$$

if there exists $u \in [t_n - T, nT]$ with $|y_i(u)| = \max_{t \in [t_n - T, nT]} |y_i(t)|$, or

$$|y_i(t_n)| \leqslant \varepsilon + |y_i(t_n)|\, u_i(\infty) \tag{2.7}$$

if $\max_{s \in [t_n - nT, t_n]} |y_i(t)| = \max_{t \in [nT, t_n]} |y_i(t)|$. Therefore, if $|y_i(t_{n-1})| \leqslant \varepsilon/[1 - u_i(\infty)]$, then $|y_i(t_n)| \leqslant \varepsilon/[1 - u(\infty)]$, and hence $|y_i(t_k)| \leqslant \varepsilon/[1 - u_i(\infty)]$ for all $k \geqslant n-1$. If $|y_i(t_n)| > \varepsilon/[1 - u_i(\infty)]$, then $|y_i(t_n)| \leqslant \varepsilon + u_i(\infty)\, |y_i(t_{n-1})|$. This implies that either there exists a positive integer K such that

$$|y_i(t_k)| \leqslant \frac{\varepsilon}{1 - u_i(\infty)} \qquad \text{for all} \quad k \geqslant K \tag{2.8}$$

or

$$|y_i(t_n)| \leqslant \varepsilon + u_i(\infty)\, |y_i(t_{n-1})| \qquad \text{for} \quad n = 1, 2, \ldots \tag{2.9}$$

In the latter case, we have

$$\begin{aligned} |y_i(t_n)| &\leqslant \varepsilon + u_i(\infty)[\varepsilon + u_i(\infty)\, |y_i(t_{n-2})|] \\ &\leqslant \cdots \\ &\leqslant \varepsilon[1 + u_i(\infty) + \cdots + u_i^n(\infty)] + u_i^{n+1}(\infty)\, M(\varphi)] \\ &\leqslant \frac{\varepsilon}{1 - u_i(\infty)} + u_i^{n+1}(\infty)\, M(\varphi) \end{aligned}$$

Therefore, in both of these cases, $\lim_{t\to\infty} y_i(t) = 0$ and thus $\lim_{t\to\infty} x_i(t) = C_i \geqslant 0$. On the other hand, $\int_0^\infty x_i(t)\, dt < \infty$, therefore $C_i = 0$. This completes the proof.

3. NONNEGATIVE PROPERTY OF SOLUTIONS

In our model equation (2.1), $x_i(t)$ denotes the amount of material in the compartment C_i and $x_i(t) - \int_0^\infty x_i(t-s)\, du_i(s)$ denotes the amount of material swallowed by C_i. Therefore it is reasonable to require that solutions corresponding to nonnegative initial condition and $\varphi_i(0) - \int_0^\infty \varphi_i(-s)\, du_i(s) \geqslant 0$, $1 \leqslant i \leqslant n$ should satisfy that $x_i(t) \geqslant 0$ and $x_i(t) - \int_0^\infty x_i(t-s)\, du_i(s) \geqslant 0$ for $1 \leqslant i \leqslant n$ and $t \geqslant 0$. The aim of this section is to present some sufficient conditions to guarantee this property of solutions to our model equation (2.1).

Our first result is as follows.

Theorem 3.1. *Assume that*

(H10) $r_{ii}(s) - \lambda_i u_i(s)$, $1 \leqslant i \leqslant n$, *are monotone nondecreasing.*

Then for any $\varphi = (\varphi_1, \ldots, \varphi_n)$, $\varphi_i \in BC((-\infty, 0], R)$, *there exists a unique solution* $(x_1(t), \ldots, x_n(t))$ *of Eq. (2.1) through* $(0, \varphi)$. *Moreover, if* $h_i(t) \geqslant 0$ *for all* $t \geqslant 0$, $\varphi_i(s) \geqslant 0$ *for* $s \leqslant 0$ *and* $\varphi_i(0) - \int_0^\infty \varphi_i(-s)\, du_i(s) \geqslant 0$ *for* $1 \leqslant i \leqslant n$, *then* $x_i(t) \geqslant 0$ *and* $x_i(t) - \int_0^\infty x_i(t-s)\, du_i(s) \geqslant 0$ *for* $t \geqslant 0$ *and* $1 \leqslant i \leqslant n$.

To prove this result, we need the following.

Lemma 3.1. *Suppose that*

(i) f: $[0, \infty) \to R$ *and* φ: $(-\infty, 0] \to R$ *are bounded and continuous;*

(*ii*) $u: [0, \infty) \to R$ *is monotone nondecreasing with* $u(0) = 0$, $u(\infty) < 1$, *and for any bounded and continuous* $x: R \to R$, *the function* $\int_0^\infty z(t-s)\,du(s)$ *is continuous for* $t \geqslant 0$; *and*

(*iii*) $\varphi(0) = \int_0^\infty \varphi(-s)\,du(s) + f(0)$.

Then the equation

$$\begin{aligned} x(t) &= \int_{-\infty}^{t} x(s)\,du(t-s) + f(t), \qquad && t \geqslant 0 \\ x(t) &= \varphi(t), && t \leqslant 0 \end{aligned} \tag{3.1}$$

has a unique solution $x(t)$ *defined for all* $t \geqslant 0$ *and satisfying*

$$|x(t)| \leqslant \frac{1}{1-u(\infty)} \max_{0 \leqslant s \leqslant t} \left| f(t) + \int_{-\infty}^{0} \varphi(s)\,du(t-s) \right|$$

Moreover, $x(t) \geqslant 0$ *for* $t \geqslant 0$ *if* $f(t) \geqslant 0$ *for* $t \geqslant 0$ *and* $\varphi(t) \geqslant 0$ *for* $t \leqslant 0$.

Proof. Equation (3.1) is equivalent to the following integral equation:

$$\begin{aligned} x(t) &= \int_{0}^{t} x(t-s)\,du(s) + F(t), \qquad && t \geqslant 0 \\ x(0) &= F(0) \end{aligned} \tag{3.2}$$

where

$$F(t) = f(t) + \int_{-\infty}^{0} \varphi(s)\,du(t-s)$$

For any given $T > 0$, let $M = \max_{0 \leqslant s \leqslant T} |F(s)|$. Define a function sequence $\{x^n\}$ on $[0, T]$ as follows:

$$\begin{aligned} x^0(t) &= F(t) \\ x^n(t) &= \int_0^t x^{(n-1)}(t-s)\,du(s) + F(t), \qquad n = 1, 2, \ldots \end{aligned}$$

It is easy to prove that

$$|x^n(t) - x^{n-1}(t)| \leqslant M u^n(\infty)$$

and

$$|x^n(t)| \leqslant \frac{M}{1-u(\infty)}$$

Therefore, $u(\infty)<1$ implies that $\{x^n(t)\}$ converges to a function $x(t)$ uniformly, which solves Eq. (3.2) and satisfies $|x(t)| \leqslant M/[1-u(\infty)]$. T is any given positive number, and thus the sequence $\{x^n\}$ converges to a solultion of (3.2) uniformly on any compact subset of $[0, \infty)$. Obviously, if $f(t) \geqslant 0$ for all $t \geqslant 0$ and $\varphi(s) \geqslant 0$ for all $s \leqslant 0$, then $x^n(t) \geqslant 0$ for all $t \geqslant 0$ and all integers n. Therefore $\lim_{n\to\infty} x^n(t) = x(t) \geqslant 0$. This completes the proof.

Now we are in the position to state the proof of Theorem 3.1. The following proof is constructive and, therefore, provides a computational procedure for finding the solution.

Proof of Theorem 3.1. It is easy to prove that Eq. (2.1) is equivalent to

$$x_i(t) = \int_0^\infty x_i(t-s)\, du_i(s) + e^{-\lambda_i t}\left[\varphi_i(0) - \int_0^\infty \varphi_i(-s)\, du_i(s)\right]$$
$$+ \int_0^t e^{-\lambda_i(t-u)} \left[\int_0^\infty \sum_{j=1}^n x_j(u-s)\, d\bar{r}_{ij}(s) + h_i(u)\right] du$$

where

$$\bar{r}_{ij}(s) = \begin{cases} r_{ij}(s), & \text{if } \ i \neq j \\ r_{ii}(s) - \lambda_i u_i(s), & \text{if } \ i = j \end{cases}$$

that is,

$$x_i(t) = \int_0^\infty x_i(t-s)\, du_i(s) + e^{-\lambda_i t}\left[\varphi_i(0) - \int_0^\infty \varphi_i(-s)\, du_i(s)\right]$$
$$+ \int_0^t e^{-\lambda_i(t-u)} \int_0^u \sum_{j=1}^n x_j(u-s)\, d\bar{r}_{ij}(s)\, du$$
$$+ \int_0^t e^{-\lambda_i(t-u)}\, h_i(u)\, du + f_i(t) \tag{3.3}$$

where

$$f_i(t) = \int_0^t e^{-\lambda_i(t-u)} \int_u^\infty \sum_{j=1}^n \varphi_j(u-s)\, d\bar{r}_{ij}(s)\, du \tag{3.4}$$

We construct now a function sequence $\{x_i^n\}\rangle$ defined by

$$x_i^0(t) = \int_0^\infty x_i^0(t-s)\, du_i(s) + F_i(t), \qquad t \geqslant 0$$
$$x_i^0(t) = \varphi(t), \qquad t \leqslant 0$$

and

$$x_i^k(t) = \int_0^\infty x_i^k(t-s)\, du_i(s)$$
$$+ \sum_{j=1}^n \int_0^t e^{-\lambda_i(t-s)} \int_0^u x_j^{k-1}(u-s)\, d\bar{r}_{ij}(s)\, du + F_i(t), \qquad t \geqslant 0$$
$$x_i^k(t) = \varphi(t), \qquad t \leqslant 0$$

for $k \geqslant 1$, where

$$F_i(t) = e^{-\lambda_i t}\left[\varphi_i(0) - \int_0^\infty \varphi_i(-s)\, du_i(s)\right]$$
$$+ \int_0^t e^{-\lambda_i(t-u)} h_i(u)\, du + \sum_{j=1}^n \int_0^t e^{-\lambda_i(t-u)} \int_u^\infty \varphi_j(u-s)\, d\bar{r}_{ij}(s)\, du$$

This sequence is well defined by Lemma 3.1, and for any $T > 0$, we have

$$|x_i^0(t) \leqslant N_i, \qquad 0 \leqslant t \leqslant T$$

where

$$N_i = \frac{1}{1-u_i(T)} \max_{0 \leqslant t \leqslant T}\left[|F_i(t)| + \left|\int_t^\infty \varphi_i(t-s)\, du_i(s)\right|\right]$$

From the definition of x_i^1 and x_i^0, it follows that

$$x_i^1(t) - x_i^0(t) = \int_0^t [x_i^1(t-s) - x_i^0(t-s)]\, du_i(s)$$
$$+ \sum_{j=1}^n \int_0^t e^{-\lambda_i(t-u)} \int_0^u x_j^0(u-s)\, d\bar{r}_{ij}(s)\, du$$

and therefore by using the same argument for Lemma 3.1, we have

$$|x_i^1(t) - x_i^0(t)| \leqslant \frac{1}{1-u_i(T)} \sup_{0 \leqslant v \leqslant t} \sum_{j=1}^n \left|\int_0^v e^{-\lambda_i(v-u)} \int_0^u x_j^0(u-s)\, d\bar{r}_{ij}(s)\, du\right|$$
$$\leqslant \frac{M_i}{1-u_i(T)} \sum_{j=1}^n \sup_{0 \leqslant v \leqslant t} \int_0^v \int_0^u N_i\, d\bar{r}_{ij}(s)\, du$$
$$\leqslant \frac{M_i N_i}{1-u_i(T)} \sum_{j=1}^n \bar{r}_{ij}(T) t$$
$$\leqslant NKt$$

where

$$M_i = \max_{0 \leqslant t \leqslant T} e^{-\lambda_i t}$$

$$K = \max_{1 \leqslant i \leqslant n} \frac{M_i}{1 - u_i(T)} \sum_{j=1}^{n} \bar{r}_{ij}(T)$$

$$N = \max_{1 \leqslant i \leqslant n} N_i$$

Generally, suppose that

$$|x^{k-1}(t) - x^{k-2}(t)| \leqslant \frac{N(Kt)^{k-1}}{(k-1)!}, \qquad 0 \leqslant t \leqslant T$$

then by using the same argument for Lemma 3.1, we obtain

$$\begin{aligned} |x_i^k(t) - x_i^{k-1}(t)| &\leqslant \frac{1}{1 - u_i(T)} \sum_{j=1}^{n} \int_0^t e^{-\lambda_i(t-u)} \\ &\quad \times \int_0^u |x_j^{k-1}(u-s) - x_j^{k-2}(u-s)| \, d\bar{r}_{ij}(s) \, du \\ &\leqslant \frac{1}{1 - u_i(T)} \sum_{j=1}^{n} \frac{NM_i}{(k-1)!} \int_0^t \int_0^u [K(u-s)]^{k-1} \, d\bar{r}_{ij}(s) \, du \\ &\leqslant N \frac{(Kt)^k}{k!}, \qquad 0 \leqslant t \leqslant T \end{aligned}$$

Therefore, by induction on k, we claim that

$$\max_{1 \leqslant i \leqslant n} |x_i^k(t) - x_i^{k-1}(t)| \leqslant N \frac{(Kt)^k}{k!}, \qquad 0 \leqslant t \leqslant T$$

from which it follows that the sequence $\{x_i^k\}$ converges to a function $\{x_i\}$ which solves Eq. (3.3). Evidently, $\int_0^t e^{-\lambda_i(t-u)} \int_0^u x_j^{k-1}(u-s)\, d\bar{r}_{ij}(s)\, du$ is nonnegative provided that x_j^{k-1} is nonnegative, and by induction as well as Lemma 3.1, we know that $x_i^k(t)$ and $x_i^k(t) - \int_0^\infty x_i^k(t-s)\, du_i(s)$ are nonnegative for $1 \leqslant i \leqslant n$, $k = 1, 2, \ldots$, and $t \geqslant 0$, and hence, $x_i(t) \geqslant 0$, $\int_0^\infty x_i(t-s)\, du_i(s) \geqslant 0$ for $1 \leqslant i \leqslant n$ and $t \geqslant 0$. This completes the proof.

The previous result imposes a strong assumption (H10) on the transit time distribution function $r_{ii}(t)$ and the function $u_i(t)$ reflecting the "active" feature of the compartment C_i. This assumption essentially requires that r_{ii}

and u_i have the same jump points and, therefore, excludes the following simple equation:

$$\frac{d}{dt}[x(t)-ax(t-\tau)] = -cx(t)+bx(t-\sigma), \qquad t \geqslant 0 \tag{3.5}$$

where $a, b, c \geqslant 0$ and $0 \leqslant \sigma \leqslant \tau$ are constants. For this scalar equation, we have the following.

Theorem 3.2. *If*

$$ae^{c\tau} < 1 \qquad \text{and} \qquad ace^{c\tau} < be^{c\sigma}$$

then the set

$$\Phi = \left\{\psi \in C([-r, 0], [0, \infty)); \psi(0) - a\psi(-\tau) - ace^{c\tau} \int_{-\tau}^{0} e^{cu}\psi(u)\, du > 0\right\}$$

contains nonidentically zero functions, and for all $\varphi \in \Phi$, the solution $x(t)$ of Eq. (3.5) through $(0, \varphi)$ remains positive for $t \geqslant 0$.

Proof. By integration, we obtain

$$x(t) = ax(t-\tau) + e^{-ct}\left[\varphi(0) - a\varphi(-\tau) - ac\int_0^t e^{cs}x(s-\tau)\, ds \right.$$
$$\left. + b\int_0^t e^{cs}x(s-\sigma)\, ds\right] \tag{3.6}$$

for all $t \geqslant 0$.

For $t \in [0, \tau]$ and $s \in [0, t]$, one has $s - \tau \leqslant 0$ and $x(s-\tau) = \varphi(s-\tau)$. Since $\varphi \in \Phi$, we find

$$\varphi(0) - a\varphi(-\tau) - ac\int_0^t e^{cs}x(s-\tau)\, ds$$
$$= \varphi(0) - a\varphi(-\tau) - ac\int_0^t e^{cs}\varphi(s-\tau)\, ds$$
$$\geqslant \varphi(0) - a\varphi(-\tau) - ac\int_0^\tau e^{cs}\varphi(s-\tau)\, ds$$
$$= \varphi(0) - a\varphi(-\tau) - ace^{c\tau}\int_{-\tau}^0 e^{cu}\varphi(u)\, du > 0$$

In this case from Eq. (3.6), it follows that

$$x(t) > be^{-ct} \int_0^t e^{cs} x(s-\sigma)\, ds \tag{3.7}$$

for all $t \in [0, \tau]$. Since $x(t) = \varphi(t) \geqslant 0$ for $-r \leqslant t \leqslant 0$, by (3.7) we find that $x(0) > 0$.

We now show that $x(t) > 0$ for all $t \in [0, \tau]$. Otherwise there exist a $t_1 \in (0, \tau]$ such that $x(t_1) = 0$ and $x(t) > 0$ for $0 \leqslant t \leqslant t_1$. But in this case, Eq. (3.7) yields

$$x(t_1) > be^{-ct_1} \int_0^{t_1} e^{cs} x(s-\sigma)\, ds \geqslant 0$$

which is a contradiction. Thus $x(t) > 0$ for all $t \in [0, \tau]$.

For $t > \tau$, we have

$$\begin{aligned} -ac \int_0^t e^{cs} x(s-\tau)\, ds + b \int_{-\sigma}^{t-\sigma} e^{c(u+\sigma)} x(u)\, du \\ = -ace^{c\tau} \int_{-\tau}^0 e^{cu} x(u)\, du + be^{c\sigma} \int_{-\sigma}^0 e^{cu} x(u)\, du \\ + (be^{c\sigma} - ace^{c\tau}) \int_0^{t-\tau} e^{cu} x(u)\, du + be^{c\sigma} \int_{t-\tau}^{t-\sigma} e^{cu} x(u)\, du. \end{aligned}$$

Thus, Eq. (3.7) yields

$$\begin{aligned} x(t) = ax(t-\tau) + e^{-ct} \Big[\varphi(0) - a\varphi(-\tau) - ace^{c\tau} \int_{-\tau}^0 e^{cu} \varphi(u)\, du \\ + be^{c\sigma} \int_{-\sigma}^0 e^{cu} \varphi(u)\, du \Big] + e^{-ct} [be^{c\sigma} - ace^{c\tau}] \int_0^{t-\tau} e^{cu} x(u)\, du \\ + e^{-ct} be^{c\sigma} \int_{t-\tau}^{t-\sigma} e^{cu} x(u)\, du \end{aligned}$$

for all $t \geqslant \tau$. But $\varphi \in \Phi$ and hence

$$\begin{aligned} x(t) > ax(t-\tau) + e^{-ct}(be^{c\sigma} - ace^{c\tau}) \int_0^{t-\tau} e^{cu} x(u)\, du \\ + e^{-ct} be^{c\sigma} \int_{t-\tau}^{t-\sigma} e^{cu} x(u)\, du, \qquad t \geqslant \tau \end{aligned} \tag{3.8}$$

Since $x(t) \geqslant 0$, $-r \leqslant t \leqslant \tau$, and $x(\tau) > 0$, by an argument similar to that given above and (3.8), we find $x(t) > 0$ for all $t \geqslant \tau$ and the proof is then complete.

As an important corollary to the following generalization of the closed compartmental system,

$$\frac{d}{dt}[x(t)-axc(t-\tau)] = -bx(t)+bx(t-\sigma), \qquad t \geqslant 0 \qquad (3.9)$$

where $a \geqslant 0$, $0 \leqslant \sigma \leqslant \tau$, and $b \geqslant 0$ are real numbers, we get the following.

Corollary 3.1. *If $ae^{b\tau} < 1$. Then for all $\varphi \in \Phi_0$, where Φ_0 is defined by*

$$\Phi_0 = \left\{\psi \in C([-\tau, 0], [0, \infty)); \psi(0) - a\psi(-\tau) - abe^{b\tau} \int_{-\tau}^{0} e^{bu}\psi(u)\, du > 0\right\}$$

the solution $x(t) = x(\varphi)(t)$ of Eq. (3.9) through $(0, \varphi)$ is positive for $t \geqslant 0$.

Remark 3.1. As we found, if each compartment produces or swallows material, then the model equation becomes a neutral equation, as opposed to the classical case where model equations are retarded functional differential equations, and the study of the nonnegative property of solutions turns out to be very difficult and requires further investigation.

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