

An Abstract Neutral Functional Differential Equation Arising From a Cell Population Model

O. Arino

*Laboratoire de Mathématiques Appliquées, I.P.R.A., Av. de l'Université,
64000 Pau, France*

and

O. Sidki

Faculté des Sciences et Techniques Fes-Saïss, B.P. 2202, Fes, Maroc

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In this article, an abstract (infinite dimensional) neutral functional differential equation arising from a cell population model is exhibited. It is then shown that a large class of such equations can be solved by means of the theory of nonlinear semigroups. Finally, application to the model equation is detailed. © 1999 Academic Press

1. INTRODUCTION

In this article, we consider the model of cell proliferation described by the equation

$$n(t, x) = 2H[N(t)] \int_0^{+\infty} \int_0^{+\infty} f(x, \phi(\tau, \xi)) \gamma(\tau, \xi) n(t - \tau, \xi) d\xi d\tau, \quad (1)$$

in which

$$N(t) = \int_0^{+\infty} \int_0^{+\infty} \int_{t-\tau}^t n(s, y) \gamma(\tau, y) ds d\tau dy.$$



This model is a modification of a model first proposed in Kimmel *et al.* [9]. The original model was linear.

Nonlinear variants were later considered in Arino and Kimmel [1, 2] and Arino and Mortabit [4]. The model is based on the subdivision of the cell cycle into four consecutive phases represented as follows:

$$\rightarrow y \begin{array}{|c|c|c|c|} \hline G_1 & S & G_2 & M \\ \hline \end{array} \rightarrow y \sim f(\cdot, x) \rightarrow$$

$$\tau \sim \gamma(\cdot, y) \quad x = \Phi(\tau, y).$$

During its progression inside the cycle, a cell keeps growing, although with a variable strength. Generally, it doubles its size from birth (as a daughter cell) to the end of the G_2 phase before the M phase (mitosis) where it divides into two identical cells, each with half the constituents of the mother cell.

The main hypothesis introduced in [9], in the case of subdivision of the cell, is that the division is not equal.

Equation (1) takes into consideration two further aspects, compared to the one aspect in [9].

One assumes here that the life duration of a cell (that is, the length of a cycle) is not determined by the initial size, but dependence is, in probability, determined by a conditional density $\gamma(\cdot, \xi)$ (conditioned on the size): $\int_{\tau_1}^{\tau_2} \gamma(\tau, \xi) d\tau = \text{Probability for the lifelength of a cell, with initial size } \xi, \text{ to lie within the interval } [\tau_1, \tau_2].$

As a result, the final size of cells cannot be expressed in terms of their initial size only (as was assumed in [9]) but it is also a function of the lifelength: $\phi(\tau, \xi)$.

A linear model based on these considerations was presented in [3]. Here, we introduce the limiting effects due to the environment in the form of a function of the total population, which decays to zero when population grows to $+\infty$. Such models were considered in [1, 2]. Equation (1) collects and extends two previous models: a linear by Arino, *et al.* [3] and a nonlinear by Arino and Kimmel [1]. Equation (1) is an integral equation and was studied as such in [1, 3].

Here we transform the integral equation into a functional differential equation of neutral type (NFDE) that we solve under suitable hypotheses. Thus, we obtain both a strict extension of previous existence results [1, 3] and novel regularity properties verified by the solutions of the NFDE.

Differentiating (formally) Eq. (1) with respect to time yields the NFDE,

$$\frac{\partial}{\partial t} n(t, \cdot) = G(n_t)(\cdot), \quad (2)$$

where G is a nonlinear operator defined from $W^{1,1}([-r, 0]; L^1(0, +\infty))$ into $L^1(0, +\infty)$ by

$$\begin{aligned}
 G(\varphi) &= 2K(\varphi)\dot{H}[\mathcal{L}(\varphi)] \\
 &\times \int_0^{+\infty} \int_0^{+\infty} f(., \phi(\tau, \xi))\gamma(\tau, \xi)\varphi(-\tau, \xi) d\xi d\tau \\
 &+ 2H[\mathcal{L}(\varphi)] \\
 &\times \int_0^{+\infty} \int_0^{+\infty} f(., \phi(\tau, \xi))\gamma(\tau, \xi)\frac{\partial}{\partial\theta}\varphi(-\tau, \xi) d\xi d\tau \quad (3)
 \end{aligned}$$

with

$$\begin{cases}
 K(\varphi) = \int_0^{+\infty} \int_0^{+\infty} \int_{-\tau}^0 \frac{\partial}{\partial\theta}\varphi(\theta, \xi)\gamma(\tau, y) d\theta d\tau dy \\
 \mathcal{L}(\varphi) = \int_0^{+\infty} \int_0^{+\infty} \int_{-\tau}^0 \varphi(\theta, \xi)\gamma(\tau, y) d\theta d\tau dy
 \end{cases} ,$$

for every $\varphi \in W^{1,1}([-r, 0]; L^1(0, +\infty))$.

Under appropriate assumptions on the parameters defining Eq. (1), one shows that, for each initial value $n_0 \in W^{1,1}([-r, 0]; L^1(0, +\infty))$ and each $T > 0$, NFDE (2) possesses one and only one solution n , $n \in W^{1,1}([-r, T]; L^1(0, +\infty))$.

Integrating (2), one obtains the solution of (1) and, in the same way as in [2], one shows that it is nonnegative for all $t \geq 0$, if $n_0 \geq 0$.

2. RESOLUTION OF THE NFDE: $\dot{x}(t) = F(x_t)$

In order to study Eq. (2), we give some results on the following class of NFDEs.

$$\frac{dx}{dt} = F(x_t), \quad x_0 = \varphi \in W^{1,1}([-r, 0]; X), \quad 0 \leq t \leq T, \quad (4)$$

where $x: [-r, T] \rightarrow X$, $0 < r < +\infty$ is the delay, X is a Banach space with norm $|\cdot|_X$, and x_t is the history defined pointwise by $x_t(\theta) = x(t + \theta)$, for all $\theta \in [-r, 0]$.

We suppose that $F: W^{1,1}([-r, 0]; X) \rightarrow X$, is Lipschitz continuous, with Lipschitz constant α ; i.e.,

$$H_{(F)}: |F(\varphi_1) - F(\varphi_2)|_X \leq \alpha\|\varphi_1 - \varphi_2\|_{1,1},$$

for all $\varphi_1, \varphi_2 \in W^{1,1}([-r, 0]; X)$.

And, we define the space $W^{1,1}([a, b]; X)$ by

$$W^{1,1}([a, b]; X) = \left\{ \begin{array}{l} f \in L^1([a, b]; X); f \text{ absolutely continuous on } [a, b], \\ f' \text{ exists a.e., } f' \in L^1([a, b]; X), \\ \text{and } f(t) = f(a) + \int_a^t f'(s) ds, \quad \forall t \in [a, b] \end{array} \right\}.$$

For all $f \in W^{1,1}([a, b]; X)$, we define the following norm:

$$\|f\|_{1,1} = \int_a^b |f(s)| ds + \int_a^b |f'(s)| ds. \quad (5)$$

Note by [5] that if $\dim X < +\infty$, or X is a reflexive Banach space, then each absolutely continuous function $x: [a, b] \rightarrow X$, is a.e differentiable, and $x(t) = x(a) + \int_a^b x'(s) ds$.

In [7], Dyson and Villella-Bressan proved the existence and uniqueness of solutions of NFDE (4), written in the form of an evolution equation

$$\frac{du}{dt} = Au,$$

where A is a nonlinear operator defined on $W^{2,1}([-r, 0]; X)$ with values in $W^{1,1}([-r, 0]; X)$ by

$$A\varphi = \dot{\varphi} \quad \text{and} \quad \varphi \in D(A) = \{\varphi \in W^{2,1}([-r, 0]; X) : \dot{\varphi}(0) = F(\varphi)\}. \quad (6)$$

These authors proved that if F satisfies $H_{(F)}$, then A is $(1 + \alpha)$ -dissipative and such that $\text{Im}(I - \lambda A) = W^{1,1}([-r, 0]; X)$, for $\lambda > 0$ small enough. Therefore, by the Crandall and Liggett theorem [6], $\lim_{n \rightarrow +\infty} (I - (t/n)A)^{-n}\varphi$ exists for all $t \geq 0$ and for all $\varphi \in W^{1,1}([-r, 0]; X)$. If we define $T(t)\varphi = \lim_{n \rightarrow +\infty} (I - \frac{t}{n}A)^{-n}\varphi$, then $T(t)$ is a nonlinear strongly continuous semigroup of type $(1 + \alpha)$ on $W^{1,1}([-r, 0]; X)$. More precisely, it is proved in [7] that:

THEOREM 1 [7]. *Let F satisfy $H_{(F)}$. Then, A defined by (6) generates a semigroup $T(t)$ of type $(1 + \alpha)$ in $W^{1,1}([-r, 0]; X)$. Set*

$$x(t) = \begin{cases} \varphi(t) & \text{if } t \in [-r, 0] \\ (T(t)\varphi)(0) & \text{if } t > 0. \end{cases}$$

Then $x(t)$ is the unique strong solution of Eq. (4) for all $\varphi \in W^{1,1}([-r, 0]; X)$. If $\varphi \in E = \{\varphi \in \mathcal{C}^1([-r, 0]; X) : \dot{\varphi}(0) = F(\varphi)\}$, then the solution is continuously differentiable.

In [10], we proposed another method. A direct approach by means of an integral equation was considered. More precisely, we proved that there exists an integer N , such that K^n is a strict contraction, for all $n \geq N$, where K is given by

$$(Kx)(t) = \begin{cases} \varphi(0) + \int_0^t F(x_s) ds & \text{if } t > 0 \\ \varphi(t) & \text{if } t \in [-r, 0] \end{cases}.$$

K is defined on the set $E_\varphi = \{y \in W^{1,1}([-r, T]; X) : y = \varphi \text{ on } [-r, 0]\}$, where $T > 0$ is arbitrary and $\varphi \in W^{1,1}([-r, 0]; X)$ is the initial datum of (4).

In [10] the following theorem was proved:

THEOREM 2. *Let F satisfy $H_{(F)}$ and $E_\varphi = \{y \in W^{1,1}([-r, T]; X) : y = \varphi \text{ on } [-r, 0]\}$. Then, NFDE (4) has a unique solution $x \in E_\varphi$, for all $T > 0$, and for each initial data $\varphi \in W^{1,1}([-r, 0]; X)$.*

Set

$$T(t)\varphi = x_t, \tag{7}$$

with

$$x_t(\theta) = \begin{cases} x(t + \theta) & \text{if } t + \theta > 0 \\ \varphi(t + \theta) & \text{if } t + \theta \leq 0 \end{cases}. \tag{8}$$

Finally, we quote the following proposition that will be used for the resolution of NFDE (2).

PROPOSITION 3 [10]. *Suppose that F verifies $H_{(F)}$. Then, (a) The family of operators $\{T(t)\}_{t \geq 0}$ defined from $W^{1,1}([-r, 0]; X)$ into $W^{1,1}([-r, 0]; X)$ by (7) is a nonlinear strongly continuous semigroup that verifies the following relation: for all $\theta \in [-r, 0]$,*

$$(T(t))\varphi(\theta) = \begin{cases} \varphi(0) + \int_0^{t+\theta} F(T(s)\varphi) ds & \text{if } t + \theta > 0 \\ \varphi(t + \theta) & \text{if } t + \theta \leq 0 \end{cases}. \tag{9}$$

(b) For all $\varphi_1, \varphi_2 \in W^{1,1}([-r, 0]; X)$ and all $t \geq 0$, we have

$$\|T(t)\varphi_1 - T(t)\varphi_2\|_{1,1} \leq e^{(\alpha+1)t} \|\varphi_1 - \varphi_2\|_{1,1}. \tag{10}$$

(c) The operator A defined by (6) is the infinitesimal generator of $T(t)$.

3. RESOLUTION OF THE NFDE: $(\partial/\partial t)n(t, \cdot) = G(n_t)(\cdot)$

The parameters of Eq. (1) are the functions f , ϕ , γ , and H . We make the following hypotheses:

$H_{(f)}$: $f \in L^1(\mathbb{R}_+^2)$, $f \geq 0$, and $\int_0^{+\infty} f(y, x) dy = 1$, for all $x \geq 0$.

$H_{(\gamma)}$: $\gamma \in L^1(\mathbb{R}_+^2)$, $\gamma \geq 0$, $\int_0^{+\infty} \gamma(\tau, x) d\tau = 1$ and there exists a constant $k > 0$, such that $|\gamma(\tau, x)| \leq k$, for all $(\tau, x) \in [0, +\infty) \times [0, +\infty)$. There exist A_1, A_2, τ_1 , and τ_2 such that $0 < \tau_1 < \tau_2$, $0 < A_1 < A_2$, and $\text{supp } \gamma(\cdot, \xi) \subset [\tau_1, \tau_2]$, for all $\xi \in [A_1, A_2]$.

$H_{(\phi)}$: $\phi \in \mathcal{C}(\mathbb{R}_+^2)$ and $\phi \geq 0$.

$H_{(H)}$: $H \in \mathcal{C}^1(\mathbb{R})$, $0 \leq H \leq 1$, and H, \dot{H} are locally Lipschitz.

We define the norm in $W^{1,1}([-r, 0]; L^1(0, +\infty))$ by

$$\|\varphi\|_{1,1} = \int_{-r}^0 |\varphi(\theta, \cdot)|_{L^1} d\theta + \int_{-r}^0 |\dot{\varphi}(\theta, \cdot)|_{L^1} d\theta \quad (11)$$

for all $\varphi \in W^{1,1}([-r, 0]; L^1(0, +\infty))$.

PROPOSITION 4. *We suppose $H_{(f)}$, $H_{(\gamma)}$, $H_{(\phi)}$, and $H_{(H)}$. Then, the map $\varphi \rightarrow G(\varphi)(\cdot)\chi_R(\|\varphi\|_{1,1})$ is Lipschitz continuous from $W^{1,1}([-r, 0]; L^1(0, +\infty))$ into $L^1(0, +\infty)$, where*

$$\chi_R(x) = \begin{cases} 1 & \text{if } |x| \leq R \\ 0 & \text{if } |x| \geq 2R \\ -\frac{1}{R}x + 2 & \text{if } R \leq x \leq 2R \\ \frac{1}{R}x + 2 & \text{if } -2R \leq x \leq -R \end{cases} \quad (12)$$

Proof. Let $\varphi_1, \varphi_2 \in W^{1,1}([-r, 0]; L^1(0, +\infty))$. For each $x \geq 0$, we will evaluate the following expression:

$$\begin{aligned} & G(\varphi_1)(x)\chi_R(\|\varphi_1\|_{1,1}) - G(\varphi_2)(x)\chi_R(\|\varphi_2\|_{1,1}) \\ &= [G(\varphi_1)(x) - G(\varphi_2)(x)]\chi_R(\|\varphi_2\|_{1,1}) \\ &\quad - G(\varphi_1)(x)[\chi_R(\|\varphi_2\|_{1,1}) - \chi_R(\|\varphi_1\|_{1,1})]. \end{aligned} \quad (13)$$

We consider three possible cases: ($\|\varphi_1\|_{1,1} \leq R$ and $\|\varphi_2\|_{1,1} \leq R$), ($\|\varphi_1\|_{1,1} \geq 2R$ and $\|\varphi_2\|_{1,1} \geq 2R$), and ($\|\varphi_1\|_{1,1} \leq R$ and $\|\varphi_2\|_{1,1} \geq 2R$).

Case I. $\|\varphi_1\|_{1,1} \geq 2R$ and $\|\varphi_2\|_{1,1} \geq 2R$. So, we have

$$G(\varphi_1)(x)\chi_R(\|\varphi_1\|_{1,1}) - G(\varphi_2)(x)\chi_R(\|\varphi_2\|_{1,1}) = 0.$$

Case II. $\|\varphi_1\|_{1,1} \leq R$ and $\|\varphi_2\|_{1,1} \geq 2R$.

From (13) one obtains

$$\begin{aligned} &|G(\varphi_1)(x)\chi_R(\|\varphi_1\|_{1,1}) - G(\varphi_2)(x)\chi_R(\|\varphi_2\|_{1,1})| \\ &= |G(\varphi_1)(x)| |\chi_R(\|\varphi_2\|_{1,1}) - \chi_R(\|\varphi_1\|_{1,1})| \\ &\leq |G(\varphi_1)(x)| |\chi_{R|\text{Lip}}| \|\varphi_2\|_{1,1} - \|\varphi_1\|_{1,1}| \\ &\leq |G(\varphi_1)(x)| |\chi_{R|\text{Lip}}| \|\varphi_2 - \varphi_1\|_{1,1}. \end{aligned}$$

So,

$$\begin{aligned} &\int_0^{+\infty} |G(\varphi_1)(x)\chi_R(\|\varphi_1\|_{1,1}) - G(\varphi_2)(x)\chi_R(\|\varphi_2\|_{1,1})| dx \\ &\leq |\chi_{R|\text{Lip}}| \|\varphi_2 - \varphi_1\|_{1,1} \int_0^{+\infty} |G(\varphi_1)(x)| dx. \end{aligned}$$

Now, we prove that there exists a constant $C > 0$, such that

$$\int_0^{+\infty} |G(\varphi_1)(x)| dx \leq C,$$

for all φ_1 , such that $\|\varphi_1\|_{1,1} \leq R$: φ_1 is defined on $[-r, 0]$, so, in (3) $\tau \in [0, r]$. By a change of variable $\tau' = -\tau$ and integrating (3) from 0 to $+\infty$, we obtain

$$\begin{aligned} &\int_0^{+\infty} |G(\varphi)(x)| dx \\ &\leq 2|K(\varphi)| |\dot{H}(\mathcal{L}(\varphi))| \\ &\quad \times \left\{ \int_0^{+\infty} \int_0^{+\infty} \int_{-r}^0 |f(x, \phi(-\tau, \xi))| |\gamma(-\tau, \xi)| |\varphi(\tau, \xi)| d\xi d\tau dx \right\} \\ &\quad + 2|H(\mathcal{L}(\varphi))| \left\{ \int_0^{+\infty} \int_0^{+\infty} \int_{-r}^0 |f(x, \phi(-\tau, \xi))| |\gamma(-\tau, \xi)| \right. \\ &\quad \left. \times |\dot{\varphi}(\tau, \xi)| d\xi d\tau dx \right\}. \end{aligned}$$

From $H_{(\gamma)}$, we have

$$\begin{aligned} |K(\varphi)| &\leq \int_0^{+\infty} \int_0^{+\infty} \int_{-r}^0 |\dot{\varphi}(\theta, y)| |\gamma(\tau, y)| d\theta d\tau dy \\ &\leq \int_0^{+\infty} \int_{-r}^0 |\dot{\varphi}(\theta, y)| d\theta dy \leq R \end{aligned} \quad (14)$$

and

$$\begin{aligned} |\mathcal{L}(\varphi)| &\leq \int_0^{+\infty} \int_0^{+\infty} \int_{-r}^0 |\varphi(\theta, y)| |\gamma(\tau, y)| d\theta d\tau dy \\ &\leq \int_0^{+\infty} \int_{-r}^0 |\varphi(\theta, y)| d\theta dy \leq R. \end{aligned} \quad (15)$$

Then, there exists a constant $k_1 > 0$, such that

$$|\dot{H}(\mathcal{L}(\varphi))| \leq k_1. \quad (16)$$

So, from $H_{(f)}$, we obtain

$$\begin{aligned} \int_0^{+\infty} |G(\varphi)(x)| dx \\ \leq 2k_1 R \int_0^{+\infty} \int_{-r}^0 |\varphi(\tau, \xi)| d\xi d\tau + 2 \int_0^{+\infty} \int_{-r}^0 |\dot{\varphi}(\tau, \xi)| d\xi d\tau \\ \leq 2(k_1 R + 1)R. \end{aligned}$$

Finally, we have

$$|G(\varphi_1)(x) \chi_R(\|\varphi_1\|_{1,1}) - G(\varphi_2)(x) \chi_R(\|\varphi_2\|_{1,1})|_{L^1} \leq \lambda_1 \|\varphi_1 - \varphi_2\|_{1,1} \quad (17)$$

with $\lambda_1 = 2(k_1 R + 1)R |\chi_R|_{\text{Lip}}$.

Case III. $\|\varphi_1\|_{1,1} \leq R$ and $\|\varphi_2\|_{1,1} \leq R$. Therefore,

$$\begin{aligned} G(\varphi_1)(x) \chi_R(\|\varphi_1\|_{1,1}) - G(\varphi_2)(x) \chi_R(\|\varphi_2\|_{1,1}) \\ = G(\varphi_1)(x) - G(\varphi_2)(x) \\ = 2K(\varphi_1) \dot{H}(\mathcal{L}(\varphi_1)) \int_0^{+\infty} \int_{-r}^0 f(x, \phi(-\tau, \xi)) \\ \times \gamma(-\tau, \xi) \varphi_1(\tau, \xi) d\xi d\tau \\ + 2H(\mathcal{L}(\varphi_1)) \int_0^{+\infty} \int_{-r}^0 f(x, \phi(-\tau, \xi)) \end{aligned}$$

$$\begin{aligned} & \times \gamma(-\tau, \xi) \dot{\varphi}_1(\tau, \xi) d\xi d\tau \\ & - 2K(\varphi_2) \dot{H}(\mathcal{L}(\varphi_2)) \int_0^{+\infty} \int_{-r}^0 f(x, \phi(-\tau, \xi)) \\ & \times \gamma(-\tau, \xi) |\varphi_2(\tau, \xi)| d\xi d\tau \\ & - 2H(\mathcal{L}(\varphi_2)) \int_0^{+\infty} \int_{-r}^0 f(x, \phi(-\tau, \xi)) \\ & \times \gamma(-\tau, \xi) \dot{\varphi}_2(\tau, \xi) d\xi d\tau. \end{aligned}$$

So, $\int_0^{+\infty} |G(\varphi_1)(x) - G(\varphi_2)(x)| dx \leq I_1 + I_2 + I_3 + I_4$, where

$$\begin{aligned} I_1 &= 2|K(\varphi_1)| |\dot{H}(\mathcal{L}(\varphi_1))| \\ & \times \int_0^{+\infty} \int_0^{+\infty} \int_{-r}^0 |f(x, \phi(-\tau, \xi))| |\gamma(-\tau, \xi)| \\ & \times |\varphi_1(\tau, \xi) - \varphi_2(\tau, \xi)| d\xi d\tau dx, \end{aligned}$$

$$\begin{aligned} I_2 &= 2|K(\varphi_1) \dot{H}(\mathcal{L}(\varphi_1)) - K(\varphi_2) \dot{H}(\mathcal{L}(\varphi_2))| \\ & \times \int_0^{+\infty} \int_0^{+\infty} \int_{-r}^0 |f(x, \phi(-\tau, \xi))| |\gamma(-\tau, \xi)| \\ & \times |\varphi_2(\tau, \xi)| d\xi d\tau dx, \end{aligned}$$

$$\begin{aligned} I_3 &= 2|H(\mathcal{L}(\varphi_2))| \\ & \times \int_0^{+\infty} \int_0^{+\infty} \int_{-r}^0 |f(x, \phi(-\tau, \xi))| |\gamma(-\tau, \xi)| \\ & \times |\dot{\varphi}_2(\tau, \xi) - \dot{\varphi}_1(\tau, \xi)| d\xi d\tau dx, \end{aligned}$$

and,

$$\begin{aligned} I_4 &= 2|H(\mathcal{L}(\varphi_1)) - H(\mathcal{L}(\varphi_2))| \\ & \times \int_0^{+\infty} \int_0^{+\infty} \int_{-r}^0 |f(x, \phi(-\tau, \xi))| |\gamma(-\tau, \xi)| |\dot{\varphi}_2(\tau, \xi)| d\xi d\tau dx. \end{aligned}$$

In view of $H_{(f)}$, $H_{(\gamma)}$, $H_{(H)}$, (14), (15), and (16), we have

$$I_1 \leq 2Rkk_1 \int_0^{+\infty} \int_{-r}^0 |\varphi_1(\tau, \xi) - \varphi_2(\tau, \xi)| d\xi d\tau \leq \lambda_2 \|\varphi_1 - \varphi_2\|_{1,1}$$

with $\lambda_2 = 2Rkk_1$,

$$\begin{aligned} I_2 &\leq 2Rk\{|K(\varphi_1) - K(\varphi_2)||\dot{H}(\Lambda(\varphi_1))| \\ &\quad + |K(\varphi_2)||\dot{H}(\mathcal{L}(\varphi_1)) - \dot{H}(\mathcal{L}(\varphi_2))|\} \\ &\leq 2Rkk_1 \int_0^{+\infty} \int_{-r}^0 |\dot{\varphi}_1(\tau, \xi) - \dot{\varphi}_2(\tau, \xi)| d\xi d\tau \\ &\quad + 2R^2k|\dot{H}|_{\text{Lip}} \int_0^{+\infty} \int_{-r}^0 |\varphi_1(\tau, \xi) - \varphi_2(\tau, \xi)| d\xi d\tau \\ &\leq \lambda_3 \|\varphi_1 - \varphi_2\|_{1,1} \end{aligned}$$

with $\lambda_3 = 2Rk(k_1 + R)$,

$$I_3 \leq 2k \int_0^{+\infty} \int_{-r}^0 |\dot{\varphi}_1(\tau, \xi) - \dot{\varphi}_2(\tau, \xi)| d\xi d\tau \leq \lambda_4 \|\varphi_1 - \varphi_2\|_{1,1}$$

with $\lambda_4 = 2k$, and

$$I_4 \leq 2|H|_{\text{Lip}} k^2 R \int_0^{+\infty} \int_{-r}^0 |\varphi_1(\tau, \xi) - \varphi_2(\tau, \xi)| d\xi d\tau \leq \lambda_5 \|\varphi_1 - \varphi_2\|_{1,1},$$

with $\lambda_5 = 2|H|_{\text{Lip}} k^2 R$.

So,

$$\begin{aligned} \int_0^{+\infty} |G(\varphi_1)(x) - G(\varphi_2)(x)| dx &\leq I_1 + I_2 + I_3 + I_4 \\ &\leq (\lambda_2 + \lambda_3 + \lambda_4 + \lambda_5) \|\varphi_1 - \varphi_2\|_{1,1}. \end{aligned}$$

Then, there exists a constant $\alpha > 0$, such that

$$|G(\varphi_1)(\cdot) \chi_R(\|\varphi_1\|_{1,1}) - G(\varphi_2)(\cdot) \chi_R(\|\varphi_2\|_{1,1})|_{L^1} \leq \alpha \|\varphi_1 - \varphi_2\|_{1,1}.$$

■

Thus, by Theorem 2, the problem

$$\begin{cases} \frac{\partial}{\partial t} n(t, \cdot) = G(n_t)(\cdot) \chi_R(\|n_t\|_{1,1}) \\ n_0 = \varphi \end{cases} \quad (18)$$

has a unique solution $n \in W^{1,1}([-r, T]; L^1(0, +\infty))$, for all $T > 0$, and for all initial data $\varphi \in W^{1,1}([-r, 0]; L^1(0, +\infty))$.

4. APPLICATION TO THE INTEGRAL EQUATION

For all $R > 0$ and for all $\varphi \in W^{1,1}([-r, 0]; L^1(0, +\infty))$, we define

$$T_R(t)\varphi = n_t. \tag{19}$$

Then, by Proposition 3, the family $\{T_R(t)\}_{t \geq 0}$ is a nonlinear strongly continuous semigroup of type $(\alpha + 1)$ on $W^{1,1}([-r, 0]; L^1(0, +\infty))$, and verifies the relation

$$(T_R(t)\varphi)(\theta, x) = \begin{cases} \varphi(0, x) + \int_0^{t+\theta} G(T_R(s)\varphi)(x) \chi_R(\|T_R(s)\varphi\|_{1,1}) ds \\ \quad \text{if } t + \theta > 0 \\ \varphi(t + \theta, x) \quad \text{if } -r \leq t + \theta \leq 0, \end{cases} \tag{20}$$

and the infinitesimal generator of $T_R(t)$ is given by

$$\begin{aligned} A_R\varphi &= \dot{\varphi} \\ D(A_R) &= \{\varphi \in W^{2,1}([-r, 0]; L^1(0, +\infty)) : \\ &\quad \dot{\varphi}(0, \cdot) = G(\varphi)(\cdot) \chi_R(\|\varphi\|_{1,1})\}. \end{aligned} \tag{21}$$

The map $t \mapsto T_R(t)\varphi$ is continuous on $[0, +\infty)$. So, for all φ in the ball $B(0, R)$, there exists $t(\varphi, R) > 0$ such that $\|T_R(t)\varphi\|_{1,1} < R$, for all $t < t(\varphi, R)$. Then we set

$$\tau_R(\varphi) = \sup\{s > 0, \|T_R(t)\varphi\|_{1,1} < R, 0 \leq t \leq s\}. \tag{22}$$

Note that the map $R \mapsto \tau_R(\varphi)$ is monotone strictly increasing on $]0, +\infty[$.

We will now prove that essentially $T_R(t)\varphi$ is independent on R , for all $\varphi \in B(0, R)$, provided that $t < t(\varphi, R)$. In fact,

PROPOSITION 5. *For all $R_1, R_2 > 0$, such that $R_2 > R_1$ and for all $\varphi \in B(0, R_1)$, we have $T_{R_1}(t)\varphi = T_{R_2}(t)\varphi$, for all $t \in [0, \tau_{R_1}(\varphi)[$.*

Proof. Let $t \in [0, \tau_{R_1}(\varphi)[$. So, $t < \tau_{R_1}(\varphi) < \tau_{R_2}(\varphi)$, therefore

$$\chi_{R_1}(\|T_{R_1}(t)\varphi\|_{1,1}) = \chi_{R_2}(\|T_{R_2}(t)\varphi\|_{1,1}) = 1$$

and

$$\begin{aligned}
& \|T_{R_1}(t)\varphi - T_{R_2}(t)\varphi\|_{1,1} \\
&= \int_0^{+\infty} \int_{-r}^0 |T_{R_1}(t)\varphi(\theta, x) - T_{R_2}(t)\varphi(\theta, x)| d\theta dx \\
&\quad + \int_0^{+\infty} \int_{-r}^0 \left| \frac{\partial}{\partial \theta} T_{R_1}(t)\varphi(\theta, x) - \frac{\partial}{\partial \theta} T_{R_2}(t)\varphi(\theta, x) \right| d\theta dx \\
&= \int_0^{+\infty} \int_{-t}^0 |T_{R_1}(t+\theta)\varphi(\mathbf{0}, x) - T_{R_2}(t+\theta)\varphi(\mathbf{0}, x)| d\theta dx \\
&\quad + \int_0^{+\infty} \int_{-t}^0 \left| \frac{\partial}{\partial \theta} T_{R_1}(t+\theta)\varphi(\mathbf{0}, x) - \frac{\partial}{\partial \theta} T_{R_2}(t+\theta)\varphi(\mathbf{0}, x) \right| d\theta dx \\
&= \int_0^{+\infty} \int_0^t |T_{R_1}(\eta)\varphi(\mathbf{0}, x) - T_{R_2}(\eta)\varphi(\mathbf{0}, x)| d\eta dx \\
&\quad + \int_0^{+\infty} \int_0^t \left| \frac{\partial}{\partial \eta} T_{R_1}(\eta)\varphi(\mathbf{0}, x) - \frac{\partial}{\partial \eta} T_{R_2}(\eta)\varphi(\mathbf{0}, x) \right| d\eta dx \\
&= \int_0^{+\infty} \int_0^t \left| \int_0^\eta [G(T_{R_1}(s)\varphi)(x) - G(T_{R_2}(s)\varphi)(x)] ds \right| d\eta dx \\
&\quad + \int_0^{+\infty} \int_0^t |G(T_{R_1}(\eta)\varphi)(x) - G(T_{R_2}(\eta)\varphi)(x)| d\eta dx \\
&\leq t\alpha \int_0^t \|T_{R_1}(s)\varphi - T_{R_2}(s)\varphi\|_{1,1} ds \\
&\quad + \alpha \int_0^t \|T_{R_1}(\eta)\varphi - T_{R_2}(\eta)\varphi\|_{1,1} d\eta \\
&\leq \alpha(1 + \tau_{R_1}(\varphi)) \int_0^t \|T_{R_1}(s)\varphi - T_{R_2}(s)\varphi\|_{1,1} ds.
\end{aligned}$$

So, by Gronwall's lemma, we have,

$$\|T_{R_1}(t)\varphi - T_{R_2}(t)\varphi\|_{1,1} = 0, \quad \text{for all } t \in [0, \tau_{R_1}(\varphi)].$$

■

From (19), we have $T_R(t)\varphi = n_t$. Thus,

$$n(t, x) = \begin{cases} (T_R(t)\varphi)(\mathbf{0}, x) & \text{if } t > 0 \\ \varphi(t, x) & \text{if } t \in [-r, 0]. \end{cases} \quad (23)$$

Let R_0 , such that $\tau_{R_0}(\varphi) = \sup_{R > \|\varphi\|_{1,1}} \tau_R(\varphi)$ and $[0, \tau_{R_0}(\varphi)[$ the maximal interval where a solution n of (18) is defined. Then, for each $T < \tau_{R_0}(\varphi)$, $n_{|[0, T]} \in W^{1,1}([0, T]; L^1(0, +\infty))$ and is unique as a solution of (18).

We will now show that $\tau_{R_0}(\varphi) = +\infty$. Indeed, we have the following:

PROPOSITION 6. *If $\tau_{R_0}(\varphi) < +\infty$, then*

$$\limsup_{t \rightarrow \tau_{R_0}^-} \|n_t\|_{1,1} = +\infty.$$

Proof. The proof is done by contradiction. Suppose that there exists $k > 0$, such that $\|n_t\|_{1,1} \leq k$, for all $t \in [0, \tau_{R_0}(\varphi)[$. Then, by (19),

$$\|T_{R_0}(t)\varphi\|_{1,1} \leq k, \quad \text{for all } t \in [0, \tau_{R_0}(\varphi)[.$$

We have $\tau_k(\varphi) \leq \tau_{R_0}(\varphi)$, therefore $k \leq R_0$. So,

$$\|T_{R_0}(t)\varphi\|_{1,1} \leq R_0 \quad \text{for all } t \in [0, \tau_{R_0}(\varphi)[.$$

There exists $T > 0$, such that $\tau_{R_0}(\varphi) - T/2 < T < \tau_{R_0}(\varphi)$. So, Eq. (18) has a unique solution on $[0, T]$, for the initial data $\tilde{\varphi} = T_{R_0}(\tau_{R_0}(\varphi) - T/2)\varphi$.

$$\|\tilde{\varphi}\|_{1,1} = \left\| T_{R_0}\left(\tau_{R_0}(\varphi) - \frac{T}{2}\right)\varphi \right\|_{1,1} < R_0 \quad \left(\text{because } \tau_{R_0}(\varphi) - \frac{T}{2} < \tau_{R_0}(\varphi) \right).$$

The solution of Eq. (18) is given by

$$n_t = T_{R_0}(t)\tilde{\varphi} = T_{R_0}(t)T_{R_0}\left(\tau_{R_0}(\varphi) - \frac{T}{2}\right)\varphi = T_{R_0}\left(t + \tau_{R_0}(\varphi) - \frac{T}{2}\right)\varphi$$

for all $t \in [0, T]$.

We denote $\xi = t + \tau_{R_0}(\varphi) - T/2$. Then, $\xi \in [0, \tau_{R_0}(\varphi) + T/2[$ and $\eta_\xi = T_{R_0}(\xi)\varphi$ is a solution of (18) on $[0, \tau_{R_0}(\varphi) + T/2[$, for the initial data φ . This is a contradiction with the maximality of interval $[0, \tau_{R_0}(\varphi)[$. So,

$$\limsup_{t \rightarrow \tau_{R_0}} \|n_t\|_{1,1} = +\infty.$$

■

From the fact that $\|n_t\|_{1,1} < R_0$, for all $t \in [0, \tau_{R_0}(\varphi)[$, we have $\tau_{R_0}(\varphi) = +\infty$. But, $\tau_{R_0}(\varphi) = \sup_{R > \|\varphi\|_{1,1}} \tau_R(\varphi) = \lim_{R \rightarrow +\infty} \tau_R(\varphi) = +\infty$.

Then, we define $T(t)\varphi = T_{R_0}(t)\varphi$ for all $t \in [0, +\infty)$ and all $\varphi \in W^{1,1}$.

So, by (20) we have for all $\varphi \in W^{1,1}$,

$$\begin{aligned} n_t(\theta, x) &= T(t)\varphi(\theta, x) \\ &= \begin{cases} \varphi(0, x) + \int_0^{t+\theta} G(T(s)\varphi)(x) ds & \text{if } t + \theta > 0 \\ \varphi(t + \theta, x) & \text{if } -r \leq t + \theta \leq 0. \end{cases} \end{aligned} \quad (24)$$

The infinitesimal generator of $T(t)$ is given by

$$A\varphi = \dot{\varphi}, \quad D(A) = \{\varphi \in W^{2,1}, \dot{\varphi}(0, \cdot) = G(\varphi)(\cdot)\}. \quad (25)$$

So,

$$n(t, x) = \begin{cases} (T(t)\varphi)(0, x) & \text{if } t > 0 \\ \varphi(t, x) & \text{if } t \in [-r, 0] \end{cases} \quad (26)$$

is the unique solution of the problem

$$\begin{cases} \frac{\partial}{\partial t}(t, \cdot) = G(n_t)(\cdot) \\ n_0 = \varphi \end{cases}. \quad (27)$$

Finally, we have the following theorem:

THEOREM 7. For all $\varphi \in W^{1,1}([-r, 0]; L^1(0, +\infty))$ and all $T \in [0, +\infty)$, problem (27) has a unique solution $n \in W^{1,1}([-r, T]; L^1(0, +\infty))$, given by (26).

For all $\varphi \in W^{1,1}([-r, 0]; L^1(0, +\infty))$, we define

$$\mathcal{L}(\varphi) = \int_0^{+\infty} \int_0^{+\infty} \int_{-\tau}^0 \varphi(\theta, y) \gamma(\tau, y) d\tau dy$$

and

$$\mathcal{A}(\varphi)(x) = \int_0^{+\infty} \int_0^{+\infty} f(x, \phi(\tau, \xi)) \gamma(\tau, \xi) \varphi(-\tau, \xi) d\xi d\tau.$$

So, $\mathcal{L}(n_t) = N(t)$ and $\mathcal{A}(n_t)(x) = \int_0^{+\infty} \int_0^{+\infty} f(x, \phi(\tau, \xi)) \gamma(\tau, \xi) n(t - \tau, \xi) d\xi d\tau$. Thus, Eq. (1) becomes

$$n(t, x) = 2H(\mathcal{L}(n_t))\mathcal{A}(n_t)(x). \quad (28)$$

In order to return to Eq. (28), we integrate (27) from 0 to t , for all $x \geq 0$:

$$\int_0^t \frac{\partial}{\partial s} n(s, x) ds = \int_0^t 2 \frac{\partial}{\partial s} H(\mathcal{L}(n_s)) \mathcal{A}(n_s)(x) ds.$$

It is equivalent to

$$n(t, x) - n(0, x) = 2H(\mathcal{L}(n_t))\mathcal{A}(n_t)(x) - 2H(\mathcal{L}(n_0))\mathcal{A}(n_0)(x),$$

i.e.,

$$n(t, x) = 2H(\mathcal{L}(n_t))\mathcal{A}(n_t)(x) + [n(0, x) - 2H(\mathcal{L}(n_0))\mathcal{A}(n_0)(x)].$$

So, an additional condition comes out:

$$n_0(0, \cdot) = 2H(\mathcal{L}(n_0))\mathcal{A}(n_0)(\cdot). \tag{29}$$

PROPOSITION 8. *Suppose $H_{(f)}$, $H_{(\gamma)}$, $H_{(\phi)}$, and $H_{(H)}$ and consider the map defined from $W^{1,1}([-r, 0]; L^1(A_1, A_2))$ into $L^1(A_1, A_2)$ by*

$$\Gamma(\varphi)(\cdot) = \varphi(0, \cdot) - 2H(\mathcal{L}(\varphi))\mathcal{A}(\varphi)(\cdot),$$

for all $\varphi \in W^{1,1}([-r, 0]; L^1(A_1, A_2))$.

Then,

(i) Γ is continuous from $W^{1,1}([-r, 0]; L^1(A_1, A_2))$ into $L^1(A_1, A_2)$.

(ii) $\mathcal{B} = \{\varphi \in W^{1,1}([-r, 0]; L^1(A_1, A_2)): \Gamma(\varphi)(\cdot) = 0\}$ is a closed and nonempty set of $W^{1,1}([-r, 0]; L^1(A_1, A_2))$.

Proof. (i) Let $\varphi_1, \varphi_2 \in W^{1,1}([-r, 0]; L^1(A_1, A_2))$ such that $\|\varphi_1 - \varphi_2\|_{1,1} \rightarrow 0$. We have

$$\begin{aligned} & \Gamma(\varphi_1)(x) - \Gamma(\varphi_2)(x) \\ &= \varphi_1(0, x) - \varphi_2(0, x) \\ &\quad - 2[H(\mathcal{L}(\varphi_1))\mathcal{A}(\varphi_1)(x) - H(\mathcal{L}(\varphi_2))\mathcal{A}(\varphi_2)(x)] \\ &= \varphi_1(0, x) - \varphi_2(0, x) \\ &\quad - 2H(\mathcal{L}(\varphi_1))[\mathcal{A}(\varphi_1)(x) - \mathcal{A}(\varphi_2)(x)] \\ &\quad + 2\mathcal{A}(\varphi_2)(x)[H(\mathcal{L}(\varphi_1)) - H(\mathcal{L}(\varphi_2))]. \end{aligned}$$

So,

$$\begin{aligned} & \int_{A_1}^{A_2} |\Gamma(\varphi_1)(x) - \Gamma(\varphi_2)(x)| dx \\ & \leq \int_{A_1}^{A_2} |\varphi_1(\mathbf{0}, x) - \varphi_2(\mathbf{0}, x)| dx \\ & \quad + 2|H(\mathcal{L}(\varphi_1))| \int_{A_1}^{A_2} |\mathcal{A}(\varphi_1)(x) - \mathcal{A}(\varphi_2)(x)| dx \\ & \quad + |H(\mathcal{L}(\varphi_1)) - H(\mathcal{L}(\varphi_2))| \int_{A_1}^{A_2} |\mathcal{A}(\varphi_2)(x)| dx, \end{aligned}$$

and

$$\begin{aligned} & \int_{A_1}^{A_2} |\mathcal{A}(\varphi_1)(x) - \mathcal{A}(\varphi_2)(x)| dx \\ & = \int_{A_1}^{A_2} \left| \int_{A_1}^{A_2} \int_{\tau_1}^{\tau_2} f(x, \phi(\tau, \xi)) \right. \\ & \quad \left. \times \gamma(\tau, \xi) [\varphi_1(-\tau, x) - \varphi_2(-\tau, x)] d\tau d\xi \right| dx \\ & \leq \int_{A_1}^{A_2} \int_{\tau_1}^{\tau_2} \gamma(\tau, \xi) |\varphi_1(-\tau, x) - \varphi_2(-\tau, x)| d\tau d\xi \leq k \|\varphi_1 - \varphi_2\|_{1,1}. \end{aligned}$$

From [10], the norm

$$\|\varphi\|_0 = |\varphi(\mathbf{0}, \cdot)|_{L^1} + \int_{-r}^0 |\dot{\varphi}(\theta, \cdot)|_{L^1} d\theta$$

is equivalent to $\|\cdot\|_{1,1}$. So,

$$\begin{aligned} & \int_{A_1}^{A_2} |\varphi_1(\mathbf{0}, x) - \varphi_2(\mathbf{0}, x)| dx \\ & = \|\varphi_1 - \varphi_2\|_0 - \int_{-r}^0 |\dot{\varphi}_1(\theta, \cdot) - \dot{\varphi}_2(\theta, \cdot)|_{L^1} d\theta. \end{aligned}$$

We have $|\mathcal{L}(\varphi_1) - \mathcal{L}(\varphi_2)| \leq \|\varphi_1 - \varphi_2\|_{1,1}$ and $H \in \mathcal{E}^1$, so, $|H(\mathcal{L}(\varphi_1)) - H(\mathcal{L}(\varphi_2))|$, $\int_{A_1}^{A_2} |\mathcal{A}(\varphi_1)(x) - \mathcal{A}(\varphi_2)(x)| dx$, and $\int_{A_1}^{A_2} |\varphi_1(\mathbf{0}, x) - \varphi_2(\mathbf{0}, x)| dx$ converges to 0 as $\|\varphi_1 - \varphi_2\|_{1,1} \rightarrow \mathbf{0}$. Hence, the result.

(ii) The function $0 \in \mathcal{B}$ and by (i) Γ is continuous, so $\mathcal{B} = \Gamma^{-1}(\{0\})$ is a nonempty closed set of $W^{1,1}([-r, 0]; L^1(A_1, A_2))$. ■

In order to determine an element in \mathcal{B} , it is sufficient to start from any function defined on $[-\tau_2, -\tau_1] \times (A_1, A_2)$. In fact, suppose $\varphi \in \mathcal{B}$: Denote φ_1 the restriction of φ to $[-\tau_2, -\tau_1] \times (A_1, A_2)$ and φ_2 the restriction to $[-\tau_1, 0] \times (A_1, A_2)$. We search $\varphi_2 \in W^{1,1}([- \tau_1, 0]; L^1(A_1, A_2))$, such that

$$\varphi_2(-\tau_1, \cdot) = \varphi_1(-\tau_1, \cdot) \quad \text{and} \quad \varphi_2(0, x) = k\mathcal{A}(\varphi_1)(x), \quad (30)$$

where $k = 2H(\mathcal{L}(\varphi))$. So

$$\begin{aligned} k &= 2H \left\{ \int_{A_1}^{A_2} \int_{\tau_1}^{\tau_2} \left[\int_{-\tau}^0 \varphi(\theta, y) d\theta \right] \gamma(\tau, y) d\tau dy \right\} \\ &= 2H \left\{ \int_{A_1}^{A_2} \int_{\tau_1}^{\tau_2} \left[\int_{-\tau}^{-\tau_1} \varphi_1(\theta, y) d\theta \right] \gamma(\tau, y) d\tau dy \right. \\ &\quad \left. + \int_{A_1}^{A_2} \int_{\tau_1}^{\tau_2} \left[\int_{-\tau_1}^0 \varphi_2(\theta, y) d\theta \right] \gamma(\tau, y) d\tau dy \right\} \\ &= 2H \left\{ \int_{A_1}^{A_2} \int_{\tau_1}^{\tau_2} \left[\int_{-\tau}^{-\tau_1} \varphi_1(\theta, y) d\theta \right] \gamma(\tau, y) d\tau dy \right. \\ &\quad \left. + \int_{A_1}^{A_2} \int_{-\tau_1}^0 \varphi_2(\theta, y) d\theta dy \right\}. \end{aligned}$$

Denote

$$I = \left[\int_{A_1}^{A_2} \int_{\tau_1}^{\tau_2} \left[\int_{-\tau}^{-\tau_1} \varphi_1(\theta, y) d\theta \right] \gamma(\tau, y) d\tau dy, +\infty[. \right.$$

If $k \in 2H(I)$, then the problem is reduced to finding φ_2 , verifying (30), and such that

$$\begin{aligned} &\int_{A_1}^{A_2} \int_{-\tau_1}^0 \varphi_2(\theta, y) d\theta dy \\ &= (2H)^{-1}(k) - \int_{A_1}^{A_2} \int_{\tau_1}^{\tau_2} \left[\int_{-\tau}^{-\tau_1} \varphi_1(\theta, y) d\theta \right] \gamma(\tau, y) d\tau dy. \quad (31) \end{aligned}$$

The set of admissible φ_2 is a nonempty closed subset of $W^{1,1}([- \tau_1, 0]; L^1(A_1, A_2))$. In fact, for all $\psi \in W^{1,1}([- \tau_2, -\tau_1]; L^1(A_1, A_2))$ and for k in $2H(I)$, we consider the map defined from $W^{1,1}([- \tau_1, 0]; L^1(A_1, A_2))$

into \mathbb{R} defined by

$$F_\psi(\tilde{\psi}) = \int_{A_1}^{A_2} \int_{-\tau_1}^0 \tilde{\psi}(\theta, y) d\theta dy - (2H)^{-1}(k) \\ + \int_{A_1}^{A_2} \int_{\tau_1}^{\tau_2} \left[\int_{-\tau}^{-\tau_1} \psi(\theta, y) d\theta \right] \gamma(\tau, y) d\tau dy.$$

It is easily verified that F_ψ is continuous on $W^{1,1}([-\tau_1, 0]; L^1(A_1, A_2))$. So, $F_\psi^{-1}(\{0\})$, is a closed, nonempty subset of $W^{1,1}([-\tau_1, 0]; L^1(A_1, A_2))$, contained in a ball of $L^1((-\tau_1, 0) \times (A_1, A_2))$. More precisely, it is the intersection of the ball with the positive cone of $L^1((-\tau_1, 0) \times (A_1, A_2))$. Moreover, one has to have $\varphi_2 \in W^{1,1}([-\tau_1, 0]; L^1(A_1, A_2))$, with $\varphi_2(-\tau_1, \cdot) = \varphi_1(-\tau_1, \cdot)$ and $\varphi_2(0, \cdot) = k\mathcal{A}(\varphi_1)(\cdot)$. These two conditions determine a closed subset of $W^{1,1}([-\tau_1, 0]; L^1(A_1, A_2))$ which is dense in the intersection of the ball with the positive cone.

PROPOSITION 9. *Suppose $H_{(f)}$, $H_{(\gamma)}$, $H_{(\phi)}$, and $H_{(H)}$. Then, for all $n_o \geq 0$, in \mathcal{B} , the solution n of (1), with n_o as initial value, is positive.*

Proof. From the fact that the parameters f , γ , ϕ , and H are positive, the proof follows the same steps as in [2]. ■

5. CONCLUDING REMARKS

In [2] and [4], Eq. (1), or a delay equation modelled on (1), is dealt with using a direct method. In the direct method, the equation is treated as an integral equation: One of the shortcomings of this approach is the lack of a suitable linearization that could be used in looking at the stability of solutions. The technique employed here allows the derivation of such a linearization. Developments along these lines are deferred to a further study.

REFERENCES

1. O. Arino and M. Kimmel, Asymptotic behavior of nonlinear semigroup describing a model of selective cell growth regulation, *J. Math. Biol.* **29** (1991), 289–314.
2. O. Arino and M. Kimmel, Asymptotic behavior of nonlinear functional integral equation of cell kinetics unequal division, *J. Math. Biol.* **27** (1989), 341–354.
3. O. Arino, M. Kimmel, and M. Zerner, Analysis of a cell population model with unequal division and random transition, *Lecture Notes in Pure and Appl. Math.* **131** (1991), 3–12.
4. O. Arino and A. Mortabit, Slow oscillations in a model of cell population dynamics, *Lecture Notes in Pure and Appl. Math.* **131** (1991).

5. H. Brezis, "Opérateurs maximaux monotones et semi-groupes de contractions sur les espaces de Hilbert," in *Mathematics Studies*, North Holland, Amsterdam, 1973.
6. M. G. Crandall and T. Liggett, Generation of semigroups of nonlinear transformations on General Banach Spaces, *Amer. J. Math.* **93** (1971), 265–298.
7. J. Dyson and R. Vilella-Bressan, A semigroup approach to nonlinear autonomous neutral functional differential equations, *J. Differential Equations* **59**, No. 2 (1985), 206–228.
8. J. Hale, "Functional Differential Equations," in *Applied Mathematics Series*, Vol. 3, Springer-Verlag, New York, 1971.
9. M. Kimmel, Z. Darzynkiewicz, O. Arino, and F. Traganos, Analysis of a cell cycle model based on unequal division of metabolic constituents to daughter cells during cytokinesis, *J. Theoret. Biol.* **110** (1984), 637–665.
10. O. Sidki, Thèse, Pau, No. 221 (1994).