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Impulsive prion disease model

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Abstract. A model of prion diseases with impulse effects is studied in this work. First we transform the model to a system of three differential equations with impulse effects in order to study the stability of periodic solution. After that we study the general model by the mean of evolution semi group in order to find conditions of existence of mild solution.

1. Introduction

In this work we consider a model describing prion polymerization, our model is inspired from those of Webb and collaborators (see [3], [6]), it is constituted by a differential equation modeling the evolution of PrP^c and a partial differential equation describing the PrP^{sc} evolution. We consider the case where the monomers are produced discretely at fixed times t_i, which is expressed by impulse equations (see [4]).

More specifically we consider the following system

$$\begin{cases} v'(t) = -\gamma v(t) - \tau v(t) \int_{x_0}^{\infty} u(t,x)dx \\ \qquad +2\int_0^{x_0} x \int_{x_0}^{\infty} \beta(y)\kappa(x,y)u(t,y)dydx, \ t \neq t_i, \quad i = 1,2,\ldots, \\ v(t_i^+) - v(t_i^-) = \lambda_i, \quad \lambda_i > 0, \quad i = 1,2,\ldots, \\ \partial_t u(t,x) + \tau v(t)\partial_x u(t,x) + (\mu(x) + \beta(x))u(t,x) \\ \qquad = 2\int_x^{\infty} \beta(y)\kappa(x,y)u(t,y)dy, \end{cases} \tag{1}$$

for $t \geq 0$, $x \in [x_0, +\infty)$ with fixed $x_0 > 0$.

The variables and parameters of the model are

- $v(t)$ is the number of PrP^c monomers at time t,
- $u(t,x)$ is the density of PrP^{sc} polymers of length x at time t,

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- x_0 is the lower bound for polymer length (that is polymers have length x with $x_0 < x < \infty$),
- λ_i is the number of monomers PrP^c produced at time t_i,
- γ is the metabolic degradation rate for PrP^c,
- τ is the rate associated with lengthening of PrP^{sc} polymers by attaching to and converting PrP^c monomers,
- $\beta(x)$ is length-dependent rate of polymer breakage,
- $\kappa(x, y)$ is the probability, when a polymer of length y breaks, that one of the two resulting polymers has length x,
- $\mu(x)$ is the length-dependent metabolic degradation rate of PrP^{sc} polymers having length x.

The kernel $\kappa(y, x)$ should satisfy the following properties

$$\kappa(y,x) \geq 0, \kappa(y,x) = \kappa(x-y,x), \quad \int_0^x \kappa(y,x)dy = 1,$$

for all $x \geq x_0$, $y \geq 0$,

$$\begin{aligned} \kappa(y,x) &= 1/x, \quad \text{if } x > x_0 \text{ and } 0 < y < x. \\ \kappa(y,x) &= 0, \quad \text{elsewhere.} \end{aligned}$$

In the following section we transform the model (1) to a system of impulsive differential equations in order to study the stability of periodic trivial solutions, in the third section we study the general model. In the last section we give some remarks.

2. Conversion to impulsive differential equations

Define the functions $V(t) = v(t)$, $U(t) = \int_{x_0}^{\infty} u(t,y)dy$ and $P(t) = \int_{x_0}^{\infty} yu(t,y)dy$ where $U(t)$ is the total number of polymers and $P(t)$ is the total number of monomers in polymers at time t.

We deduce from model (1) the following system of impulsive differential equations

$$\begin{aligned} \dot{V}(t) &= \lambda - \gamma V(t) - \tau V(t)U(t) + 2\beta x_0^2 U(t) = F_1(V(t), U(t), P(t)), \\ \dot{U}(t) &= -\mu U(t) + \beta P(t) - 2\beta x_0 U(t) = F_2(V(t), U(t), P(t)), \\ \dot{P}(t) &= \tau V(t)U(t) - \mu P(t) - \beta x_0^2 U(t) = F_3(V(t), U(t), P(t)), \\ V(t_i^+) &= V(t_i) + \lambda_i = \Theta_1(V(t_i), U(t_i), P(t_i)), \lambda_i > 0, i \in \mathbb{N}^*, \\ U(t_i^+) &= U(t) = \Theta_2(V(t_i), U(t_i), P(t_i)), \\ P(t_i^+) &= P(t) = \Theta_3(V(t_i), U(t_i), P(t_i)). \end{aligned} \tag{2}$$

In this section we consider the case where $\lambda_i = \lambda_0 > 0$ and $t_i = \tau \; \forall i \in \mathbb{N}^*$.

We are interested by the existence and stability of periodic solutions of (2).

A solution $\xi = (V, U, P)$ of the problem (2) is a function defined in $\mathbb{R}_+$, with non-negative components, continuously differentiable in $\mathbb{R}_+ - \{t_i\}_{i \geq 0}$, with $t_0 = 0$ and satisfying (2).

The function $\xi = (V, 0, 0)$ is the trivial solution of problem (2) where $V(t) = V_0 e^{-\gamma t}$. Also ξ is called trivial T_0-periodic solution if it is a trivial solution with $\xi(nT_0) = \xi((n+1)T_0)$ for all $n \geq 0$.
We have $F_2(V, 0, 0) \equiv \Theta_2(V, 0, 0) \equiv 0$ and $F_2(V, 0, 0) \equiv \Theta_2(V, 0, 0) \equiv 0$.
Our main objective is to study the stability of the trivial periodic solution and the loss of stability for some values of the parameters.

Let Φ be the flow associated to (2), we have $\Phi(t, X_0) = \xi(t), 0 < t \le T_0$ where $\xi(0) = X_0 = \xi(0) = (V(0), U(0), P(0))$.
Let Ψ be the operator defined by

$$\Psi(\tau, X_0) = \Theta(\Phi(\tau, X_0)),$$

we denote by $D_X\Psi$ the derivative of Ψ with respect to X. Then $\xi = \Phi(\cdot, X_0)$ is a τ-periodic solution of (2) if and only if $\Psi(\tau, X_0) = X_0$ *i.e.* X_0 is a fixed point of $\Psi(\tau, \cdot)$, and it is exponentially stable if $\rho(D_X\Psi(\tau, \cdot)) < 1$.

Let V_s be a T_0-periodic function defined by $V_s(t) = \lambda_0 \frac{e^{-\gamma t}}{1-e^{-\gamma T_0}}$ for $0 < t \le T_0$.
For $U = P = 0$ the problem (2) has T_0-periodic solution $\xi = (V_s, 0, 0)$.
Consider the following hypothesis

(H1) $\max\left(\frac{(1-e^{-\gamma T_0})}{\beta\tau}\left[2\beta^2 x_0^2 - \left(\frac{2}{T_0} - (\mu+\beta x_0)\right)^2\right], \frac{(1-e^{-\gamma T_0})}{\beta\tau}\left[2\beta^2 x_0^2 - (\mu+\beta x_0)^2\right]\right) < \lambda_0 < \frac{2\beta x_0^2(1-e^{-\gamma T_0})}{\tau}$.

(H2) $\frac{2\beta x_0^2(1-e^{-\gamma T_0})}{\tau} < \lambda_0 < \left(\frac{1-(1-(\mu+\beta x_0)T_0)^2}{T_0^2} + 2\beta^2 x_0^2\right)\frac{(1-e^{-\gamma T_0})}{\beta\tau}$.

We have the following result.

Theorem 2.1: *If one of the hypothesis* **(H1)** *or* **(H2)** *is satisfied, then there exists* $\epsilon_0 > 0$ *such that for* $0 < T_0 < \epsilon_0$ *the trivial periodic solution is exponentially stable.*

Proof: We have $D_X\Psi(T_0, X) = D_X\Theta(\Phi(T_0, X))\frac{\partial\Phi}{\partial X}(T_0, X)$, then for $X_0 = (V(0), U(0), P(0))$ we obtain

$$D_X\Psi(T_0, X) = \begin{pmatrix} \frac{\partial\Theta_1}{\partial V} & \frac{\partial\Theta_1}{\partial U} & \frac{\partial\Theta_1}{\partial P} \\ \frac{\partial\Theta_2}{\partial V} & \frac{\partial\Theta_2}{\partial U} & \frac{\partial\Theta_2}{\partial P} \\ \frac{\partial\Theta_3}{\partial V} & \frac{\partial\Theta_3}{\partial U} & \frac{\partial\Theta_3}{\partial P} \end{pmatrix} \begin{pmatrix} \frac{\partial\Phi_1}{\partial V} & \frac{\partial\Phi_1}{\partial U} & \frac{\partial\Phi_1}{\partial P} \\ \frac{\partial\Phi_2}{\partial V} & \frac{\partial\Phi_2}{\partial U} & \frac{\partial\Phi_2}{\partial P} \\ \frac{\partial\Phi_3}{\partial V} & \frac{\partial\Phi_3}{\partial U} & \frac{\partial\Phi_3}{\partial P} \end{pmatrix}(T_0, X_0)$$

$$= \begin{pmatrix} \frac{\partial\Phi_1}{\partial V} & \frac{\partial\Phi_1}{\partial U} & \frac{\partial\Phi_1}{\partial P} \\ \frac{\partial\Phi_2}{\partial V} & \frac{\partial\Phi_2}{\partial U} & \frac{\partial\Phi_2}{\partial P} \\ \frac{\partial\Phi_3}{\partial V} & \frac{\partial\Phi_3}{\partial U} & \frac{\partial\Phi_3}{\partial P} \end{pmatrix}(T_0, X_0).$$

From the variational equation we find

$$\frac{d}{dt}\begin{pmatrix} \frac{\partial\Phi_1(t,X_0)}{\partial V} & \frac{\partial\Phi_1(t,X_0)}{\partial U} & \frac{\partial\Phi_1(t,X_0)}{\partial P} \\ \frac{\partial\Phi_2(t,X_0)}{\partial V} & \frac{\partial\Phi_2(t,X_0)}{\partial U} & \frac{\partial\Phi_2(t,X_0)}{\partial P} \\ \frac{\partial\Phi_3(t,X_0)}{\partial V} & \frac{\partial\Phi_3(t,X_0)}{\partial U} & \frac{\partial\Phi_3(t,X_0)}{\partial P} \end{pmatrix} = \begin{pmatrix} -\gamma & -\tau V_s(t) + \beta x_0^2 & 0 \\ 0 & -(\mu+2\beta x_0) & -\tau V_s(t) + \beta x_0^2 \\ 0 & \beta & -\mu \end{pmatrix}\begin{pmatrix} \frac{\partial\Phi_1(t,X_0)}{\partial V} & \frac{\partial\Phi_1(t,X_0)}{\partial U} & \frac{\partial\Phi_1(t,X_0)}{\partial P} \\ \frac{\partial\Phi_2(t,X_0)}{\partial V} & \frac{\partial\Phi_2(t,X_0)}{\partial U} & \frac{\partial\Phi_2(t,X_0)}{\partial P} \\ \frac{\partial\Phi_3(t,X_0)}{\partial V} & \frac{\partial\Phi_3(t,X_0)}{\partial U} & \frac{\partial\Phi_3(t,X_0)}{\partial P} \end{pmatrix}.$$

Then we obtain

$$\frac{\partial\dot{\Phi}_1(t, X_0)}{\partial V} = -\gamma\frac{\partial\Phi_1(t, X_0)}{\partial V} + (-\tau V_s(t) + \beta x_0^2)\frac{\partial\Phi_2(t, X_0)}{\partial V} \tag{3}$$

$$\frac{\partial\dot{\Phi}_2(t, X_0)}{\partial V} = -(\mu+2\beta x_0)\frac{\partial\Phi_2(t, X_0)}{\partial V} + (-\tau V_s(t) + \beta x_0^2)\frac{\partial\Phi_3(t, X_0)}{\partial V} \tag{4}$$

$$\frac{\partial \dot{\Phi}_3(t, X_0)}{\partial V} = \beta \frac{\partial \Phi_2(t, X_0)}{\partial V} - \mu \frac{\partial \Phi_3(t, X_0)}{\partial V} \tag{5}$$

$$\frac{\partial \dot{\Phi}_1(t, X_0)}{\partial U} = -\gamma \frac{\partial \Phi_1(t, X_0)}{\partial U} + (-\tau V_s(t) + \beta x_0^2) \frac{\partial \Phi_2(t, X_0)}{\partial U} \tag{6}$$

$$\frac{\partial \dot{\Phi}_2(t, X_0)}{\partial U} = -(\mu + 2\beta x_0) \frac{\partial \Phi_2(t, X_0)}{\partial U} + (-\tau V_s(t) + \beta x_0^2) \frac{\partial \Phi_3(t, X_0)}{\partial U} \tag{7}$$

$$\frac{\partial \dot{\Phi}_3(t, X_0)}{\partial U} = \beta \frac{\partial \Phi_2(t, X_0)}{\partial U} - \mu \frac{\partial \Phi_3(t, X_0)}{\partial U} \tag{8}$$

$$\frac{\partial \dot{\Phi}_1(t, X_0)}{\partial P} = -\gamma \frac{\partial \Phi_1(t, X_0)}{\partial P} + (-\tau V_s(t) + \beta x_0^2) \frac{\partial \Phi_2(t, X_0)}{\partial P} \tag{9}$$

$$\frac{\partial \dot{\Phi}_2(t, X_0)}{\partial P} = -(\mu + 2\beta x_0) \frac{\partial \Phi_2(t, X_0)}{\partial P} + (-\tau V_s(t) + \beta x_0^2) \frac{\partial \Phi_3(t, X_0)}{\partial P} \tag{10}$$

$$\frac{\partial \dot{\Phi}_3(t, X_0)}{\partial P} = \beta \frac{\partial \Phi_2(t, X_0)}{\partial P} - \mu \frac{\partial \Phi_3(t, X_0)}{\partial P} \tag{11}$$

From (3)–(4) we obtain $\frac{\partial \Phi_2(t,X_0)}{\partial V} = 0$, $\frac{\partial \Phi_3(t,X_0)}{\partial V} = 0$ and $\frac{\partial \Phi_1(t,X_0)}{\partial V} = e^{-\gamma t}$.

To solve the system (3)–(10) we use power series.

Put

$$\frac{\partial \Phi_1(T_0, X_0)}{\partial U} = \sum_{n \geq 0} a_n T_0^n, \quad a_0 = 0,$$

$$\frac{\partial \Phi_1(T_0, X_0)}{\partial P} = \sum_{n \geq 0} b_n T_0^n, \quad b_0 = 0,$$

$$\frac{\partial \Phi_2(T_0, X_0)}{\partial U} = \sum_{n \geq 0} c_n T_0^n, \quad c_0 = 1,$$

$$\frac{\partial \Phi_2(T_0, X_0)}{\partial P} = \sum_{n \geq 0} d_n T_0^n, \quad d_0 = 0,$$

$$\frac{\partial \Phi_3(T_0, X_0)}{\partial U} = \sum_{n \geq 0} e_n T_0^n, \quad e_0 = 0,$$

$$\frac{\partial \Phi_3(T_0, X_0)}{\partial P} = \sum_{n \geq 0} f_n T_0^n, \quad f_0 = 1.$$

Hence

$$det(D_X \Psi(T_0, X) - \nu I) = (e^{-\gamma T_0} - \nu)(\nu^2 + A\nu + B)$$

where

$$A = -\left(\sum_{n\geq 0} c_n T_0^n + \sum_{n\geq 0} a_n T_0^n\right),$$

$$B = \left(\sum_{n\geq 0} c_n T_0^n\right)\left(\sum_{n\geq 0} a_n T_0^n\right) + \left(\sum_{n\geq 0} d_n T_0^n\right)\left(\sum_{n\geq 0} e_n T_0^n\right).$$

We have an eigenvalue $\nu_1 = e^{-\gamma T_0} < 1$, it remains to find the two other eigenvalues ν_2 and ν_3.

The discriminant of the polynom $\nu^2 + A\nu + B$ is

$$\Delta = 4\beta T_0^2 \left(2\beta x_0^2 - \tfrac{\tau\lambda_0}{1-e^{-\gamma T_0}}\right) + o(T_0^2) = 4\beta T_0^2 \Delta_1 + o(T_0^2)$$

where $\Delta_1 = 2\beta x_0^2 - \frac{\tau\lambda_0}{1-e^{-\gamma T_0}}$.

For T_0 small enough, we deduce the sign of Δ from that of Δ_1.

1. $\Delta_1 > 0$ if an only if $\lambda_0 < \frac{2\beta x_0^2(1-e^{-\gamma T_0})}{\tau}$.
   For T_0 small enough, we have

$$\nu_{2,3} = 1 - (\mu + \beta x_0)T_0 \pm T_0\sqrt{2\beta^2 x_0^2 - \frac{\beta\tau\lambda_0}{1-e^{-\gamma T_0}} + o(1)}.$$

   The solution ξ is exponentially stable if

$$|\nu_i| < 1 \text{ for } i = 1, 2, 3.$$

   That is

$$T_0 < \frac{2}{\mu + \beta x_0},$$

$$\lambda_0 > \frac{(1-e^{-\gamma T_0})}{\beta\tau}\left[2\beta^2 x_0^2 - \left(\frac{2}{T_0} - (\mu + \beta x_0)\right)^2 + o(1)\right],$$

   and

$$\lambda_0 > \frac{(1-e^{-\gamma T_0})}{\beta\tau}\left[2\beta^2 x_0^2 - (\mu + \beta x_0)^2 + o(1)\right].$$

   Then we deduce that ξ is exponentially stable if (**H1**) is satisfied and $\epsilon_0 \leq \frac{2}{\mu+\beta x_0}$.

2. $\Delta_1 < 0$ if an only if $\lambda_0 > \frac{2\beta x_0^2(1-e^{-\gamma T_0})}{\tau}$.
   For T_0 small enough, we have

$$\nu_{2,3} = 1 - (\mu + \beta x_0)T_0 \pm i T_0\sqrt{-2\beta^2 x_0^2 + \frac{\beta\tau\lambda_0}{1-e^{-\gamma T_0}} + o(1)}.$$

   That is

$$\lambda_0 < \left(\frac{1 - (1 - (\mu + \beta x_0)T_0)^2}{T_0^2} + 2\beta^2 x_0^2 + o(1)\right)\frac{(1-e^{-\gamma T_0})}{\beta\tau}.$$

   Then we deduce that ξ is exponentially stable if (**H2**) is satisfied and $\epsilon_0 \leq \frac{2}{\mu+\beta x_0}$.

□

3. Analysis of the general model

In this section we consider the general model (1), we use the evolution semi group theory to prove the existence of mild solutions (see [4]).

We consider the case where $\beta(x) \equiv \beta$ and $\mu(x) \equiv \mu$ are constant. Then for $t \in J$, $x \in Y := [x_0, +\infty)$, $u^0 \in D$ and $u \in L^1(Y)$, we may rewrite (1.1) as

$$\begin{cases} v'(t) = -\gamma v(t) - \tau v(t)|u|_1 + \beta x_0^2 |\kappa u|_1, & t \neq t_i, \\ v(t_i^+) - v(t_i) = \lambda_i, \lambda_i > 0, i \in n^*, \\ v(0) = v^0, \end{cases} \tag{12}$$

and

$$\begin{cases} \partial_t u(t,x) + \tau v(t) \partial_x u(t,x) + (\mu+\beta) u(t,x) = 2\beta \int_x^\infty \kappa(x,y) u(y) dy, \\ u(t,x_0) = 0, u(0,x) = u^0(x), \end{cases} \tag{13}$$

where $|u|_1 = \int_{x_0}^\infty |u(y)| dy$.

Set $D := \left\{ u^0 \in L^1(Y) \cap W^{1,1}(\mathbb{R}) : x^2 u^0, (u^0)', x(u^0)' \in L^1(Y), u^0(x) = 0 \text{ for } x \leq x_0 \right\}$.

Let $J_i = (t_i, t_{i+1})$, $i = 0, \ldots, p$, and v_i be the restriction of a function y to J_i.

Consider the following spaces

$PC = \{ v\colon J \to X,\ v_i \in C(J_i, X),\ i = 0, \ldots, p,$ such that $v(t_i^-)$ and $v(t_i^+)$ exist and satisfy $v(t_k^-) = v(t_k)$ for $i = 0, \ldots, p \}$

with the norm $\|v\|_{PC} = \max\{\|v_k\|_\infty, \quad i = 0, \ldots, p\}$,

$PC^1(J, \mathbb{R}) = \left\{ v \in PC : v \in C^1(J_i, \mathbb{R}), \exists v'(t_i^+), v'(t_i^-), i = 1, \ldots, p \right\}$

with the norm $\|v\|_{PC^1} = \max\{\|v\|_{PC}, \|v'\|_{PC}\}$ and

$X := L^1(Y; (a+x)dx)$ where $a > 0$, with the norm defined by $\|y\|_X = a|y|_1 + |xy|_1$.

Then $(PC, \|\cdot\|_{PC})$, $(PC^1, \|\cdot\|_{PC^1})$ and $(X, \|\cdot\|_X)$ are Banach spaces.

For $\overline{u} \in C(J, X)$, the solution of (12) is given by

$$v_{\overline{u}}(t) = \sum_{0 < t_j \leq t \leq b} \lambda_j e^{\left(-\gamma(t-t_j) - \tau \int_{t_j}^t |\overline{u}(s)|_1 ds\right)} + v^0 e^{\left(-\gamma t - \tau \int_0^t |\overline{u}(s)|_1 ds\right)}$$
$$+ \beta x_0^2 \int_0^t |\kappa \overline{u}(s)|_1 e^{\left(-\gamma(t-s) - \tau \int_s^t |\overline{u}(\sigma)|_1 d\sigma\right)} ds$$

Let $v = v_{\overline{u}}$, the problem (13) is written as

$$\begin{cases} u'(t) + A_v(t) u(t) = f(t, u(t)), & t \in J, \\ u(0) = u_0. \end{cases} \tag{14}$$

where

$$A_{v_{\overline{u}}}(.)(u(x)) = v_{\overline{u}}(.) \partial_x u(x) + (\mu+\beta) u(x), \qquad \text{for } x \in Y$$

and

$$f(t, u(t,x)) = 2\beta \int_x^\infty \kappa(x,y) u(t,y) dy, \quad \text{with} \qquad f : J \times X \to X.$$

Then for $(s,t) \in \Delta := \{(t,s) \in J^2, t \geq s\}$, the evolution problem for (13) is given by (see [1], [5])

$$\left[U_{v_{\overline{u}}}(t,s) u^0 \right](x) = u^0 \left(x - \int_s^t v_{\overline{u}}(\sigma) d\sigma \right) e^{-\phi(t,s)}, \tag{15}$$

where $\phi(t,s) = (\mu+\beta)(t-s)$.

Remark 3.1: *The two parameter family linear operators $U_{v_{\overline{u}}}(t,s)$ is an exponentially bounded evolution semi-group system (see [4]).*

For $v = v_{\overline{u}}$ the solution of (13) is given by

$$u(t) = U_{v_{\overline{u}}}(t,0)u^0 + \int_0^t U_{v_{\overline{u}}}(t,s)f(s,u(s))ds. \tag{16}$$

Theorem 3.2: *The problem (13) has a unique mild solution $u \in C(J,X)$.*

Proof: Let $u_1, u_2 \in X$ then for $t \in J$ and $x \geq x_0$, we have

$$\begin{aligned}
\|f(t,u_1) - f(t,u_2)\|_X &\leq \int_{x_0}^{\infty} 2\beta \left|\int_x^{\infty} \kappa(x,y)(u_1(y)-u_2(y))dy\right|(a+x)dx \\
&\leq 2\beta \int_{x_0}^{\infty} |u_1(y)-u_2(y)|dy \int_{x_0}^{y} \kappa(x,y)(a+x)dx \\
&\leq 2\beta \int_{x_0}^{\infty} |u_1(y)-u_2(y)| \frac{\left(ay+\frac{y^2}{2}\right)}{y} dy \\
&\leq 2\beta \int_{x_0}^{\infty} |u_1(y)-u_2(y)|(a+y)dy \\
&\leq 2\beta \|u_1-u_2\|_X .
\end{aligned}$$

Then we deduce that (13) has a unique mild solution in X given by (16). □

Theorem 3.3: *For $v^0 > 0$ and $u^0 \in X$, the problem (12) and (13) has a unique global positive solution $(v,u) \in PC^1(J,\mathbf{R}) \times C(J,X)$.*

Proof: Let $\overline{u}_1,\ \overline{u}_2 \in C(J,X)$, from the explicit representation of $v_{\overline{u}}$ we have

$$|v_{\overline{u}_1}(t) - v_{\overline{u}_2}(t)| \leq\leq b\tau \left(\sum_{0\leq t_j\leq t} \lambda_j + v^0 + \beta x_0\right) \|\overline{u}_1 - \overline{u}_2\|_{\infty} .$$

Let $\Lambda(\overline{u})(t) = U_{v_{\overline{u}}}(t,0)u^0$, for $t \in J$ and $\overline{u} \in C(J,X)$.
Next we show that $\Lambda : C(J,X) \to C(J,X)$ is a contraction, which would imply existence and uniqueness of the solution of (12) and (13) (see [2]).
In fact, for $\overline{u}_1,\ \overline{u}_2 \in C(J,X)$ and $t \in J$, we have

$$\|\Lambda(\overline{u}_1)(t) - \Lambda(\overline{u}_2)(t)\|_X \leq \left|u^0\right|_1 b^2\tau \left(\sum_{0\leq t_j\leq t} \lambda_j + v^0 + \beta x_0\right) \|\overline{u}_1 - \overline{u}_2\|_{\infty} .$$

Hence Λ is a contraction for $\left|u^0\right|_1 \left(\sum_{0\leq t_j\leq b} \lambda_j + v^0 + \beta x_0\right) < \frac{1}{b^2\tau}$.

Now, we prove the existence and uniqueness of solution for (12) and (13). Let $r > 0$ such that $u^0 \in B(0,r) \subset X$, then there exists $K > 0$ such that

$$\|U_{v_u}(t,s)\| \leq K \quad \text{for all } u \in B(0,r).$$

Let $u \in C(J,X)$ such that $u(t) = U_{v_u}(t,0)u^0 + \int_0^t U_{v_u}(t,s)f(s,u(s))ds,\quad t \in J$ and $u(t) \in B(0,r)$, $t \in J$, then

$$\|u(t)\|_X \leq |u^0|_1 K + 2\beta K b r.$$

Assume that $|u^0|_1 K + 2\beta K b r \leq r$ and set $C = \{u \in C(J,X) :\ \|u\|_{\infty} \leq r\}$.

Now, we show that $N : C \to C$ has a unique fixed point.
Let $u_1, u_2 \in C$, thus

$$\|(Nu_1)(t) - (Nu_2)(t)\|_X \leq e^{\mu t}\left(c + \frac{2\beta(Kx_0+r)}{x_0\mu}\right)\|u_1 - u_2\|_*$$

where $\|u\|_* = \sup_{t\in J} e^{-\mu t}\|u(t)\|_X, c = \left|u^0\right|_1 b^2\tau\left(\sum_{0\leq t_j\leq t}\lambda_j + v^0 + \beta x_0\right)$ and $\mu > 0$ large enough such that $C_0 = c + \frac{2\beta(Kx_0+r)}{x_0\mu} < 1$.

Hence $\|Nu_1 - Nu_2\|_* \leq C_0\|u_1 - u_2\|_*$.
To prove the positivity of the solution of (13), we proceed by induction.
For $n \geq 1$ we put

$$u_{n+1}(t) = u_1(t) + \int_s^t U_v(t,s)f(s,u_n(s))ds,\ \ t \geq 0.$$

And we conclude that the solution for the problem (13) is positive. □

4. Remarks

In this work we have studied a prion disease model with impulse effects. First we have transformed the general model into impulsive differential equation system, which help to study the exponential stability of the trivial periodic equilibrium. After that, we have studied the general problem, we have proved the existence of solutions under conditions on the parameters of the model. It will be very interesting to search a global solutions on $\mathbb{R}_+$ in order to study their stabilities and to give numerical simulations to illustrate the results obtained.

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