DELAY EQUATIONS: ANALYSIS OF A MODEL WITH FEEDBACK USING TOPOLOGICAL DEGREE

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Abstract: We prove the existence of at least one positive θ-periodic solution of a system of delay differential equations for models with feedback arising on regulatory mechanisms in which self-regulation is relevant, e.g. in cell physiology
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1 INTRODUCTION

We study a model for the cycle of the Testosterone hormone (shown in Fig.1). We follow the notation of [3] for the concentration of the Luteinising Hormone (LH) from Hypotalamus, Luteinising Hormone Releasing Hormone ($LHRH$) from Pituitary gland and Testosterone Hormone (TH) from Testes in man. In 1989, Murray studied a more simple system (based on a model by Smith from 1980) also mentioned in [2] and [4]. For details, see [3].

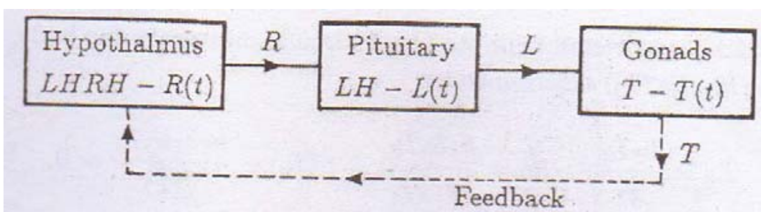

Figure 1: Hormone Testosterone cycle

A general mathematical model describing the biochemical interaction of the hormones LH, $LHRH$ and TH in the male is presented. The model structure consists of a negative feedback system of three delay differential equations.
In this paper we study existence of solutions in a more general model, namely the following system of delay differential equations

$$\frac{dR}{dt} = F(t, T(t-\tau)) - b_1(R(t)),$$
$$\frac{dL}{dt} = G(t, R(t-\tau), T(t-\tau)) - b_2(L(t)), \tag{1}$$
$$\frac{dT}{dt} = H(t, L(t-\tau)) - b_3(T(t))$$

where $\tau > 0$ is a fixed delay.
The features of the model read as follows.

1. $F, H : \mathbb{R} \times [0, +\infty) \to [0, \infty)$ and $G : \mathbb{R} \times [0, +\infty)^2 \to [0, \infty)$ are continuous and θ-periodic in the first coordinate.

2. $b_i : [0, +\infty) \to [0, +\infty)$ is an increasing, unbounded homeomorphism and $b_i(0) = 0$ for $i = 1, 2, 3$

3. F is nonincreasing in its second coordinate and $F(t,x) > 0$ for all $x \geq 0$.

4. H is nondecreasing in its second coordinate and $H(t,x) > 0$ for all $x > 0$.

5. G is nondecreasing in its second coordinate and nonincreasing in its third coordinate, with $G(t,x,y) > 0$ for $x > 0$.

Remark. It is seen from the model that high levels of T affect the concentration of R and L.

It shall be seen that under conditions $1-5$ the system has at least one positive θ-periodic solution.

2 Abstract setting

We shall write our equation as $Lu = Nu$, where $u := (R,L,T)$, L is the linear operator given by $Lu := u'$ and N is defined as the right-hand side of system (1). We shall apply the continuation method in the Banach space

$$C_\theta = \{u \in C(\mathbb{R},\mathbb{R}^3) : u(t) = u(t+\theta) \text{ for all } t\}$$

equipped with the standard uniform norm. Note that the nonlinear operator N is defined over the positive cone $K := \{u \in C_\theta : R,T,L \geq 0\}$.

For convenience, the average of a function u shall be denoted by $\overline{u}$, namely $\overline{u} := \frac{1}{\theta}\int_0^\theta u(t)\,dt$. Also, identifying $\mathbb{R}^3$ with the subset of constant functions of C_θ we may define the function $\phi : [0,+\infty)^3 \to \mathbb{R}^3$ given by $\phi(x) = \overline{Nx}$.

The following continuation theorem can be easily deduced from the standard topological degree methods (see e.g. [1]).

Theorem 1 *Assume there exists $\Omega \subset K$ open and bounded such that:*

a) The problem $Lu = \lambda Nu$ has no solutions in $\partial\Omega$ for $0 < \lambda < 1$.

b) $\phi(u) \neq 0$, $u \in \partial\Omega \cap \mathbb{R}^3$.

c) $deg(\phi, \Omega \cap \mathbb{R}^3, 0) \neq 0$, where 'deg' stands for the Brouwer degree.

Then (1) has at least one solution in $\overline{\Omega}$.

3 Existence of solutions

In this section, we shall prove the existence of at least one θ-periodic solution (R,L,T) such that $R(t), L(t), T(t) > 0$ for all t. More precisely,

Theorem 2 *If conditions $1-5$ are satisfied, then the system (1) has at least one positive θ-periodic solution.*

Proof.

In order to apply Theorem 1 to our problem, let us assume that $u = (R,L,T) \in K$ is a solution of the system $Lu = \lambda Nu$ for some $\lambda \in (0,1)$. We shall obtain bounds that will allow an appropriate choice of the subset Ω.

In the first place, suppose that R achieves its maximum R^* at some value t^*, then $R'(t^*) = 0$ and hence

$$b_1(R^*) = F(t^*, T(t^*-\tau)) \leq F(t^*, 0).$$

Thus, fixing a constant $\mathcal{R} > b_1^{-1}(F(t,0))$ for all t we conclude that $R^* < \mathcal{R}$. Next, observe that if L achieves its maximum L^* at some t^*, then

$$b_2(L^*) = G(t^*, R(t^*-\tau), T(t^*-\tau)) \leq G(t^*, R^*, 0) \leq G(t^*, \mathcal{R}, 0).$$

Thus, we may fix a constant $\mathcal{L} > b_2^{-1}(G(t,\mathcal{R},0))$ for all t and it is deduced that $L^* < \mathcal{L}$. In the same way, the maximum T^* of the function T satisfies $T^* < \mathcal{T}$ for any arbitrary constant $\mathcal{T} > b_3^{-1}(F(t,\mathcal{L}))$ for all t.

In order to obtain lower bounds, assume firstly that R achieves its minimum R_* at some t_*, then

$$b_1(R_*) = F(t_*, T(t_* - \tau)) \geq F(t_*, T^*) \geq F(t_*, \mathcal{T}) > 0$$

so we may fix a positive constant $\mathfrak{r} < b_1^{-1}(F(t, \mathcal{T}))$ for all t and deduce that $R_* > \mathfrak{r}$. In the same way, it is seen that if $\mathfrak{l} > 0$ is such that $\mathfrak{l} < b_1^{-2}(\min G(t, \mathfrak{r}, \mathcal{T}))$ for all t then $L_* > \mathfrak{l}$. Finally, fix a positive constant $\mathfrak{t}$ such $\mathfrak{t} < b_3^{-1}(H(t, \mathfrak{l}))$ for all t, then it is verified that $T_* > \mathfrak{t}$.

In other words, if

$$\Omega := \{(R, L, T) \in C_\theta : \mathfrak{r} < R(t) < \mathcal{R}, \mathfrak{l} < L(t) < \mathcal{L}, \mathfrak{t} < T(t) < \mathcal{T} \text{ for all } t\},$$

then the first condition of the continuation theorem is satisfied.

Moreover, observe that $\Omega \cap \mathbb{R}^3$ is a parallelepiped, namely

$$Q := \Omega \cap \mathbb{R}^3 = (\mathfrak{r}, \mathcal{R}) \times (\mathfrak{l}, \mathcal{L}) \times (\mathfrak{t}, \mathcal{T}).$$

It is clear, from our choice of the bounds, that ϕ does not vanish on the boundary of Q, so the second condition of Theorem 1 is also fulfilled.

It remains to prove that $deg(\phi, Q, 0) \neq 0$. With this aim, consider the homotopy $\vartheta : \overline{Q} \times [0, 1] \to \mathbb{R}^3$ given by

$$\vartheta(x, \lambda) = (1 - \lambda)(\mathfrak{p} - x) + \lambda\phi(x)$$

where $\mathfrak{p}$ is the center of Q, that is

$$\mathfrak{p} = \left(\frac{\mathcal{R} + \mathfrak{r}}{2}, \frac{\mathcal{L} + \mathfrak{l}}{2}, \frac{\mathcal{T} + \mathfrak{t}}{2} \right).$$

Since

$$\phi(x_1, x_2, x_3) = \frac{1}{\theta} \int_0^\theta \big(F(t, x_3), G(t, x_1, x_3), H(t, x_2)\big)\, dt - (b_1(x_1), b_2(x_2), b_3(x_3)),$$

it is readily seen that ϑ does not vanish for $x \in \partial$Q. By the homotopy invariance of the Brouwer degree, we conclude that

$$deg(\phi, Q, 0) = deg(\mathfrak{p} - Id, Q, 0) = -1$$

and the proof is complete. □

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