Global asymptotic stability of the periodic solution for a periodic model of hematopoiesis with impulses

Teresa Faria[a], José J. Oliveira[b]

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(a) Faculdade de Ciências da Universidade de Lisboa, CMAF
(b) Departamento de Matemática, CMAT, Universidade do Minho

Hematopoiesis models

Mackey and Glass [1], proposed the following models to describe the hematopoiesis process (the process of production, multiplication, and specialization of blood cells in the bone marrow):

- Hematopoieses with monotone prodution rate

$$z'(t) = -\gamma z(t) + \frac{F_0 \eta^n}{\eta^n + z(t-\tau)^n}, \qquad n > 0; \tag{1}$$

- Hematopoiesis with unimodal prodution rate

$$z'(t) = -\gamma z(t) + \frac{F_0 \eta^n z(t-\tau)}{\eta^n + z(t-\tau)^n}, \qquad n > 1; \tag{2}$$

$z(t)$ density of cells at time t; τ time delay; γ destruction rate; F_0 maximal prodution rate (only for (1)); η a shape parameter.

[1] M.C.Mackey, L. Glass, Science 197 (1977) 287-289.

Hematopoiesis model with several delays

$$y'(t) = -a(t)y(t) + \sum_{i=1}^{m} \frac{\beta_i(t)}{1 + y(t - \tau_i(t))^n}, \qquad t \geq 0$$

Notation: $\tau(t) = \max_i \tau_i(t)$ and $\overline{\tau} = \sup_t \tau(t)$

Hematopoiesis model with linear impulses

For $(t_k)_k$ an increasing sequence such that $t_k \to \infty$, we consider

$$\begin{cases} y'(t) = -a(t)y(t) + \displaystyle\sum_{i=1}^{m} \frac{\beta_i(t)}{1 + y(t - \tau_i(t))^n}, & 0 \le t \ne t_k, \\ y(t_k^+) = (1 + b_k)y(t_k), & k \in \mathbb{N} \end{cases} \quad (3)$$

$$y(t_k^+) = (1 + b_k)y(t_k) \Leftrightarrow y(t_k^+) - y(t_k) = b_k y(t_k)$$

$$PC_0^+ = \left\{ \varphi \in PC : \varphi(\theta) \ge 0 \text{ for } \theta \in [-\overline{\tau}, 0),\ \varphi(0) > 0 \right\}$$

- **Periodic Hematopoiesis model with linear impulses**

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- **(H1)** $a, \beta_i \in C(\mathbb{R}; (0, \infty))$ and $\tau_i \in C(\mathbb{R}; [0, \infty))$ are ω-periodic, for some $\omega > 0$;

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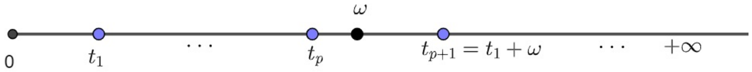
- **(H2)** $\exists p \in \mathbb{N}$ such that $0 < t_1 < \cdots < t_p < \omega$ and

$$t_{k+p} = t_k + \omega, \qquad b_{k+p} = b_k, \qquad k \in \mathbb{N};$$



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- **(H3)** $1 + b_k > 0$, $\forall k \in \mathbb{N}$;
- **(H4)** $\prod_{k=1}^{p}(1 + b_k) < e^{\int_0^\omega a(t)dt}$

Goal

To establish sufficient conditions for global asymptotic stability (GAS) of a positive ω-periodic solution of (3).

Existence of periodic solution

- **Theorem 2** Faria & Oliveira [3]:
  Assume **(H1)-(H4)**.
  Then system (3) has at least one positive ω-periodic solution.

[3] T. Faria and J.J. Oliveira, *Existence of positive periodic solution for scalar delay differential equations with and without impulses*, J. Dyn. Differ. Equ., 31 (2019), 1223-1245.

Existence of periodic solution

- **Theorem 2** Faria & Oliveira [3]:
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- In what follows, we fix $y^*(t)$ a positive ω-periodic solution of system (3).

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Global asymptotic stability

In [4,5], global stability criteria were obtained for the general impulsive model

$$\begin{cases} x'(t) = -a(t)x(t) + \sum_{i=1}^{m} f_i(t, x(t - \tau_i(t))), & t \neq t_k, \\ x(t_k^+) = (1 + b_k)x(t_k), & k \in \mathbb{N} \end{cases}, \qquad (4)$$

where, for each i, $f_i : [0, \infty) \times \mathbb{R} \to \mathbb{R}$ is piecewise continuous and continuous in the second variable.

- [4] T. Faria and J.J. Oliveira, *On stability for impulsive delay differential equations and applications to a periodic Lasota-Wazewska model*, Disc. Cont. Dyn. Systems Series B, 21 (2016), 2451-2472.
- [5] T. Faria and J.J. Oliveira, *A note on stability of impulsive scalar delay differential equations*, Electron. J. Qual. Theory Differ. Equ., Paper No. 69 (2016), 1-14.

- **Theorem 5** Faria & Oliveira, [4,5]:
  Assume **(H2)-(H3)** and $a(t) \not\equiv 0$ ω-periodic continuous.
  The zero solution of (4) is globally asymptotically stable if

(A1) (**Yorke Condition**)

(A2) ($\frac{3}{2}$-**Condition**)

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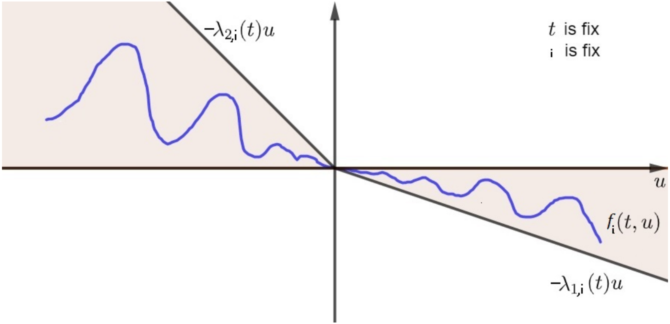
  Assume **(H2)-(H3)** and $a(t) \not\equiv 0$ ω-periodic continuous.
  The zero solution of (4) is GAS if

(A1) (**Yorke Condition**) There are $\lambda_{1,i}, \lambda_{2,i} : [0,\infty) \to [0,\infty)$ piecewise continuous such that, for $t \geq 0$ and $u \in \mathbb{R}$,

$$-\lambda_{1,i}(t)\max\{u,0\} \leq f_i(t,u) \leq \lambda_{2,i}(t)\max\{-u,0\};$$



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(A1) (**Yorke Condition**)

(A2) ($\frac{3}{2}$-**Condition**) There is $T > 0$ such that

$$\alpha_1^* \alpha_2^* < 1 \text{ or } \alpha_1 \alpha_2 < \frac{9}{4} \tag{5}$$

where $\alpha_j^* = \sup_{t \geq T} \alpha_j^*(t)$, $\alpha_j = \sup_{t \geq T} \alpha_j^*(t)\, e^{\int_{t-\tau(t)}^{t} a(u)du}$ $(j = 1, 2)$,

$$\alpha_j^*(t) = \int_{t-\tau(t)}^{t} \sum_{i=1}^{m} \lambda_{j,i}(s) B_i(s)\, e^{-\int_s^t a(u)du}\, ds, \qquad j = 1, 2.$$

$$\text{with } B_i(s) = \prod_{k: t-\tau_i(t) \leq t_k < t} (1 + b_k)^{-1}, \qquad i = 1, \ldots, m.$$

Proof of the main results (idea)

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- System (3) is transformed into

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where:

- for $t \geq 0$ and $u \geq -y^*(t-\tau_i(t))$, $f_i(t,u) = \beta_i(t)g_i(t,u)$ with

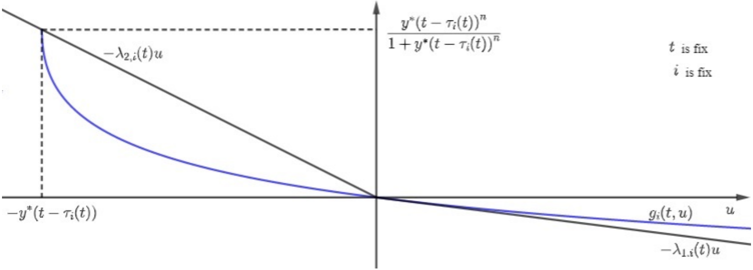
$$g_i(t,u) = \frac{1}{1+[u+y^*(t-\tau_i(t))]^n} - \frac{1}{1+y^*(t-\tau_i(t))^n}, \quad (6)$$

$$S = \left\{ \varphi \in PC : \varphi(\theta) \geq -y^*(\theta) \text{ for } \theta \in [-\overline{\tau}, 0),\ \varphi(0) > -y^*(0) \right\}$$

Let $n \in (0, 1]$.
Considering $g_i(t, u)$ defined in (6), we have

$$\frac{\partial g_i}{\partial u}(t, u) < 0 \text{ and } \frac{\partial^2 g_i}{\partial u^2}(t, u) > 0, \qquad \forall u > -y^*(t - \tau_i(t)), \forall t \geq 0$$

with $\frac{\partial g_i}{\partial u}(t, 0) = -\frac{ny^*(t - \tau_i(t))^{n-1}}{[1 + y^*(t - \tau_i(t))^n]^2}$.



$$\lambda_{1,i}(t) = \frac{ny^*(t - \tau_i(t))^{n-1}}{[1 + y^*(t - \tau_i(t))^n]^2}, \qquad \lambda_{2,i}(t) = \frac{y^*(t - \tau_i(t))^{n-1}}{1 + y^*(t - \tau_i(t))^n}.$$

- **Theorem 3**: Assume **(H1)-(H4)** and $n \in (0,1]$.
  The periodic solution $y^*(t)$ of (3) is GAS, in the set of positive solutions, if there is $T > 0$ such that

$$\alpha_1^* \alpha_2^* < 1 \quad \text{or} \quad \alpha_1 \alpha_2 < \frac{9}{2},$$

where $\alpha_j^* = \sup_{t \geq T} \alpha_j^*(t)$, $\alpha_j = \sup_{t \geq T} \alpha_j^*(t)\, e^{\int_{t-\tau(t)}^t a(u)du}$ $(j = 1,2)$,
and

$$\alpha_1^*(t) = \int_{t-\tau(t)}^t \sum_{i=1}^m \beta_i(s) \frac{n y^*(s-\tau_i(s))^{n-1}}{[1 + y^*(s-\tau_i(s))^n]^2} B_i(s)\, e^{-\int_s^t a(u)\, du}\, ds$$

$$\alpha_2^*(t) = \int_{t-\tau(t)}^t \sum_{i=1}^m \beta_i(s) \frac{y^*(s-\tau_i(s))^{n-1}}{1 + y^*(s-\tau_i(s))^n} B_i(s)\, e^{-\int_s^t a(u)\, du}\, ds$$

$$\text{with } B_i(s) = \prod_{k: t-\tau_i(t) \leq t_k < t} (1 + b_k)^{-1}, \qquad i = 1, \dots, m.$$

Let $n \in (1, \infty)$.
In this case, $g_i(t,u)$ defined in (6) verifies

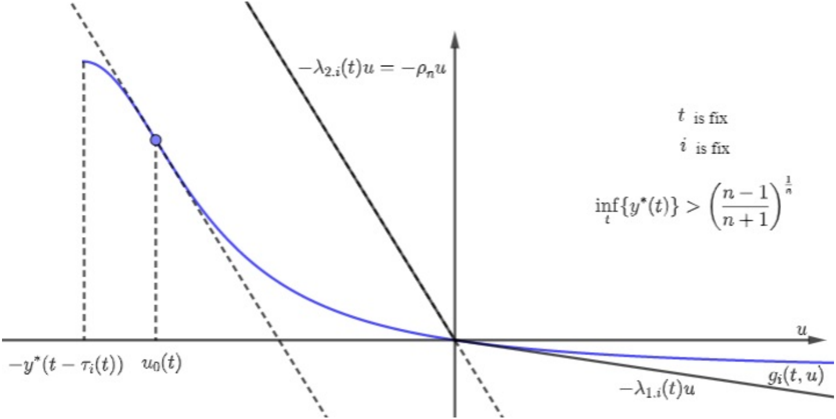
$$\frac{\partial g_i}{\partial u}(t,u) < 0, \qquad \forall u > -y^*(t-\tau_i(t)),\ \forall t \geq 0,$$

and

$$\begin{cases} \dfrac{\partial^2 g_i}{\partial u^2}(t,u) > 0 \text{ for } u > u_0(t), \\ \\ \dfrac{\partial^2 g_i}{\partial u^2}(t,u) < 0 \text{ for } u \in (-y^*(t-\tau_i(t)), u_0(t)), \end{cases}$$

where $u_0(t) := -y^*(t-\tau_i(t)) + \left(\frac{n-1}{n+1}\right)^{\frac{1}{n}}$ is the unique inflection point of $u \mapsto g_i(t,u)$.

We have $\frac{\partial g_i}{\partial u}(t, u_0(t)) = -\rho_n = -\frac{(n+1)^2}{4n}\left(\frac{n-1}{n+1}\right)^{\frac{n-1}{n}}$.


$-\lambda_{2,i}(t)u = -\rho_n u$
t is fix
i is fix
$\inf_t\{y^*(t)\} > \left(\frac{n-1}{n+1}\right)^{\frac{1}{n}}$
u
$-y^*(t-\tau_i(t))$
$u_0(t)$
$g_i(t,u)$
$-\lambda_{1,i}(t)u$

Theorem 4: Assume **(H1)-(H4)** and $n > 1$.
The periodic solution $y^*(t)$ of (3) is GAS (in PC_0^+) if, for some $T > 0$, one of the following conditions holds:

(i) $\left(\alpha_1\gamma < \frac{9}{4} \text{ or } \alpha_1^*\gamma^* < 1\right)$ and $\inf_t\{y^*(t)\} \geq \left(\frac{n-1}{n+1}\right)^{\frac{1}{n}}$;

(ii) $\left(\alpha_1\gamma < \frac{9}{4} \text{ or } \alpha_1^*\gamma^* < 1\right)$ and $\sup_t\{y^*(t)\} \leq \left(\frac{n-1}{n+1}\right)^{\frac{1}{n}}$;

(iii) $\gamma < \frac{3}{2}$ or $\gamma^* < 1$,

where $\gamma^* = \sup_{t \geq T} \gamma^*(t)$, $\gamma = \sup_{t \geq T} \gamma^*(t)\, e^{\int_{t-\tau(t)}^t a(u)du}$, with

$$\gamma^*(t) = \rho_n \int_{t-\tau(t)}^t \sum_{i=1}^m \beta_i(s) B_i(s)\, e^{-\int_s^t a(u)\, du}\, ds,$$

with $\rho_n = \frac{(n+1)^2}{4n}\left(\frac{n-1}{n+1}\right)^{\frac{n-1}{n}}$, $B_i(s)$, α_1, and α_1^* as above.

In case that $y^*(t)$ is unknown, we have the estimate

$$\mathfrak{m} \le y^*(t) \le \mathfrak{M}, \qquad t \ge 0,$$

where

$$\mathfrak{M} = \min\left\{ M\beta\overline{B}, M\overline{B}(e^{A(\omega)} - 1)\, e^{A(\omega)} \left(\max_{t\in[0,\omega]} \frac{\sum_{i=1}^m \beta_i(t)}{a(t)} \right) \right\}$$

$$\mathfrak{m} = \frac{e^{-A(\omega)}\, M\underline{B}}{1+\mathfrak{M}^n} \max\left\{ \beta, (e^{A(\omega)} - 1) \left(\min_{t\in[0,\omega]} \frac{\sum_{i=1}^m \beta_i(t)}{a(t)} \right) \right\}$$

with $\beta = \int_0^\omega \sum_{i=1}^m \beta_i(s) ds$, $A(\omega) = \int_0^\omega a(u) du$,
$M = \left(\prod_{k=1}^p (1+b_k)^{-1} - e^{-A(\omega)} \right)^{-1}$,
$\overline{B} = \max\left\{1, \prod_{k=j}^{j+l} (1+b_k)^{-1} : j = 1, \dots, p, l = 0, \dots, p-1 \right\}$, and
$\underline{B} = \min\left\{1, \prod_{k=j}^{j+l} (1+b_k)^{-1} : j = 1, \dots, p, l = 0, \dots, p-1 \right\}$.

- One delay multiple of the period ($m = 1$, $\tau(t) = q\omega$, $q \in \mathbb{N}$)

$$\begin{cases} y'(t) = -a(t)y(t) + \dfrac{\beta(t)}{1 + y(t - q\omega)^n}, & 0 \le t \ne t_k, \\ y(t_k^+) = (1 + b_k)y(t_k), & k \in \mathbb{N} \end{cases} \tag{7}$$

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- **Theorem 5**: Assume **(H2)-(H4)** and $a, \beta : [0, \infty) \to (0, \infty)$ ω-periodic continuous functions.
  Then (7) has a positive periodic solution which is GAS if:
  case $n > 1$

$$\rho_n B_0^q \sup_{t \geq T} \int_{t-q\omega}^{t} \beta(s)\, e^{-\int_s^t a(u)du}\, ds < \max\left\{1, \frac{3}{2}\, e^{-q\int_0^\omega a(u)du}\right\},$$

or, case $0 < n \leq 1$,

$$\sqrt{n} B_0^q \sup_{t \geq T} \int_{t-q\omega}^{t} \beta(s)\, e^{-\int_s^t a(u)du}\, ds < \mathfrak{m} \max\left\{1, \frac{3}{2}\, e^{-q\int_0^\omega a(u)du}\right\}$$

where $B_0 = \prod_{k=1}^{p}(b_k + 1)^{-1}$.

- **Remark:** Saker and Alzabut [6] proved the existence of a positive periodic solution of (7) and its GAS assuming (H1), (H3), $n \in \mathbb{N}$, the function

$$t \mapsto \prod_{k:t_k \in [0,t)} (1+b_k) \text{ is } \omega\text{-periodic}, \tag{8}$$

and the "3/2-type condition"

$$\rho_n q \int_0^\omega \beta(s)ds < \frac{3}{2}\, \mathrm{e}^{-q\int_0^\omega a(u)du}. \tag{9}$$

[6] S.H. Saker and JO. Alzabut, *On the impulsive delay hematopoiesis model with periodic coefficients*, Rocky Mountain J. Math. 39 (2009) 1657-1688.

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- Condition (8) is stronger than (H2)+(H3).

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- Condition (9) is stronger than

$$\rho_n B_0^q \sup_{t \geq T} \int_{t-q\omega}^t \beta(s) \, e^{-\int_s^t a(u)du} \, ds < \max \left\{ 1, \frac{3}{2} \, e^{-q \int_0^\omega a(u)du} \right\},$$

Thus Theorem 5 improves the stability criterion in [6].

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- No impulsive case ($b_k = 0$, $\forall k \in \mathbb{N}$)

$$y'(t) = -a(t)y(t) + \sum_{i=1}^{m} \frac{\beta_i(t)}{1 + y(t - \tau_i(t))^n}, \quad t \geq 0, \qquad (10)$$

[7] G. Liu, J. Yan and F. Zhang, J. Math. Anal. Appl. 334 (2007), 157-171.

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$$\rho_n \sup_{t\in[0,\omega]} \int_{t-\tau(t)}^{t} \sum_{i=1}^{m} \beta_i(s)\, e^{-\int_s^t a(u)du}\, ds < \max\left\{1, \frac{3}{2}\, e^{-\mathcal{A}}\right\},$$

where $\mathcal{A} = \sup_{t\in[0,\omega]} \int_{t-\tau(t)}^{t} a(u)du$, then there is a positive ω-periodic solution of (10) which is GAS.

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where $\mathcal{A} = \sup_{t\in[0,\omega]} \int_{t-\tau(t)}^{t} a(u)du$, then there is a positive ω-periodic solution of (10) which is GAS.

- Liu et al [7] proved the existence of a positive periodic solution of (10) and its GAS assuming (H1), $n > 1$, and

$$(n-1)^{\frac{n-1}{n}} \frac{\mathrm{e}^{A(\omega)}}{\mathrm{e}^{A(\omega)} - 1} \int_0^{\omega} \sum_{i=1}^{m} \beta_i(s)ds \leq 1.$$

[7] G. Liu, J. Yan and F. Zhang, J. Math. Anal. Appl. 334 (2007), 157-171.

Numerical example

Consider the 1-periodic model

$$
\begin{aligned}
y'(t) &= -\left(1+\frac{1}{2}\cos(2\pi t)\right)y(t)+\frac{\eta_1\left(1+\frac{1}{2}\cos(2\pi t)\right)}{1+y(t-6-\cos(2\pi t))^n}\\
&\quad+\frac{\eta_2\left(1+\frac{1}{2}\sin(2\pi t)\right)}{1+y(t-7-\cos(2\pi t))^n}+\frac{\eta_3\left(1+\frac{1}{2}\cos(2\pi t)\right)}{1+y(t-15-\cos(2\pi t))^n},
\end{aligned}
$$

where η_1, η_2, η_3 are positive real numbers.

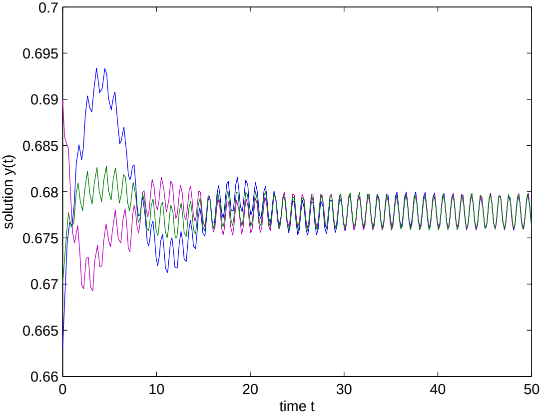

Figure: Numerical simulation of three solutions where $\eta_1 = 1.1$, $\eta_2 = 0.03$, $\eta_3 = 0.001$ and $n = 1.03$, with initial condition $\varphi(\theta) = 0.67$, $\varphi(\theta) = 0.65(1 + 0.02\cos(\theta))$, and $\varphi(\theta) = 0.69(1 + 0.02\sin(\theta))$, for $\theta \in [-16, 0]$, respectively.

Thank you

The presented results are published in

[8] T. Faria and J.J. Oliveira, *Global asymptotic stability for a periodic delay hematopoiesis model with impulses*, Applied Mathematical Modelling 79 (2020) 843-864.