Stability for a Periodic Delay Hematopoiesis Model with Impulses

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Model: A periodic hematopoiesis model with impulses and time-delays:[1]

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

(H1) $a(t), \beta_i(t), \tau_i(t)$ are continuous, nonnegative and ω-periodic (for some $\omega > 0$), with $a(t) > 0, \beta(t) := \sum_{i=1}^{m} \beta_i(t) > 0$;

(H2) there is $p \in \mathbb{N}$ such that $0 < t_1 < t_2 < \cdots < t_p < \omega$ and $t_{k+p} = t_k + \omega,\ b_{k+p} = b_k, \quad k \in \mathbb{N}$

$0 \quad t_1 \quad t_2 \cdots t_p \quad \omega \quad t_{p+1} \quad t_{p+2} \cdots t_{2p} \quad 2\omega \quad \cdots \quad 3\omega$

(H3) the constants $b_1, \dots, b_p \in \mathbb{R}$ satisfy $b_k > -1$;

(H4) $\displaystyle\prod_{k=1}^{p} (1 + b_k) < e^{\int_0^\omega a(t)dt}$.

[1] CMAFcIO In: Applied Mathematical Modelling, 79 (2020) 843–864. Ciências ULisboa

Motivation & Applications:

- Hematopoiesis is the process of production, multiplication, regulation and specialization of blood cells (red blood cells, white blood cells and platelets) in the bone marrow, until they become mature blood cells for release in the circulation bloodstream. It begins with the differentiation and division of the multipotent *hematopoietic stem cells*.
- The stem cells take time to multiply and specialize into mature blood cells, thus time delays occur. Typically, it takes between days and several weeks to replace the different types of blood cells (e.g. 2 week for neutrophils, 7 days for basophils).
- Mackey & Glass models (Science 197(1977)): $y'(t) + \gamma y(t) = \dfrac{\beta}{1 + y(t-\tau)^n}$
- As shown in several studies (e.g. Bélair et al., J.Math.Biol. 75 (2017); Berezansky, Braverman, J.Math.Anal.Appl. 450 (2017)), delay differential equations with **two or more different delays** appear naturally in hematological models, as well as in other real-world physiological phenomena.
- Some evolutionary systems go through abrupt changes, due to predictable or sudden external phenomena, such as radiation, drug administration or other forms of stress. To account for these phenomena, impulses are introduced.

Some Main Results: assume (H1)-(H4)

Theorem 1. There exists at least one **positive ω-periodic solution** $y^*(t)$.

Theorem 2. The ω-periodic solution $y^*(t)$ is a **global attractor** IF:

- Case $n \in (0, 1]$: $\dfrac{\mathfrak{m}^{n-1}\sqrt{n}}{[1 + \mathfrak{m}^n]^{3/2}} \mathcal{B} < \max\left\{1, \dfrac{3}{2} e^{-\mathcal{A}}\right\}$,
- Case $n > 1$: one of the following conditions holds:

(i) $\dfrac{\sqrt{n\rho_n \mathfrak{m}^{n-1}}}{1 + \mathfrak{m}^n} \mathcal{B} < \max\left\{1, \dfrac{3}{2} e^{-\mathcal{A}}\right\}$ and $\mathfrak{m} \ge \left(\frac{n-1}{n+1}\right)^{\frac{1}{n}}$;

(ii) $\dfrac{\sqrt{n\rho_n \mathfrak{M}^{n-1}}}{1 + \mathfrak{M}^n} \mathcal{B} < \max\left\{1, \dfrac{3}{2} e^{-\mathcal{A}}\right\}$ and $\mathfrak{M} \le \left(\frac{n-1}{n+1}\right)^{\frac{1}{n}}$;

(iii) $\rho_n \mathcal{B} < \max\left\{1, \frac{3}{2} e^{-\mathcal{A}}\right\}$.

$$\mathcal{A} := \sup_{t\in[0,\omega]} \int_{t-\tau(t)}^{t} a(u)du, \quad \mathcal{B} := \sup_{t\in[0,\omega]} \int_{t-\tau(t)}^{t} \sum_{i=1}^{m} \beta_i(s) B_i(s) e^{-\int_s^t a(u)\,du}\, ds,$$

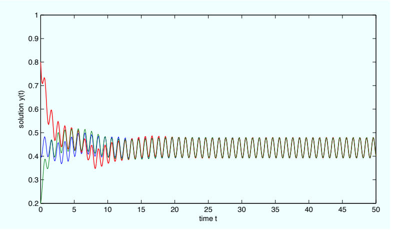
$$B_i(t) := \prod_{k: t-\tau_i(t) \le t_k < t} (1 + b_k)^{-1}, \quad \underline{B} = \min B_i(t), \quad \overline{B} = \max B_i(t)$$

$$\mathfrak{M} = c_2 e^{-A(\omega)} M \overline{B} (e^{A(\omega)} - 1), \quad \mathfrak{m} = c_1 e^{-A(\omega)} M \underline{B}, \quad M = \left(\prod_{k=1}^{p} (1 + b_k)^{-1} - e^{-A(\omega)} \right)^{-1},$$

$$\rho_n = \frac{(n+1)^2}{4n} \left(\frac{n-1}{n+1}\right)^{\frac{n-1}{n}}, \quad c_1(t) = \min_{t\in[0,\omega]} \frac{\beta(t)}{a(t)}, c_2(t) = \max_{t\in[0,\omega]} \frac{\beta(t)}{a(t)}$$

Example: $m = 3$, no impulses, period =1

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



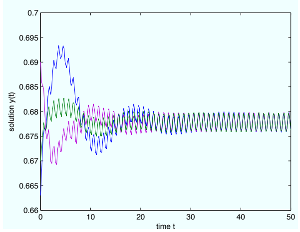


Fig 1. Three solutions of (2) where $\eta_1 = 0.03$, $\eta_2 = 0.43$, $\eta_3 = 0.001$, and $n = 3$, with initial condition $\varphi(\theta) = 0.4(\frac{1}{2}\sin(\theta) + 1)$, $\varphi(\theta) = 0.8e^{\theta}$, and $\varphi(\theta) = 0.2e^{\theta}$, for $\theta \in [-16, 0]$, respectively.

Fig 2.Three solutions of (2) 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.