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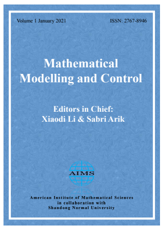

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Research article

Lipschitz stability analysis of fractional-order gene regulatory networks with impulsive perturbations and distributed delays

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Abstract: A model of fractional-order discontinuous impulsive delayed gene regulatory networks (GRNs) was investigated in this paper. The impulsive perturbations were at fixed moments of time and measured the impulsive control effects which can be controlled appropriately. A fractional-order modeling approach was applied and distributed delays were taken into account for greater model flexibility. In this paper, rather than studying the classical Lyapunov-type stability of an equilibrium point, we addressed the extended Lipschitz stability behavior of the considered GRNs. By applying the impulsive fractional Lyapunov functions technique, new criteria were derived to ensure the global uniform Lipschitz stability for the fractional impulsive delayed GRNs. Furthermore, the effects of considering uncertain parameters were also analyzed. Finally, an illustrating example was given to support the obtained theoretical results.

Keywords: gene regulatory networks; impulses; distributed delays; fractional order; Lipschitz stability

1. Introduction

Due to their importance as models in the fields of cell and molecular biology and medicine, a particular class of GRNs have gained popularity in recent years [1–4]. The use of systems of differential equations is a common modeling formalism that allows for the quantitative determination of molecular concentrations. A classical ODE model of GRNs is represented in the following form [1]:

$$\begin{cases} \dot{\mathcal{M}}_k(t) = -a_k\mathcal{M}_k(t) + \sum_{j=1}^{n} w_{kj} f_j(\mathcal{P}_j(t)) + B_k, \\ \dot{\mathcal{P}}_k(t) = -c_k\mathcal{P}_k(t) + d_k\mathcal{M}_k(t), \ t \geq 0, \end{cases} \tag{1.1}$$

where $\mathcal{M}_k(t)$ and $\mathcal{P}_k(t)$ represent the concentration of the k-th mRNA molecule and k-th protein molecule, respectively; a_k and c_k are the decay rates of mRNA and protein, respectively; d_k is the translation rate, $f_j(\cdot)$ is the regulatory function; w_{kj} is the coupling coefficient; and B_k represents the basal transcriptional rate of the repressor of gene k, $k = 1, 2, \ldots, n$.

A considerable amount of research results on integer-order GRNs also considered time delay terms. In fact, time-lag effects cannot be ignored in the process of gene expression regulation and such effects can lead to undesired dynamics, including oscillation, divergence, or even instability of GRNs. Hence, numerous researches take fixed delays and time-variable delays into consideration when modeling GRNs [5–7]. There are also several interesting results on the dynamics of GRNs with distributed delays [8, 9]. Indeed, GRNs with distributed delays account for variable time delays that occur in biological processes like transcription and translation, which are more biologically realistic than fixed or time-varying delays. In addition, distributed time-delayed signals reflect the distributed signal propagation in neurons during a time span in parallel pathways including different axon lengths and sizes [10].

Due to some sudden changes at certain times that usually exist in the process of interactions between genes (mRNA) and proteins, impulsive phenomena are inevitable in GRNs. Such short-term environmental changes are mainly due to environmental changes and can affect the concentrations of mRNA molecules and proteins. This explains the existing number of investigations on integer-order GRNs with impulsive conditions, as it is much more important to discuss the dynamics of impulsive GRN models [11–13]. Note that, the research results on impulsive GRNs with distributed delays are very rare and very recent [14, 15]. Also, from the perspective of control theory, research on impulsive control strategies can provide in-depth insight into the mechanism of implementing control signals at certain points in time [16, 17]. Therefore, it is important to investigate the influence of impulsive control strategies on the behavior of GRNs [18, 19]. Impulsive differential equations [20, 21] have been widely used to analyze impulsive and impulsively controlled GRNs.

The fact that GRNs represent complex processes that provide a powerful tool in the study of the gene regulatory mechanism has led to the development of novel approaches for modeling and analysis. Recently, the concept of fractional calculus was applied in order to improve and generalize the existing integer-order GRN models [22–24]. The main motivations of using the fractional calculus modeling approach are the generalizations and the substantial degree of reliability and accuracy in the fractional-order models [25–28]. Since most fractional-order derivatives are non-local, and possess memory effects and hereditary properties, very recently the fractional calculus approach has been applied in the mathematical modeling of impulsive fractional GRNs with and without delays. The existence and uniqueness of the equilibrium point of a fractional-order impulsive GRN with time delays was investigated in [29] and an asymptotic stability analysis was conducted. The paper [30] offers criteria for the boundedness, existence, uniqueness, and asymptotic stability of impulsive delayed fractional GRNs. In the paper [31], a novel fractional-order GRN model was proposed with a controller that involves saturated impulsive control. The finite-time Mittag–Leffler stabilization problem for the proposed model was studied. The existence of an almost periodic solution of a factional-order impulsive delayed reaction-diffusion GRN model and its perfect Mittag–Leffler stability were the main subjects in the paper [32]. An impulsive control strategy was proposed in [33] for the Mittag–Leffler stability behavior of fractional GRNs without delays.

However, to the best of the authors' knowledge, there are no corresponding results in the existing literature for impulsive fractional GRNs with distributed delays, which is one of the goals in this research.

As it is seen from the above cited references, the problem of stability analysis of GRN models has been studied by many researchers [4–6, 8, 9, 18, 19, 29, 30, 33]. It is also seen that much of the existing research in the literature considers stability, asymptotic stability, or exponential stability in the Lyapunov sense. Recently, there has been renewed interest in stability analysis in the sense of Lipschitz for numerous applied systems [34–37], including some neural network models [38, 39]. The Lipschitz stability notion has been applied to impulsive systems [40] and to fractional-order systems [41, 42]. However, the concept of Lipschitz stability has not been studied for GRNs. This extended stability concept is very appropriate for biological neural network models because it is important in determining the amount of the output of the network that is changed in response to the changes in the input. For robustness and stability, a small Lipschitz constant is suggested. Hence, the Lipschitz stability behavior is essential for security and robustness of a neural network model. The concept was introduced in [43], and for linear systems it is identical to the uniform stability notion [40]. For nonlinear systems, rather than stability in the Lyapunov sense, the Lipschitz stability refers to a neural network system that is less susceptible to attacks. Therefore, there is a need to study the Lipschitz stability behavior of impulsive fractional-order GRNs, which is the main aim of our paper.

In this research, we introduce and analyze the Lipschitz stability of fractional-order impulsive GRNs with distributed delays. Caputo fractional derivatives are used for the formulated system. These fractional-order derivatives seem to be more natural for models with delays and impulsive perturbations, since they allow classical initial and impulsive conditions to be included in the formulation of the problem. The qualitative analysis is based on the use of the fractional

Lyapunov approach [44] applied to piecewise continuous Lyapunov functions [21,28] together with some comparison results for fractional-order systems [28]. Efficient criteria for global uniform Lipschitz stability are proved. Also, the uncertain case is considered and a robust Lipschitz stability analysis is designed. Indeed, the robust stability is crucial for GRN models as extrinsic and intrinsic noises and data errors may lead to parameter uncertainties. The beneficial effects of the analyzed Lipschitz stability concept and the results obtained can be applied to other neural network models.

The significance of the present research is as follows:

(i) A hybrid GRN model is introduced that incorporates distributed delays to account for phenomena like translation and transcription, impulsive (short-term) effects to allow for the application of impulsive control strategies, and fractional-order derivatives to capture hereditary and "intrinsic memory" effects [45];

(ii) The extended concept of Lipschitz stability is introduced to discontinuous impulsive fractional GRNs with distributed delays for the first time in the literature;

(iii) New criteria for global uniform Lipschitz stability are provided.

In addition, a noteworthy reference for researchers interested in impulsive and fractional GRN models is provided describing the existing literature and demonstrating the latest progress in their qualitative research.

The plan of the rest of the paper is as follows. In Section 2 some fractional calculus definitions are given. Then, the fractional-order impulsive GRNs with distributed delays are formulated. Definitions and lemmas related to the global uniform Lipschitz stability notion and the Lyapunov approach are also presented. The main Lipschitz stability results are established in Section 3. The robust Lipschitz stability case is studied in Section 4. Section 5 offers an example. Section 6 is the conclusion section where a brief review of the main results of our research and their significance is presented and extensions of our work are suggested.

2. Preliminaries

In this paper, the Euclidean space of dimension n will be denoted by $\mathbb{R}^n$, $||u|| = \sum_{k=1}^{n} |u_k|$ denotes the norm of $u = (u_1, u_2, \dots, u_n)^T$ in $\mathbb{R}^n$, $\mathbb{R}_+ = [0, \infty)$, and $\mathbb{R}^n_+ = \mathbb{R}_+ \times \cdots \times \mathbb{R}_+$. Given an interval $I \subset \mathbb{R}$, the class of all continuous functions $\varphi : I \to \mathbb{R}$ will be denoted by $C[I, \mathbb{R}]$, and $C^1[I, \mathbb{R}]$ denotes the class of continuously differentiable functions $\varphi : I \to \mathbb{R}$. Next, the space of all piecewise continuous functions $\varphi : I \to \mathbb{R}$ with a finite number of points of discontinuity $\tilde{\xi} \in I$ at which $\varphi(\tilde{\xi}^-)$ and $\varphi(\tilde{\xi}^+)$ exist and $\varphi(\tilde{\xi}^-) = \varphi(\tilde{\xi})$ will be denoted by $PC[I, \mathbb{R}]$, $PC_\infty = PC[(-\infty, 0], \mathbb{R}^n]$, and $\mathcal{PCB}[(-\infty, 0], \mathbb{R}^n]$ denotes the space of all functions $\varphi \in PC_\infty$ that are bounded. The norm in PC_∞ will be defined by

$$||\varphi||_\infty = \sup_{\upsilon \in (-\infty, 0]} ||\varphi(\upsilon)||.$$

2.1. Fractional calculus definitions

Let $\xi_0 \in \mathbb{R}_+, \varphi \in C^1[[\xi_0, \omega], \mathbb{R}]$, $\varphi = \varphi(t)$, $t \in [\xi_0, \omega]$, and $\omega > \xi_0$.

Definition 2.1. *The Caputo fractional derivative of order q, $0 < q < 1$, with the lower limit ξ_0 for the function φ, is given by*

$${}^{C}_{\xi_0}D^q_t \varphi(t) = \frac{1}{\Gamma(1-q)} \int_{\xi_0}^{t} \frac{\varphi'(h)}{(t-h)^q} dh,$$

where Γ denotes the Gamma function.

For $\xi_0 = 0$, we denote

$${}^{C}D^q_t \varphi(t) = {}^{C}_{0}D^q_t \varphi(t) = \frac{1}{\Gamma(1-q)} \int_{0}^{t} \frac{\varphi'(h)}{(t-h)^q} dh.$$

The standard Mittag–Leffler function with one parameter is defined as $E_q(z) = \sum_{\kappa=0}^{\infty} \frac{z^\kappa}{\Gamma(q\kappa + 1)}$, where $q > 0$ and z is a complex variable.

More in-depth information on the theory of fractional calculus is available in the books [26–28] and some of the references cited therein.

2.2. The GRN model's formulation

Let the moments $\xi_1, \xi_2, \dots, \xi_i, \dots \in \mathbb{R}$ be such that

$$0 = \xi_0 < \xi_1 < \xi_2 < \cdots < \xi_i < \xi_{i+1} < \dots, \ \lim_{i \to \infty} \xi_i = \infty.$$

We introduce the following impulsive control fractional GRNs given by

$$\begin{cases} {}^{C}D_t^q u_k^m(t) = -\alpha_k u_k^m(t) + \sum_{l=1}^{n} \beta_{kl} \int_{-\infty}^{t} \mathcal{K}_l(t-\sigma) f_l(u_l^p(\sigma)) d\sigma \\ \qquad\qquad + \Theta_k, \ t \neq \xi_i, \\ {}_0^C D_t^q u_k^p(t) = -\gamma_k u_k^p(t) + \delta_k \int_{-\infty}^{t} \mathcal{K}_k(t-\sigma) u_k^m(\sigma) d\sigma, \ t \neq \xi_i, \\ u_k^m(\xi_i^+) = u_k^m(\xi_i) + \Omega_{ki}(u_k^m(\xi_i)), \\ u_k^p(\xi_i^+) = u_k^p(\xi_i) + \Pi_{ki}(u_k^p(\xi_i)), \end{cases} \tag{2.1}$$

where the concentration of the k-th mRNA molecule and k-th protein molecule are denoted by u_k^m and u_k^p, respectively, $u^m = (u_1^m, u_2^m, \ldots, u_n^m)^T$, $u^p = (u_1^p, u_2^p, \ldots, u_n^p)^T$, the positive real constants α_k and γ_k represent the decay rates of mRNA and protein, respectively, the translation rates are denotes by the positive real constants δ_k, the regulatory functions f_l are of the Hill form:

$$f_l(\omega) = \frac{(\omega/\chi_l)^{H_l}}{1 + (\omega/\chi_l)^{H_l}}, \ l = 1, 2, \ldots, n,$$

in which χ_l are real positive constants, H_l denote the Hill coefficients, the connecting parameters are the real constants β_{kl}, given as

$$\beta_{kl} = \begin{cases} \zeta_{kl}, & \text{if } l \text{ is an activator of gene } k, \\ -\zeta_{kl}, & \text{if } l \text{ is a repressor of gene } k, \\ 0, & \text{if there is no link between the node } l \\ & \text{and the gene } k, \end{cases}$$

the basal level of the repressor of gene k is denoted as Θ_k and $\Theta_k = \sum_{l \in J_k} \zeta_{kl}$, J_k denotes the collection of all the l which are repressors of the gene k, $\mathcal{K}_l$ is the delay kernel, and $k, l = 1, 2, \ldots, n$. Also, the variables $u_k^m(\xi_i) = u_k^m(\xi_i^-)$ and $u_k^p(\xi_i) = u_k^p(\xi_i^-)$ denote the concentration of the k-th mRNA and k-th protein at the instance ξ_i (before any impulsive perturbation), respectively, the amounts $u_k^m(\xi_i^+)$ and $u_k^p(\xi_i^+)$ represent the concentration of the k-th mRNA and k-th protein after an impulsive disruption at the moment ξ_i, respectively, the continuous in $\mathbb{R}$ functions Ω_{ki} and Π_{ki} measure the amount of abrupt changes of $u_k^m(t)$ and $u_k^p(t)$ at the impulsive moments ξ_i, and we have $\Delta u_k^m(\xi_i) = u_k^m(\xi_i^+) - u_k^m(\xi_i) = \Omega_{ki}(u_k^m(\xi_i))$ and $\Delta u_k^p(\xi_i) = u_k^p(\xi_i^+) - u_k^p(\xi_i) = \Pi_{ki}(u_k^p(\xi_i))$, $k = 1, 2, \ldots, n$, $i = 1, 2, \ldots$.

Remark 2.1. *The proposed impulsive fractional GRN model (2.1) generalizes several recently introduced neural network models in the theory of gene regulations. For example, it generalizes the model proposed in [8] to the impulsive and fractional-order settings. It also extends the impulsive models with distributed delays studied in [14, 15, 18] to the fractional-order case. In addition, the model (2.1) extends the impulsive fractional GRN model investigated in [33] considering distributed delays. This significantly increases the flexibility in terms of delays and includes many specific cases. Hence, the suggested model is new. It is a hybrid model that includes more general distributed delays, impulsive perturbations, and fractional-order derivatives.*

Remark 2.2. *The impulsive functions Ω_{ki} and Π_{ki}, $k = 1, 2, \ldots, n$, $i = 1, 2, \ldots$, in (2.1) can be used for controlling the qualitative behavior of the concentration of the k-th mRNA molecule and k-th protein molecule during the process of regulation.*

We consider the impulsive fractional GRN model (2.1) under the initial conditions

$$\begin{cases} u_k^m(\upsilon; 0, \psi^m) = \psi_k^m(\upsilon), \ -\infty < \upsilon \leq 0, \\ u_k^p(\upsilon; 0, \psi^p) = \psi_k^p(\upsilon), \ -\infty < \upsilon \leq 0, \\ u_k^m(0^+; 0, \psi^m) = \psi_k^m(0), \ u_k^p(0^+; 0, \psi^p) = \psi_k^p(0), \end{cases} \tag{2.2}$$

where $k = 1, 2, \ldots, n$, ψ^m, $\psi^p \in \mathcal{PCB}[(-\infty, 0], \mathbb{R}^n]$, $\psi^m = (\psi_1^m, \psi_2^m, \ldots, \psi_n^m)^T$, $\psi^p = (\psi_1^p, \psi_2^p, \ldots, \psi_n^p)^T$.

The solution of the initial value problem (IVP) (2.1), (2.2) will be denoted by $u(t; 0, \psi)$, i.e.,

$$u(t; 0, \psi) = (u^m(t; 0, \psi^m), u^p(t; 0, \psi^p))^T.$$

We will consider the following assumption throughout this work:

(A) The delay kernel functions $\mathcal{K}_l$ defined on $\mathbb{R}$ are nonnegative, continuous, and satisfy the estimate

$$\int_{-\infty}^{t} \mathcal{K}_l(\sigma) d\sigma \leq K_l$$

for some positive constants K_l and all $l = 1, 2, \ldots, n$.

Also, the form of the considered regulatory functions f_l guarantees that for all $l = 1, 2, \ldots, n$ and any $v, \bar{v} \in \mathbb{R}$, $v \neq \bar{v}$, there exist constants f_l^L such that [24, 33]

$$0 \leq \frac{f_l(v) - f_l(\bar{v})}{v - \bar{v}} \leq f_l^L. \quad (2.3)$$

2.3. Lipschitz stability definitions

Consider an equilibrium of the model (2.1) $(u^{m^*}, u^{p^*})^T = (u_1^{m^*}, u_2^{m^*}, \ldots, u_n^{m^*}, u_1^{p^*}, u_2^{p^*}, \ldots, u_n^{p^*})^T$, i.e., a constant solution that satisfies the following system:

$$\begin{cases} \alpha_k u_k^{m^*} = \sum_{l=1}^{n} \beta_{kl} \int_{-\infty}^{t} \mathcal{K}_l(t-\sigma) f_l(u_l^{p^*}) d\sigma + \Theta_k, \ t \neq \xi_i, \\ \gamma_k u_k^{p^*}(t) = \delta_k \int_{-\infty}^{t} \mathcal{K}_k(t-\sigma) u_k^{m^*} d\sigma, \ t \neq \xi_i, \\ \Omega_{ki}(u_k^{m^*}) = 0, \\ \Pi_{ki}(u_k^{p^*}) = 0, \end{cases} \quad (2.4)$$

$k = 1, 2, \ldots, n, \ i = 1, 2, \ldots$.

The Lipschitz stability concept will be adopted to system (2.1) by the next definition.

Definition 2.2. *The equilibrium $(u^{m^*}, u^{p^*})^T$ of system (2.1) is said to be globally uniformly Lipschitz stable if there exists a constant $A > 0$ such that for $\psi^m, \ \psi^p \in \mathcal{PCB}[(-\infty, 0], \mathbb{R}^n]$, we have $\|u^m(t) - u^{m^*}\| + \|u^p(t) - u^{p^*}\| \leq A(\|\psi^m - u^{m^*}\|_\infty + \|\psi^p - u^{p^*}\|_\infty)$ for $t \geq 0$.*

2.4. Lyapunov approach definitions and lemmas

The application of the Lyapunov analysis approach to impulsive systems requires the use of piecewise continuous Lyapunov-type functions $\Lambda : \mathbb{R}_+ \times \mathbb{R}^{2n} \to \mathbb{R}_+$, $\Lambda = \Lambda(t, u^m, u^p)$ such that:

(i) $\Lambda(t, u^m, u^p)$ is continuous in $(\xi_{i-1}, \xi_i) \times \mathbb{R}^{2n}$, $i = 1, 2, \ldots$, locally Lipschitz continuous with respect to the arguments (u^m, u^p), and $\Lambda(t, 0, 0) = 0$ for $t \geq 0$,

(ii) For each $i = 1, 2, \ldots$ and $(u^m, u^p)^T \in \mathbb{R}^{2n}$, there exist the finite limits

$$\Lambda(\xi_i^-, u^m, u^p) = \lim_{\substack{t \to \xi_i \\ t < \xi_i}} \Lambda(t, u^m, u^p),$$

$$\Lambda(\xi_i^+, u^m, u^p) = \lim_{\substack{t \to \xi_i \\ t > \xi_i}} \Lambda(t, u^m, u^p),$$

and $\Lambda(\xi_i^-, u^m, u^p) = \Lambda(\xi_i, u^m, u^p)$.

The class of all the functions $\Lambda = \Lambda(t, u^m, u^p)$ of the above type will be denoted by Λ^0.

Consider the following impulsive fractional-order system:

$$\begin{cases} {}^C D_t^q u(t) = F(t, u_t), \ t \neq \xi_i, \\ \Delta u(t) = P_i(u(t)), \ t = \xi_i, \ i = 1, 2, \ldots, \end{cases} \quad (2.5)$$

where $u_t(\sigma) = u(t+\sigma)$, $-\infty < \sigma \leq 0$, $F : \mathbb{R}_+ \times \mathcal{PCB}[(-\infty, 0], \mathbb{R}^{2n}] \to \mathbb{R}^{2n}$, $P_i : \mathbb{R}^{2n} \to \mathbb{R}^{2n}$, $\xi_i < \xi_{i+1}$, $i = 1, 2, \ldots$, and $\lim_{i \to \infty} \xi_i = \infty$.

Let the function $\Lambda \in \Lambda^0$ and $\phi = (\phi_1, \phi_2)^T$, $\phi_j \in PC_\infty$, $j = 1, 2$. For $t \neq \xi_i$, $i = 1, 2, \ldots$, we will use the derivative ${}^C D^q \Lambda(t, \phi)$ of the function Λ of order q, $0 < q < 1$, with respect to model (2.5) defined by

$${}^C D^q \Lambda(t, \phi(0)) = \lim_{h \to 0^+} \sup \frac{1}{h^q} [\Lambda(t, \phi(0)) - \Lambda(t-h, \phi(0) - h^q F(t, \phi))].$$

The following lemmas are crucial for the proof of our main results.

Lemma 2.1. [28] *Assume that the function $\Lambda \in \Lambda^0$ is such that for $t \in \mathbb{R}_+$, $\phi = (\phi_1, \phi_2)^T$, $\phi_j \in PC_\infty$, $j = 1, 2$,*

$$\Lambda(t^+, \phi(0) + P_i(\phi)) \leq \tilde{R}_i(\Lambda(t, \phi(0))), \ t = \xi_i, \ i = 1, 2, \ldots,$$

for continuous and non-decreasing functions $\tilde{R}_i(\chi) = \chi + R_i(\chi)$, $R_i \in C[\mathbb{R}_+, \mathbb{R}_+]$, $i = 1, 2, \ldots$, and the inequality

$${}^C D^q \Lambda(t, \phi(0)) \leq \Phi(t, \Lambda(t, \phi(0))), \ t \neq \xi_i, \ i = 1, 2, \ldots,$$

holds whenever $\Lambda(t+\sigma, \phi(\sigma)) \leq \Lambda(t, \phi(0))$ for $-\infty < \sigma \leq 0$, $\Phi \in PC[\mathbb{R}_+ \times \mathbb{R}_+, \mathbb{R}]$.

Then, $\sup_{-\infty < \sigma \leq 0} \Lambda(0^+, \psi(\sigma)) \leq \chi_0$ *implies*

$$\Lambda(t, u(t; 0, \psi)) \leq \chi^+(t; 0, \chi_0), \ t \in \mathbb{R}_+,$$

where $\chi^+(t; 0, \chi_0)$ is the maximal solution of the scalar comparison equation ${}^C D_t^q \chi(t) = \Phi(t, \chi)$, $t \neq \xi_i$, $\Delta\chi(\xi_i) = \chi(\xi_i^+) - \chi(\xi_i) = R_i(\chi(\xi_i))$, $i = 1, 2, \ldots$, $\chi(0) = \chi_0$.

Lemma 2.2. [44] If $\varphi \in C^1[\mathbb{R}_+, \mathbb{R}]$, $\varphi = \varphi(t)$, then the inequality

$${}^C D_t^q \varphi^2(t) \leq 2\varphi(t) {}^C D_t^q \varphi(t), \ 0 < q \leq 1,$$

holds for all $t \in \mathbb{R}_+$.

3. Main Lipschitz stability results

Denote $\tilde{u}^m(t) = u^m(t) - u^{m^*}$, $\tilde{u}^p(t) = u^p(t) - u^{p^*}$, $t \in \mathbb{R}_+$, and consider the system

$$\begin{cases} {}^C D_t^q \tilde{u}_k^m(t) = -\alpha_k \tilde{u}_k^m(t) + \sum_{l=1}^n \beta_{kl} \int_{-\infty}^t \mathcal{K}_l(t-\sigma)\tilde{f}_l(\tilde{u}_l^p(\sigma))d\sigma, \\ \qquad\qquad t \neq \xi_i, \\ {}_0^C D_t^q \tilde{u}_k^p(t) = -\gamma_k \tilde{u}_k^p(t) + \delta_k \int_{-\infty}^t \mathcal{K}_k(t-\sigma)\tilde{u}_k^m(\sigma)d\sigma,\ t \neq \xi_i, \\ \tilde{u}_k^m(\xi_i^+) = \tilde{u}_k^m(\xi_i) + \tilde{\Omega}_{ki}(\tilde{u}_k^m(\xi_i)), \\ \tilde{u}_k^p(\xi_i^+) = \tilde{u}_k^p(\xi_i) + \tilde{\Pi}_{ki}(\tilde{u}_k^p(\xi_i)), \end{cases} \tag{3.1}$$

where $\tilde{f}_l \tilde{u}_l^p(t)) = f_l(\tilde{u}_l^p(t) + u_l^{p^*}) - f_l(u_l^{p^*})$, $\tilde{\Omega}_{ki}(\tilde{u}_k^m(\xi_i)) = \Omega_{ki}(\tilde{u}_k^m(\xi_i) + u_k^{m^*})$, $\tilde{\Pi}_{ki}(\tilde{u}_k^p(\xi_i)) = \Pi_{ki}(\tilde{u}_k^p(\xi_i)) + u_k^{p^*})$, $k = 1,2,\dots,n$, $i = 1,2,\dots$.

Theorem 3.1. *Let the assumption (A) be satisfied, and:*

(1) The model's parameters, are such that

$$\min_{1\le k\le n}\left\{2\alpha_k - \sum_{l=1}^n |\beta_{kl}|K_l f_l^L,\ 2\gamma_k - \delta_k K_k\right\}$$

$$\ge \max_{1\le k\le n}\left\{\delta_k K_k,\ K_k f_k^L \sum_{l=1}^n |\beta_{lk}|\right\} + \mu,\ \mu > 0;$$

(2) The impulsive functions $\tilde{\Omega}_{ki}$ and $\tilde{\Pi}_{ki}$ are such that

$$\tilde{\Omega}_{ki}(\tilde{u}_k^m(\xi_i)) = -\zeta_{ki}^m \tilde{u}_k^m(\xi_i),\ 0 < \zeta_{ki}^m < 2,$$

$$\tilde{\Pi}_{ki}(\tilde{u}_k^p(\xi_i)) = -\zeta_{ki}^p \tilde{u}_k^p(\xi_i),\ 0 < \zeta_{ki}^p < 2,$$

$k = 1,2,\dots,n$, $i = 1,2,\dots$.

Then, the equilibrium $(u^{m^*}, u^{p^*})^T$ of the model (2.1) is globally uniformly Lipschitz stable.

Proof. Given $t \in \mathbb{R}_+$, let $u(t;0,\psi)$,

$$u(t;0,\psi) = (u^m(t;0,\psi^m), u^p(t;0,\psi^p))^T,$$

be the solution of the IVP (2.1), (2.2) with ψ^m, $\psi^p \in \mathcal{PCB}[(-\infty,0],\mathbb{R}^n]$, $\psi^m = (\psi_1^m,\psi_2^m,\dots,\psi_n^m)^T$, $\psi^p = (\psi_1^p,\psi_2^p,\dots,\psi_n^p)^T$. Consider the equilibrium $(u^{m^*}, u^{p^*})^T$.

Construct a Lyapunov-type function

$$\Lambda_1(t,\tilde{u}^m,\tilde{u}^p) = \sqrt{\sum_{k=1}^n (u_k^m(t) - u_k^{m^*})^2 + \sum_{k=1}^n (u_k^p(t) - u_k^{p^*})^2}, \tag{3.2}$$

and consider the function $\Lambda(t) = \Lambda_1(t,\tilde{u}^m(t),\tilde{u}^p(t))$.

For any $t \neq \xi_i$, $i = 1,2,\dots$, using (A), (2.3), (3.1), and condition 1 of Theorem 3.1, the following estimate holds:

$$\begin{aligned} &{}^C D_t^q \Lambda(t) \\ &\le \sum_{k=1}^n \Big[-2\alpha_k(\tilde{u}_k^m(t))^2 + 2\sum_{l=1}^n |\beta_{kl}| f_l^L K_l \sup_{-\infty<\sigma\le 0} |\tilde{u}_l^p(\sigma)||\tilde{u}_k^m(t)|\Big] \\ &\quad + \sum_{k=1}^n \Big[-2\gamma_k(\tilde{u}_k^p(t))^2 + 2\delta_k K_k \sup_{-\infty<\sigma\le 0} |\tilde{u}_k^m(\sigma)||\tilde{u}_k^p(t)|\Big] \\ &\le \sum_{k=1}^n \Big[-2\alpha_k(\tilde{u}_k^m(t))^2 + \sum_{l=1}^n |\beta_{kl}| f_l^L K_l (\sup_{-\infty<\sigma\le 0} (\tilde{u}_l^p(\sigma))^2 + (\tilde{u}_k^m(t))^2)\Big] \\ &\quad + \sum_{k=1}^n \Big[-2\gamma_k(\tilde{u}_k^p(t))^2 + \delta_k K_k (\sup_{-\infty<\sigma\le 0} (\tilde{u}_k^m(\sigma))^2 + (\tilde{u}_k^p(t))^2)\Big] \\ &\le -\min_{1\le k\le n}\left\{2\alpha_k - \sum_{l=1}^n |\beta_{kl}|K_l f_l^L,\ 2\gamma_k - \delta_k K_k\right\}\Lambda(t) \\ &\quad + \max_{1\le k\le n}\left\{\delta_k K_k,\ K_k f_k^L \sum_{l=1}^n |\beta_{lk}|\right\} \sup_{-\infty<\sigma\le 0} \Lambda(t+\sigma). \end{aligned}$$

Thus, for $\phi = (\phi_1,\phi_2)^T$, $\phi_j \in PC_\infty$, $j = 1,2$, it can be derived that the inequality

$${}^C D^q \Lambda_1(t,\phi(0)) \le -\mu \Lambda_1(t,\phi(0)),\ t \neq \xi_i,\ i = 1,2,\dots \tag{3.3}$$

holds whenever $\Lambda_1(t+\sigma,\phi(\sigma)) \le \Lambda_1(t,\phi(0))$ for $-\infty < \sigma \le 0$.

At the instances $t = \xi_i$, $i = 1,2,\dots$, we have

$$\Lambda(\xi_i^+) = \sqrt{\sum_{k=1}^n (\tilde{u}_k^m(\xi_i) + \tilde{\Omega}_{ki}(\tilde{u}_k^m(\xi_i)))^2 + \sum_{k=1}^n (\tilde{u}_k^p(\xi_i) + \tilde{\Pi}_{ki}(\tilde{u}_k^p(\xi_i)))^2}.$$

Using condition 2 of Theorem 3.1, we obtain

$$\begin{aligned} \Lambda(\xi_i^+) &= \sqrt{\sum_{k=1}^n (1-\tilde{\gamma}_{ki}^m)^2(\tilde{u}_k^m(\xi_i))^2 + \sum_{k=1}^n (1-\tilde{\gamma}_{ki}^p)^2(\tilde{u}_k^p(\xi_i))^2} \\ &< \sqrt{\sum_{k=1}^n (\tilde{u}_k^m(\xi_i))^2 + \sum_{k=1}^n (\tilde{u}_k^p(\xi_i))^2} = \Lambda(\xi_i). \end{aligned}$$

The last estimate implies that for $t = \xi_i$, $i = 1,2,\dots$, and $\phi = (\phi_1,\phi_2)^T$, $\phi_j \in PC_\infty$, $j = 1,2$, we have

$$\Lambda_1(t^+,\phi(0) + \Delta(\phi)) \le \Lambda_1(t,\phi(0)). \tag{3.4}$$

Hence, from (3.3) and (3.4), applying Lemma 2.1, we derive

$$\Lambda_1(t,\tilde{u}(t;0,\psi)) \le \chi^+(t;0,\chi_0),\ t \in \mathbb{R}_+, \tag{3.5}$$

where $\chi^+(t;0,\chi_0)$ is the maximal solution of the scalar comparison equation

$$ {}^C D_t^q \chi(t) = -\mu\chi(t),\ t \neq \xi_i,\ \Delta\chi(\xi_i) = 0,\ i = 1, 2, \ldots, \quad (3.6)$$

$\chi(0) = \chi_0 = \sup_{-\infty<\sigma\leq 0} \Lambda_1(0^+, \psi(\sigma))$.

Since the zero solution of the scalar comparison Eq (3.6) is globally uniformly Lipschitz stable [39], then, there exists a constant $A > 0$ such that for $\chi_0 > 0$, we have $\chi^+(t;0,\chi_0) \leq A\chi_0$ for $t \geq 0$.

Hence, in view of (3.5) and using the Cauchy–Schwarz inequality, we obtain

$$\begin{aligned}
& ||u^m(t) - u^{m^*}|| + ||u^p(t) - u^{p^*}|| \\
= & \sum_{k=1}^{n} |u_k^m(t) - u_k^{m^*}| + \sum_{k=1}^{n} |u_k^p(t) - u_k^{p^*}| \\
\leq & \sqrt{\sum_{k=1}^{n}(u_k^m(t) - u_k^{m^*})^2 + \sum_{k=1}^{n}(u_k^p(t) - u_k^{p^*})^2}\,\sqrt{n} \\
= & \Lambda_1(t, \tilde{u}(t;0,\psi))\sqrt{n} \\
\leq & \chi^+(t;0,\chi_0)\sqrt{n}.
\end{aligned}$$

The global uniform Lipschitz stability of the zero solution of (3.6) implies that for $\chi_0 = \sup_{-\infty<\sigma\leq 0} \Lambda_1(0^+, \psi(\sigma)) < \eta$, we have

$$||u^m(t) - u^{m^*}|| + ||u^p(t) - u^{p^*}|| \leq A\sqrt{n} \sup_{-\infty<\sigma\leq 0} \Lambda_1(0^+, \psi(\sigma)).$$

Finally, we apply the Minkowski inequality to derive

$$||u^m(t)-u^{m^*}||+||u^p(t)-u^{p^*}|| \leq A\sqrt{n}(||\psi^m-u^{m^*}||_\infty+||\psi^p-u^{p^*}||_\infty)$$

for $t \geq 0$, ψ^m, $\psi^p \in \mathcal{PCB}[(-\infty, 0], \mathbb{R}^n]$, $||\psi^m - u^{m^*}||_\infty + ||\psi^p - u^{p^*}||_\infty < \eta$, which proves the global uniform Lipschitz stablity of the equilibrium $(u^{m^*}, u^{p^*})^T$ of the model (2.1). □

Remark 3.1. *Theorem 3.1 provides the first, in the existing literature, global uniform Lipschitz stability criteria for a GRN model that involves impulsive perturbations, fractional-order derivatives, and distributed delay. Hence, the result established contributes to the development of their theory. Also, as in some practical cases where classical Lyapunov-type stability concepts considered in [29–31, 33] are not appropriate, the Lipschitz stability is an option. The Lipschitz stability implies that the model's solution changes more gradually and predictably in response to initial data changes. In addition, since the model considered is very general, the obtained criteria can be applied to models with constant and time-varying delays, as well as to integer-order models and models without impulsive perturbations.*

Remark 3.2. *From the perspectives of impulsive control, the result obtained can be applied in the investigations of Lipschitz-type synchronization of the impulsive fractional GRN model (2.1) to an impulse free fractional GRN model. The functions Ω_{ki}^m and Π_{ki}^p characterize the controllers' effects of synchronizing impulses at the instances ξ_i, $i = 1, 2, \ldots$, $k = 1, 2, \ldots, n$.*

Remark 3.3. *More Lipschitz stability criteria, similar to those offered in Theorem 3.1, can be obtained using different norms and different Lyapunov-type functions. For example, in the use of the Lyapunov-type function $\Lambda_2(t, \tilde{u}^m, \tilde{u}^p) = ||u^m(t) - u^{m^*}|| + ||u^p(t) - u^{p^*}||$, the smallest Lipschitz constant A is obtained.*

4. Robust Lipschitz stability analysis

As uncertain parameters often exist in the real-world models [6, 8, 15, 22, 46] and, in addition, the concept of Lipschitz stability is closely related to robustness, in this section we will study the robust Lipschitz stability behavior of the model (2.1). To this end we consider the uncertain model

$$\begin{cases}
{}^C D_t^q u_k^m(t) = -(\alpha_k + \tilde{\alpha}_k)u_k^m(t) \\
\qquad + \sum_{l=1}^{n}(\beta_{kl} + \tilde{\beta}_{kl}) \int_{-\infty}^{t} \mathcal{K}_l(t-\sigma) f_l(u_l^p(\sigma))d\sigma \\
\qquad + \Theta_k + \tilde{\Theta}_k,\ t \neq \xi_i, \\
{}_0^C D_t^q u_k^p(t) = -(\gamma_k + \tilde{\gamma}_k)u_k^p(t) \\
\qquad + (\delta_k + \tilde{\delta}_k) \int_{-\infty}^{t} \mathcal{K}_k(t-\sigma) u_k^m(\sigma)d\sigma,\ t \neq \xi_i, \\
u_k^m(\xi_i^+) = u_k^m(\xi_i) + \Omega_{ki}(u_k^m(\xi_i)) + \Omega_{ki}^1(u_k^m(\xi_i)), \\
u_k^p(\xi_i^+) = u_k^p(\xi_i) + \Pi_{ki}(u_k^p(\xi_i)) + \Pi_{ki}^1(u_k^p(\xi_i)),
\end{cases} \quad (4.1)$$

where the positive real constants $\tilde{\alpha}_k$, $\tilde{\gamma}_k$, $\tilde{\delta}_k$, the real constants $\tilde{\beta}_{kl}$ and $\tilde{\Theta}_k$, $k, l = 1, 2, \ldots, n$, are the uncertain parameters in the continuous part, and Ω_{ki}^1, Π_{ki}^1, $k = 1, 2, \ldots, n$, $i = 1, 2, \ldots$, are uncertainties in the impulsive control functions.

Definition 4.1. *The equilibrium $(u^{m^*}, u^{p^*})^T$ of the impulsive* *control fractional delayed GRN model (2.1) is robustly globally uniformly Lipschitz stable if for ψ^m, $\psi^p \in \mathcal{PCB}[(-\infty, 0], \mathbb{R}^n]$, the uncertain model (4.1) is globally uniformly Lipschitz stable for uncertain parameters $\tilde{\alpha}_k$, $\tilde{\gamma}_k$, $\tilde{\delta}_k$, $\tilde{\beta}_{kl}$, $\tilde{\Theta}_k$, $k, l = 1, 2, \ldots, n$, Ω^1_{ki}, Π^1_{ki}, $k = 1, 2, \ldots, n$, $i = 1, 2, \ldots,$ taking values in some bounded sets.*

Theorem 4.1. *Let the assumption (A) and condition 2 of Theorem 3.1 be satisfied:*

(1) The model's parameters are such that

$$\min_{1\le k\le n} \{(\alpha_k + \tilde{\alpha}_k), (\gamma_k + \tilde{\gamma}_k)\}$$

$$\ge \max_{1\le k\le n} \left\{(\delta_k + \tilde{\delta}_k)K_k,\ K_k f_k^L \sum_{l=1}^{n}(|\beta_{lk}| + |\tilde{\beta}_{lk}|)\right\} > 0;$$

(2) The uncertain functions Ω^1_{ki}, Π^1_{ki}, $k = 1, 2, \ldots, n$, $i = 1, 2, \ldots,$ are such that

$$\Omega^1_{ki}(u_k^m(\xi_i)) = -\nu^m_{ki} u^m_k(\xi_i),\ 0 < \nu^m_{ki} < 2 - \zeta^m_{ki},$$

$$\Pi^1_{ki}(u_k^p(\xi_i)) = -\nu^p_{ki} u^p_k(\xi_i),\ 0 < \nu^p_{ki} < 2 - \zeta^p_{ki},$$

$k = 1, 2, \ldots, n$, $i = 1, 2, \ldots.$

Then, the equilibrium $(u^{m^*}, u^{p^*})^T$ of the model (2.1) is robustly globally uniformly Lipschitz stable.

Proof. The Lyapunov proof strategy is similar to that in the proof of Theorem 3.1. The Lyapunov-type function $\Lambda_2(t, u^m, u^p) = ||u^m(t) - u^{m^*}|| + ||u^p(t) - u^{p^*}||$ is used. □

5. An example

We consider the impulsive fractional delayed GRN model (2.1) with $n = 2$, and the following parameters $\alpha_1 = \alpha_2 = 2$, $\Theta_1 = \Theta_2 = 0$, $\gamma_1 = \gamma_2 = 0.6$, $\delta_1 = 0.2$, $\delta_2 = 0.1$, $f_l(u_l^p) = \frac{(u_l^p)^2}{1+(u_l^p)^2}$, $K_l(s) = e^{-s}$, $l = 1, 2$, $\beta_{kl} = \begin{pmatrix} \beta_{11} & \beta_{12} \\ \beta_{21} & \beta_{22} \end{pmatrix} = \begin{pmatrix} 0.5 & -0.4 \\ -0.3 & 0.4 \end{pmatrix}$, $\Omega_{ki}(u_k^m(\xi_i)) = -\frac{1}{4}u_k^m(\xi_i)$, $\Pi_{ki}(u_k^p(\xi_i)) = -\frac{1}{3}u_k^p(\xi_i)$, $k = 1, 2$, $i = 1, 2, \ldots.$

We can check that $f_k^L = 1$, $K_k = 1$, $k = 1, 2$, and

$$\begin{aligned} 1 &= \min_{1\le k\le n}\left\{2\alpha_k - \textstyle\sum_{l=1}^n |\beta_{kl}| K_l f_l^L,\ 2\gamma_k - \delta_k K_k\right\} \\ &\ge \max_{1\le k\le n}\left\{\delta_k K_k,\ K_k f_k^L \textstyle\sum_{l=1}^n |\beta_{lk}|\right\} + \mu = 0.8 + \mu. \end{aligned}$$

Hence, condition 1 of Theorem 3.1 is met for $0 \le \mu \le 0.2$. Since the zero solution of (3.6) is globally uniformly Lipschitz stable, then by Theorem 3.1, we conclude that the zero equilibrium of the model (2.1) is globally uniformly Lipschitz stable.

In addition, we consider the model (2.1) as a "nominal" model for the uncertain model (4.1). If the uncertain parameters satisfy the boundedness condition

$$\min_{1\le k\le n} \{(1 + \tilde{\alpha}_k), (0.6 + \tilde{\gamma}_k)\}$$

$$\ge \max_{1\le k\le n} \left\{(0.2 + \tilde{\delta}_k)K_k,\ K_k f_k^L \sum_{l=1}^{n}(0.8 + |\tilde{\beta}_{lk}|)\right\} > 0$$

and the uncertainties in the impulsive functions Ω^1_{ki}, Π^1_{ki}, $k = 1, 2, \ldots, n$, $i = 1, 2, \ldots$ satisfy condition 2 of Theorem 4.1 with $0 < \nu^m_{ki} < \frac{3}{4}$, $0 < \nu^p_{ki} < \frac{5}{3}$, $k = 1, 2, \ldots, n$, $i = 1, 2, \ldots,$ then according to Theorem 4.1 the zero equilibrium of the model (2.1) is robustly globally uniformly Lipschitz stable.

6. Conclusions

In this paper, a hybrid modeling approach is applied to extend the class of GRNs. The extended model has all the advantages of impulsive models with distributed delays applied as frameworks for the modeling of such systems [18]. In addition, it has the flexibility provided by the use of fractional-order derivatives. The extended concept of Lipschitz stability is introduced into the model, and new criteria that guarantee the global uniform Lipschitz stability of the model's equilibrium are established. Robust stability analysis is also provided considering the effect of uncertain parameters. The results obtained are of interest to applied researchers when a Lyapunov stability strategy cannot be used. Hence, the concept of Lipschitz stability can be applied to other models studied in mathematical biology. A future direction of our investigations is also related to some extensions of the introduced model applying the conformable calculus approaches. In addition, since the computer simulation, experimentation, and practical implementation of the obtained stability criteria require a discretization of the proposed fractional-order neural network model, the study of its discrete analogous form becomes very important.

Author contributions

All authors contributed equally and significantly in writing this paper. All authors read and approved the final manuscript.

Use of Generative-AI tools declaration

The authors declare they have not used Artificial Intelligence (AI) tools in the creation of this article.

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Conflict of interest

The authors declare that there are no conflicts of interest in this paper.

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