Robustness and Performance Analysis of Cyclic Interconnected Dynamical Networks *

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Abstract

The class of *cyclic* interconnected dynamical networks plays a crucial role in modeling of certain biochemical reaction networks. In this paper, we consider cyclic dynamical networks with loop topology and quantify bounds on various performance measures. First, we consider robustness of autonomous cyclic dynamical networks with respect to external stochastic disturbances. The $\mathcal{H}_2$–norm of the system is used as a robustness index to measure the expected steady-state dispersion of the state of the entire network. In particular, we explicitly quantify how the robustness index depends on the properties of the underlying digraph of a cyclic network. Next, we consider a class of cyclic dynamical networks with control inputs. Examples of such cyclic networks include a class of interconnected dynamical networks with some specific autocatalytic structure, e.g., glycolysis pathway. We characterize fundamental limits on the ideal performance of such cyclic networks by obtaining lower bounds on the minimum L_2–gain disturbance attenuation. We show that how emergence of such fundamental limits result in essential tradeoffs between robustness and efficiency in cyclic networks.

1 Introduction

The class of dynamical networks with cyclic interconnection topologies has been focus of numerous studies during the past decade. Examples of dynamical networks with cyclic structures include, only to name a few, gene regulation networks [1], metabolic pathways [2–5], and cellular signaling pathways [6].

The results of this paper has been motivated by cyclic dynamical systems arising in biological networks. In [1], the authors propose a sufficient stability condition for unperturbed cyclic interconnected networks. Later on, these results were extended to show that global asymptotic stability conditions for cyclic dynamical networks can be obtained using diagonal stability and passivity properties of subsystems in the form of secant conditions [7]. In various applications such cyclic dynamical networks must operate in uncertain environments, e.g., under external stochastic disturbances. Therefore, one of the central and relevant challenges is to study robustness properties of cyclic dynamical networks under external stochastic disturbances. In the first part of the paper, we focus our attention on robustness analysis of a class of autonomous cyclic dynamical networks with respect to external stochastic disturbances (see Figure 1). We use the $\mathcal{H}_2$–norm of the network as a robustness measure. The $\mathcal{H}_2$–norm measures the expected steady-state dispersion of the state of the entire network with respect to white random process. We derive explicit formulae for the $\mathcal{H}_2$–norm of the network. In particular, we show that the robustness measure depends on the properties of the underlying digraph of the network as well as the size of the network. Our approach in the first part of the paper is close in spirit to [8] where only symmetric networks with ring and lattice structures are considered. In this paper, we consider cyclic networks with asymmetric structures.

In the second part of the paper, we turn our attention to quantification of fundamental limits on ideal performance of cyclic networks with control inputs (see Figure 3). This problem belongs to a larger class of problems where the objective is to characterize fundamental limitations of feedback control laws for interconnected dynamical networks. The interest in this research area spans through various applications, ranging from biology and physics to engineering and economics. Recent research results in understanding hard limits in networks and their corresponding tradeoffs have created a paradigm shift in the way networks are analyzed, designed, and built. There have been some recent progress in characterization of fundamental limitations of feedback control laws for some class of interconnected dynamical networks. In [9], the authors give conditions for string instability in an array of linear time-invariant autonomous vehicles with communication constraints, reference [10] provides a lower bound on the achievable quality of disturbance rejection using a decentralized controller for stable discrete time linear systems with time delays, and reference [11] studies the performance of spatially invariant plants interconnected

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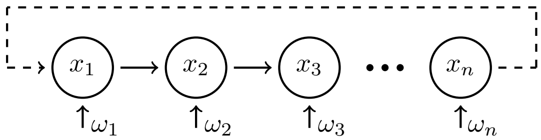

Figure 1: The schematic diagram of a cyclic dynamical network with a negative feedback structure. The system is driven by external stochastic noise inputs. The dashed link indicates a negative (inhibitory) feedback signal.

through a static network. In Section 3, we characterize fundamental limits on the ideal performance of cyclic dynamical networks. As a motivating case study, we consider cyclic networks arising in modeling of metabolic pathways. In particular, we look at autocatalytic networks with cyclic structures. In an interconnected control system with autocatalytic structure, the system's product (output) is necessary to power and catalyze its own production. The destabilizing effects of such "positive" autocatalytic feedback can be countered by negative regulatory feedback [2–5, 12]. We explicitly quantify hard limits (in the form of lower bounds) on the minimum L_2–gain disturbance attenuation. We show that how these existing hard limits result in emergence of fundamental tradeoffs between robustness and productivity of such interconnected networks.

2 Robustness analysis of autonomous cyclic networks

In this section, we consider a class of dynamical networks with cyclic interconnection topologies. One typical example of such networks is a sequence of biochemical reactions where the system's product (output) is necessary to power and catalyze the first reaction. We consider a group of LTI systems $\mathcal{G}_i$ with the following state-space models

$$\begin{aligned} \dot{x}_i &= -a_i x_i + u_i, \\ y_i &= c_i x_i, \end{aligned} \tag{2.1}$$

for $i = 1, 2, \ldots, n$ and $a_i, c_i > 0$. The signals $u_i(t) \in \mathbb{R}$, $y_i(t) \in \mathbb{R}$ and $x_i(t) \in \mathbb{R}$ are input, output and state variables of the i'th subsystem, respectively. A cyclic interconnection of subsystems $\mathcal{G}_i$ for $i = 1, 2, \ldots, n$ with input-output constraints

$$u_1 = y_n \quad \text{and} \quad u_i = y_{i-1} \quad \text{for} \quad i = 2, \ldots, n,$$

is shown in Figure 1. The governing differential equations of the cyclic network are given by

$$\begin{aligned} \dot{x}_1 &= -a_1 x_1 - y_n + \omega_1, \\ \dot{x}_2 &= -a_2 x_2 + y_1 + \omega_2, \\ &\vdots \\ \dot{x}_n &= -a_n x_n + y_{n-1} + \omega_n, \end{aligned} \tag{2.2}$$

where ω_i for $i = 1, 2, \ldots, n$ are independent white random processes with identical density. The dynamics of the network can be represented in the following compact form

$$\dot{x}(t) = Ax(t) + \omega(t), \tag{2.3}$$

where

$$A = \begin{bmatrix} -a_1 & 0 & \ldots & 0 & -c_n \\ c_1 & -a_2 & \ldots & 0 & 0 \\ \vdots & \vdots & \ddots & \vdots & \vdots \\ 0 & 0 & \ldots & -a_{n-1} & 0 \\ 0 & 0 & \ldots & c_{n-1} & -a_n \end{bmatrix}, \tag{2.4}$$

and $\omega(t) \in \mathbb{R}^n$ is a zero-mean continuous time white random process with covariance matrix $\mathbb{E}[\omega(t)\omega(\tau)^{\mathrm{T}}] = \frac{1}{2} I_n \delta(t-\tau)$.

In the following, our goal is to perform a robustness analysis for the cyclic interconnected network (2.3) driven by external stochastic disturbances. To this end, we consider the steady-state variance of the state of the network as a robustness measure, i.e.,

$$H^2 := \lim_{t \to \infty} \mathbb{E}[x(t)^{\mathrm{T}} x(t)].$$

Our first result shows that there is a hard limit on this robustness measure which is a function of the size of the network.

THEOREM 2.1. *Suppose that for the cyclic network (2.3), the stability condition* $\frac{c_1 c_2 \cdots c_n}{a_1 a_2 \cdots a_n} < \sec^n(\frac{\pi}{n})$ *holds. Then, the steady-state variance of the state of the network is lower and upper bounded as follows*

$$-\sum_{i=1}^{n} \frac{1}{2\mathbf{Re}\{\lambda_i(A)\}} \leq H^2 \leq -\sum_{i=1}^{n} \frac{1}{\lambda_i(A_s)}, \tag{2.5}$$

where $A_s = A^T + A$ *is the symmetric part of matrix* A. *Moreover, if* $a := a_1 = a_2 = \cdots = a_n$ *, then*

$$-\sum_{i=1}^{n} \frac{1}{2\mathbf{Re}\{\lambda_i(A)\}} = \begin{cases} \frac{n \tan \frac{\beta}{2}}{2r \sin \frac{\beta}{n}}, & q < 1 \\ \frac{n^2}{2r}, & q = 1 \\ \frac{n \tanh \frac{\beta}{2}}{2r \sinh \frac{\beta}{n}}, & q > 1 \end{cases} \tag{2.6}$$

where

$$r = \sqrt[n]{c_1 c_2 \cdots c_n}, \quad q = \frac{a}{r}$$

$$\beta := \begin{cases} \operatorname{arcos}(q) n, & q \leq 1 \\ \operatorname{arcosh}(q) n, & q > 1 \end{cases} \tag{2.7}$$

Proof. The stability condition $\frac{c_1 c_2 \cdots c_n}{a_1 a_2 \cdots a_n} < \sec^n(\frac{\pi}{n})$ implies that A is Hurwitz. Therefore, we can compute the robustness measure of the network which is the $\mathcal{H}_2$–norm of the system and is given by $[\mathbf{Tr}(P)]^{\frac{1}{2}}$ (see [13, 14]), where P is the solution of the Lyapunov equation

$$AP + PA^{\mathrm{T}} = -I. \tag{2.8}$$

First, we show that

$$H^2 \leq -\sum_{i=1}^{n} \frac{1}{\lambda_i(A_s)}.$$

The secant criterion (i.e., $\frac{c_1 c_2 \cdots c_n}{a_1 a_2 \cdots a_n} < \sec^n(\frac{\pi}{n})$) implies that all he eigenvalues of A have negative real parts. Hence, the unique positive definite solution of (2.8) is given by

$$P = \int_0^\infty e^{A^{\mathrm{T}} t} e^{At} dt. \tag{2.9}$$

According to [22], we have

$$\mathbf{Tr}(e^{A^{\mathrm{T}} t} e^{At}) \leq \mathbf{Tr}(e^{A^{\mathrm{T}} + A}). \tag{2.10}$$

From (2.9) and (2.10), it follows that

$$\mathbf{Tr}(P) = \int_0^\infty \mathbf{Tr}(e^{A^{\mathrm{T}} t} e^{At}) dt \leq \int_0^\infty \mathbf{Tr}(e^{A_s t}) dt. \tag{2.11}$$

The trace and sum are linear operators. Hence, they commute with the integral. From (2.11), we get

$$\begin{aligned} H^2 = \mathbf{Tr}(P) &\leq \int_0^\infty \mathbf{Tr}(e^{A_s t}) dt \\ &= \int_0^\infty \sum_{i=1}^{n} e^{\lambda_i(A_s) t} dt = -\sum_{i=1}^{n} \frac{1}{\lambda_i(A_s)}. \end{aligned} \tag{2.12}$$

Next, we show that

$$-\sum_{i=1}^{n} \frac{1}{2\mathbf{Re}\{\lambda_i(A)\}} \leq H^2.$$

According to Schur decomposition theorem, there exist a unitary matrix $V \in \mathbb{C}^{N \times N}$ such that $A = V(\Gamma + N)V^{\mathrm{H}}$ where $\Gamma = \mathbf{diag}(\lambda_1, \cdots, \lambda_N)$ and N is strictly upper triangular. We have

$$\begin{aligned} \mathbf{Tr}(e^{A^{\mathrm{T}} t} e^{At}) &= \mathbf{Tr}(e^{A^{\mathrm{H}} t} e^{At}) \\ &= \mathbf{Tr}(e^{V(\Gamma^{\mathrm{H}} + N^{\mathrm{H}})V^{\mathrm{H}} t} e^{V(\Gamma + N)V^{\mathrm{H}} t}) \\ &= \mathbf{Tr}(V e^{(\Gamma^{\mathrm{H}} + N^{\mathrm{H}})t} V^{\mathrm{H}} V e^{(\Gamma + N)t} V^{\mathrm{H}}) \\ &= \mathbf{Tr}(e^{(\Gamma^{\mathrm{H}} + N^{\mathrm{H}})t} V^{\mathrm{H}} V e^{(\Gamma + N)t} V^{\mathrm{H}} V) \\ &= \mathbf{Tr}(e^{(\Gamma^{\mathrm{H}} + N^{\mathrm{H}})t} e^{(\Gamma + N)t}) \end{aligned} \tag{2.13}$$

Furthermore, we get

$$\begin{aligned} e^{(\Gamma + N)t} &= e^{\Gamma t} + M_t, \\ e^{(\Gamma^{\mathrm{H}} + N^{\mathrm{H}})t} &= e^{\Gamma^{\mathrm{H}} t} + M_t^{\mathrm{H}}, \end{aligned} \tag{2.14}$$

where M_t is an upper-triangular Nilpotent matrix. Using (2.14), we have

$$\begin{aligned} \mathbf{Tr}(e^{(\Gamma^{\mathrm{H}} + N^{\mathrm{H}})t} e^{(\Gamma + N)t}) &= \mathbf{Tr}(e^{\Gamma t} e^{\Gamma^{\mathrm{H}} t} + M_t M_t^{\mathrm{H}})) \\ &\geq \mathbf{Tr}(e^{(\Gamma^{\mathrm{H}} + \Gamma)t}). \end{aligned} \tag{2.15}$$

From (2.13) and (2.15), it follows that

$$\begin{aligned} \mathbf{Tr}(e^{A^{\mathrm{T}} t} e^{At}) &= \mathbf{Tr}(e^{(\Gamma^{\mathrm{H}} + N^{\mathrm{H}})t} e^{(\Gamma + N)t}) \\ &\geq \mathbf{Tr}(e^{(\Gamma^{\mathrm{H}} + \Gamma)t}) = \mathbf{Tr}(e^{2\mathbf{Re}(\Gamma)t}). \end{aligned} \tag{2.16}$$

Finally, form (2.9) and (2.16) we get the desired result

$$H^2 \geq -\sum_{i=1}^{n} \frac{1}{2\mathbf{Re}\{\lambda_i(A)\}}.$$

If we assume that $a = a_1 = a_2 = \cdots = a_n$, then it is straightforward to verify that that the characteristic equation of A is given by $(\lambda + a)^n + c_1 c_2 \cdots c_n = 0$. Therefore, the eigenvalues of the matrix are $\lambda_k = -a + re^{i(\frac{\pi}{n} + \frac{2\pi k}{n})}$ for $k = 0, 1, \cdots, n-1$ and $r = \sqrt[n]{c_1 c_2 \cdots c_n}$. By substituting the value of the eigenvalues into (2.5), we get

$$\begin{aligned} -\sum_{i=1}^{n} \frac{1}{2\mathbf{Re}\{\lambda_i(A)\}} &= \sum_{k=0}^{n-1} \frac{1}{2\mathbf{Re}\left\{a - re^{i(\frac{\pi}{n} + \frac{2\pi k}{n})}\right\}} \\ &= \sum_{k=0}^{n-1} \frac{1}{2r\left(q - \cos(\frac{\pi}{n} + \frac{2\pi k}{n})\right)}. \end{aligned} \tag{2.17}$$

By substituting $q = \cos(\frac{\beta}{n})$ for $q < 1$ in (2.17), we get

$$\begin{aligned} -\sum_{i=1}^{n} \frac{1}{2\mathbf{Re}\{\lambda_i(A)\}} &= \frac{1}{2r} \sum_{k=0}^{n-1} \frac{1}{\cos(\frac{\beta}{n}) - \cos(\frac{\pi}{n} + \frac{2\pi k}{n})} \\ &= \frac{1}{4r} \sum_{k=0}^{n-1} \csc(\tfrac{(2k+1)\pi}{2n} + \tfrac{\beta}{2n}) \csc(\tfrac{(2k+1)\pi}{2n} - \tfrac{\beta}{2n}) \\ &= \frac{n \tan \frac{\beta}{2}}{2r \sin \frac{\beta}{n}}. \end{aligned}$$

We use the Birkhoffs ergodic theorem to prove the last equation. Similar steps can be taken for $q > 1$ and $q = 1$ by substituting q from (2.7) in (2.17) in order to get (2.6). □

REMARK 1. *When $a_1 = a_2 = \cdots = a_n$, the classical secant criterion [1, 7] for cyclic network (2.3) implies that the unperturbed system (2.3) is stable if and only if $q > \cos(\frac{\pi}{n})$. Therefore, if we keep the value of parameter β (given by (2.7)) fixed, changing the number of intermediate subsystems does not change the stability behavior of the cyclic network. However, according to Theorem 2.1, in this case, the lower bound of the robustness measure H increases when the size of the network grows. When β is fixed, it is* *straightforward to show that the lower bound of H grows by $\mathcal{O}(n)$ and it can be approximated by*

$$(2.18)\qquad \begin{cases} \sqrt{\frac{\tan\frac{\beta}{2}}{2r\beta}n} & , \quad q<1 \\ \sqrt{\frac{1}{2r}n} & , \quad q=1 \\ \sqrt{\frac{\tanh\frac{\beta}{2}}{2r\beta}n} & , \quad q>1 \end{cases}.$$

This means that as the number of intermediate reactions n grows, the robustness price increases at least linearly with the size of the cyclic network n (see Figure 2).

REMARK 2. *If we assume $y = x_n$, then the steady-state output dispersion is bounded above with*

$$H^2 := \mathbb{E}[y(t)^2] \leq \frac{1}{2(a - r\cos(\frac{\pi}{n}))}.$$

REMARK 3. *The results of Theorem 2.1 can be generalized to the case when A is only assumed to be Hurwitz. Using a similar approach, we can show that*

$$(2.19)\qquad -\sum_{i=1}^{n} \frac{1}{2\mathbf{Re}\{\lambda_i(A)\}} \leq H^2 \leq -\sum_{i=1}^{n} \frac{1}{\lambda_i(A_s)}.$$

We refer to [19] for more details.

REMARK 4. *We emphasize that when A is Hurwitz and normal the results of Theorem 2.1 reduces to*

$$(2.20)\qquad H^2 = -\sum_{i=1}^{n} \frac{1}{2\mathbf{Re}\{\lambda_i(A)\}} = -\sum_{i=1}^{n} \frac{1}{\lambda_i(A_s)}.$$

It can be shown that matrix A is normal when $a = a_1 = \cdots = a_n$ and $c = c_1 = \cdots = c_n$. Thus, based on Remark 4 and Theorem 2.1, we have the following result

$$(2.21)\qquad H^2 = \begin{cases} \frac{n\tan\frac{\beta}{2}}{2c\sin\frac{\beta}{n}} & , \quad a<c \\ \frac{n^2}{2c} & , \quad a=c \\ \frac{n\tanh\frac{\beta}{2}}{2c\sinh\frac{\beta}{n}}, & \quad a>c \end{cases}.$$

3 Fundamental limitations of feedback control laws in cyclic dynamical networks

In the section, we consider networks with autocatalytic structures as shown in Figure 3. In an interconnected control system with autocatalytic structure, the systems product (output) is necessary to power and catalyze its own production. The destabilizing effects of such positive autocatalytic feedback can be countered by negative regulatory feedback. We focus on a class of nonlinear dynamical networks with cyclic feedback structures driven only by output disturbance. We

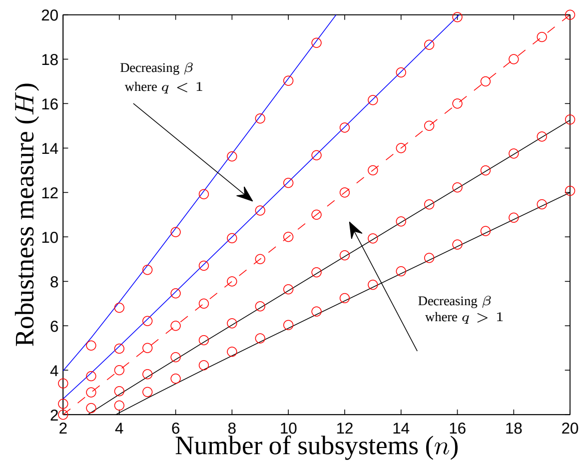

Figure 2: The red circles (○) depict the actual value of the $\mathcal{H}_2$–norm of the dynamical networks (2.3) versus the number of subsystems in the network. The solid lines represent the linear approximation of the lower bound of the $\mathcal{H}_2$–norm of the dynamical network as shown in (2.18).

consider a group of nonlinear systems $\mathcal{G}_i$ with state-space modela

$$(3.22)\qquad \begin{cases} \dot{x}_i &= -f_i(x_i) + u_i, \\ y_i &= g_i(x_i), \quad \text{for } 1 \leq i \leq n-1, \end{cases}$$

$$(3.23)\qquad \begin{cases} \dot{x}_n &= -f_n(x_n) + u_n - u, \\ y_n &= d_n u, \end{cases}$$

where $f_i(\cdot)$ and $g_i(\cdot)$ for $i = 1, \ldots, n$ are increasing functions. Moreover, $u_i(t)$, $y_i(t)$ and $x_i(t)$ are input, output and state variables of each subsystem, respectively. The state-space representation of the nonlinear cyclic interconnected network shown in Figure 3 is given by

$$(3.24)\qquad \begin{aligned} \dot{x}_1 &= -f_1(x_1) + y_n, \\ \dot{x}_2 &= -f_2(x_2) + y_1, \\ &\vdots \\ \dot{x}_n &= -f_n(x_n) + y_{n-1} - u + \delta, \\ y &= x_n. \end{aligned}$$

We assume that the origin is an equilibrium point of the unperturbed system (3.24), i.e., when $\delta = 0$. Moreover, it is assumed that

$$(3.25)\qquad a := f_1'(0) = f_2'(0) = \cdots = f_{n-1}'(0),$$

where $f_i'(0) := \left.\frac{\mathrm{d}f_i}{\mathrm{d}x_i}\right|_{x_i=0}$.

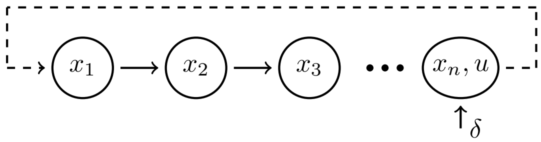

Figure 3: The schematic diagram of the nonlinear network (3.24) with a cyclic feedback structure with an output disturbance δ and control input u.

3.1 Hard limit on disturbance attenuation. The simplest robust performance requirement for (3.23) is that the concentration of y remains nearly constant when there is a small constant disturbance in output consumption δ (see [5, 12]). For example, in glycolytic pathway even temporary ATP (output) depletion can result in cell death. Therefore, we are interested in a more detailed monitoring of the transient response of the network to external disturbances. In the following, we show that there exists a hard limit on the best achievable disturbance attenuation, denoted by γ^*, for system (3.23) such that the problem of disturbance attenuation with internal stability is solvable for all $\gamma > \gamma^*$, i.e.,

$$\int_0^T y^2(t)dt \;\leq\; \gamma^2 \int_0^T \delta^2(t)dt, \tag{3.26}$$

for all $T \geq 0$ and all $\delta \in L_2(0,T)$ and $y(0) = 0$, and is not solvable for all $\gamma < \gamma^*$. In other words, disturbance attenuation problem can be solved only for those values of parameter γ greater than γ^*.

The interesting fact is that the optimal disturbance attenuation γ^* is indeed a hard limit function for system (3.23). This hard limit quantifies a fundamental barrier in achieving better performance indecies. It is known that for linear systems, optimal disturbance attenuations can be calculated using the zero-dynamics subsystem of the system [16, 20]. The ideal performance (hard limit function) is zero if and only if the disturbance δ does not affect the unstable part of the zero-dynamics (as defined in [20] for nonlinear systems).

THEOREM 3.1. *For cyclic networks (3.24), if*

$$r := \left(g_1'(0)g_2'(0)\cdots g_{n-1}'(0)d_n\right)^{\frac{1}{n-1}} > a, \tag{3.27}$$

then there exists a hard limit on the best achievable disturbance attenuation (i.e., $\gamma^* > 0$) for system (3.23) such that the regional state feedback L_2–gain disturbance attenuation problem with stability constraint is solvable for all $\gamma > \gamma^*$ and is not solvable for all $\gamma < \gamma^*$. Furthermore, the hard limit function is given by

$$\gamma^* \geq H = \frac{1}{f_n'(0) + r - a}. \tag{3.28}$$

Proof. In the first step, we introduce a new auxiliary variable $z_1 = x_1 + d_n x_n$. We can cast the linearized zero-dynamics of (3.23) in the following form

$$\dot{z} \;=\; A_0 z \;+\; B_0 y \;+\; C_0 \delta, \tag{3.29}$$

where $z = [z_1, x_2, \cdots, x_{n-1}]^{\mathrm{T}}$,

$$A_0 = \begin{bmatrix} -a & 0 & \dots & 0 & d_n g_{n-1}'(0) \\ g_1'(0) & -a & \dots & 0 & 0 \\ \vdots & \vdots & \ddots & \vdots & \vdots \\ 0 & 0 & \dots & -a & 0 \\ 0 & 0 & \dots & g_{n-2}'(0) & -a \end{bmatrix},$$

$$B_0 = \begin{bmatrix} ad_n - f_n'(0)d_n \\ -g_1'(0)d_n \\ \vdots \\ 0 \\ 0 \end{bmatrix}, \text{ and } C_0 = \begin{bmatrix} d_n \\ 0 \\ \vdots \\ 0 \\ 0 \end{bmatrix}. \tag{3.30}$$

Then, we consider the characteristic equation of matrix A_0 which is given by

$$(\lambda + a)^{n-1} - r^{n-1} = 0. \tag{3.31}$$

From (3.27) and (3.31), it follows that $\lambda_1 = r - a$ is the eigenvalue of A with the largest real-part value with left eigenvector

$$v_1 = \left[\, 1\,,\ \frac{r}{g_1'(0)}\,,\ \dots\,,\ \frac{r^{n-2}}{g_1'(0)g_2'(0)\cdots g_{n-2}'(0)} \,\right]^{\mathrm{T}}.$$

The unstable subsystem of (3.29) is characterized by

$$\dot{z} \;=\; \lambda_1 z + \left(a - f_n'(0) - r\right) d_n y + d_n \delta. \tag{3.32}$$

From the results of [17] and [20], the formula to compute the optimal value of γ reduces to

$$\gamma_L^* = \frac{1}{f_n'(0) + r - a}. \tag{3.33}$$

We emphasize that according to Proposition 6 in reference [21], γ_L^* is a lower bound for the optimal γ^* for the nonlinear system (3.24). □

In following example, we apply our results to an interesting metabolic pathway and quantify its existing hard limits.

EXAMPLE 1. *We consider a minimal representation of autocatalytic glycolysis pathway which consists of three biochemical reactions with a single intermediate metabolite reaction (3.34)-(3.35) (see [5] for more details),*

$$s + \alpha y \;\xrightarrow{f}\; x_1 \;\xrightarrow{k_x}\; (\alpha+1)y + x_1' \tag{3.34}$$

$$y \;\xrightarrow{k_y,\delta}\; \varnothing \tag{3.35}$$

where in the final reaction the effect of disturbance δ in ATP (output y) demand is considered. A set of ordinary differential equations that govern the changes in concentrations x_1 and y can be written as

$$\dot{x}_1 = -k_x x_1 + \frac{Vy^q}{1+\gamma y^h} \tag{3.36}$$

$$\dot{y} = -k_y y + (\alpha+1)k_x x_1 - \frac{\alpha V y^q}{1+\gamma y^h} + \delta, \tag{3.37}$$

for $x_1 \geq 0$, $y \geq 0$. The exogenous disturbance disturbance input is assumed to be $\delta \in L_2([0,\infty))$. To highlight fundamental tradeoffs due to autocatalytic structure of the system, we normalize the concentration such that steady-states are $y^* = 1$ and $x^* = \frac{k_y}{k_x}$. In glycolysis model (3.36)-(3.37), expression $\frac{\alpha V y^q}{1+\gamma y^h}$ can be interpreted as the regulatory feedback control employed by nature which captures inhibition of the catalyzing enzyme. Hence, we can derive a control system model for glycolysis as follows

$$\dot{x} = -k_x x + \frac{1}{\alpha} u, \tag{3.38}$$

$$\dot{y} = -k_y y + (\alpha+1)k_x x - u + \delta, \tag{3.39}$$

where u is the control input. Now, it follows from Theorem 3.1 that

$$\gamma > \frac{\alpha}{k_x + \alpha k_y}. \tag{3.40}$$

Equation (3.40) illustrates a tradeoff between robustness and efficiency (as measured by complexity and metabolic overhead). From (3.40) the glycolysis mechanism is more robust efficient if k_x and k_y are large. On the other hand, large k_x requires either a more efficient or a higher level of enzymes, and large k_y requires a more complex allosterically controlled PK enzyme; both would increase the cells metabolic load. We note that the existing hard limit is an increasing function of α. This implies that increasing α (more energy investment for the same return) can result in worse performance. It is important to note that these results are consistent with results in [5], where a linearized model with a different performance measure is used.

4 Conclusion

We exploit structural properties of cyclic networks in order to characterize their robustness properties and fundamental limits on their ideal performance. First, we consider an autonomous cyclic network driven by external stochastic disturbances. We explicitly calculate the $\mathcal{H}_2$–norm of the cyclic network as a robustness measure, which measures the expected steady-state dispersion of the state of the entire network. It is shown that the proposed robustness measure depends on characteristics of the underlying digraph of the network as well as the size of the network. Next, a cyclic dynamical networks with control inputs is considered. The fundamental limitations of feedback control laws are studied. As a motivating example, we look at cyclic networks with some specific autocatalytic structure. The hard limits are obtained as lower bounds on the minimum L_2–gain disturbance attenuation. The existence of these hard limits often impose undesirable fundamental tradeoffs on optimal performance and robustness in such networks.

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