Maximal-Robustness-Minimal-Fragility Controller: A Compromise between Robustness and Fragility of Biochemical Networks

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Abstract. Establishing a trade-off between robustness and fragility has been an active research topic in constructing biochemical networks. In this paper, we formulate a compromise between robustness and fragility as a cooperative game, based on which a dynamical incomplete information game is constructed. In addition, three channels are chosen as players, and eight pure control strategies are created. Algorithms in seeking the perfect Bayesian-Nash equilibrium are consequently constructed. Based on the perfect Bayesian-Nash equilibrium, Maximal-Robustness-Minimal-Fragility controller (MRMFc) is derived, and MRMFc is effectively applied to biochemical networks. And computer simulations demonstrate that the biochemical network achieves a good balance between robust stability and dynamical performance. Consequently, an attractive solution in attacking the problem of the trade-offs between robustness and fragility is therefore laid out in this paper.

Keywords: $\mu/H_2/H_\infty$ control; Biochemical networks; Maximal-Robustness-Minimal-Fragility controller; Perfect Bayesian-Nash equilibrium.

1 Introduction

A system-level understanding of a biological system can be divided into two steps: (1) System modeling. It is meant to derive a mathematical model from the system structure. (2) Controller devising [1-2]. It is meant to apply control theory to the biological mathematical model, and devise the negative controller to get better robustness and dynamical performance. In general, biological robustness is an essential property of biological systems [3-5]. The biological robustness is usually related to the feedback control [3-6]. The robustness of perfect adaptation is the result of the integral feedback control [5], and biological complexity is the interplay between complexity,

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robustness, modularity, feedback and fragility [6]. In literature [7], a simple graphical method was presented to analyze the presence of multi-stability, bifurcations, and hysteretic behavior of positive-feedback systems.

The trade-offs among robustness, fragility and performance exist often in biological systems at different levels [8] while robustness and fragility are the important features of biological systems [9]. Robustness is generally viewed as robust stability while fragility is viewed as dynamic performance. While fragility is considered bad, the dynamic performance is deemed good. Therefore, it is a vital research problem that the biological system should achieve a good balance between robust stability and optimal dynamic performance. To solve this problem, we employ the game theory [10-11] to perform the task. Multi-objective control theory offers a very flexible design framework in which a control engineer can freely select arbitrary performance channels and uncertainty models, and the most appropriate norm to represent the design specification for each channel can be provided [12-14]. Mixed $\mu/H_2/H_\infty$ control incorporates all three control methods, i.e, μ control for improving the stability of uncertainty[15-17], H_2 control for improving dynamic performance, and H_∞ control for improving robust stability. We choose the structured singular value to represent the stability of uncertainty when we select μ control. Moreover, we employ H_2 norm to represent dynamic performance, H_∞ norm to represent the robust stability. Consequently, we can readily formulate a mixed $\mu/H_2/H_\infty$ control.

2 Mathematical Model

Since S-system [18] is a universal biological system, we transform it into linear system in order to construct robust control model. Generally, S-system is a type of power-law formalism. The equation of the S-system can incorporate the robustness and dynamical performance of a biological system. Using S-system steady-state evaluation, the control analysis of a given system can be easily established. Assuming reactant X_i is concentration, α_i and β_i are rate constants, g_{ij} and h_{ij} are the values of interactive effect of X_i and X_j, thus we can have [18,20]

$$\dot{x}_i = \alpha_i \prod_{j=1}^{n+m} x_j^{g_{ij}} - \beta_i \prod_{j=1}^{n+m} x_j^{h_{ij}} \qquad (i = 1,2\cdots n) \tag{1}$$

Considering $\dot{x}_i = 0$, we can obtain:

$$\alpha_i \prod_{j=1}^{n+m} x_j^{g_{ij}} = \beta_i \prod_{j=1}^{n+m} x_j^{h_{ij}} \tag{2}$$

$$\ln \alpha_i + \sum_{j=1}^{n+m} g_{ij} \ln x_j - \ln \beta_i - \sum_{j=1}^{n+m} h_{ij} \ln x_j = 0 \tag{3}$$

$$\sum_{j=1}^{n} (g_{ij} - h_{ij}) \ln x_j + \sum_{j=n+1}^{n+m} (g_{ij} - h_{ij}) \ln x_j + \ln(\frac{\alpha_i}{\beta_i}) = 0 \tag{4}$$

Now, define $y_j = \ln x_j, a_{ij} = g_{ij} - h_{ij}, b_i = \ln(\frac{\alpha_i}{\beta_i})$ equation (4) can be denoted as $AY + B_\omega \boldsymbol{\omega} + B_u u = 0$, where

$$A=\begin{pmatrix} a_{11} & \cdots & a_{1n} \\ \vdots & \ddots & \vdots \\ a_{n1} & \cdots & a_{nn} \end{pmatrix} \quad B_u=\begin{pmatrix} a_{1n+k+1} & \cdots & a_{1n+m} \\ \vdots & \ddots & \vdots \\ a_{nn+k+1} & \cdots & a_{nn+m} \end{pmatrix} \quad B_\omega=\begin{pmatrix} a_{11} & \cdots & a_{1n} & 1 & \cdots & 0 \\ \vdots & \ddots & \vdots & \vdots & \ddots & \vdots \\ a_{n1} & \cdots & a_{nn} & 0 & \cdots & 1 \end{pmatrix} \tag{5}$$

We could obtain state-space equation when $X_g = Y$: $AX_g + B_\omega \boldsymbol{\omega} + B_u u = 0$

And , the state-space equation could be derived when $\dot{x}_i \neq 0$:

$$\begin{cases} F(\dot{x}_g) = \boldsymbol{A}\boldsymbol{x}_g + \boldsymbol{B}_\omega \boldsymbol{\omega}_1 + \boldsymbol{B}_u \boldsymbol{u} \\ \boldsymbol{z}_1 = \boldsymbol{C}_1 \boldsymbol{x}_g + \boldsymbol{D}_{11}\boldsymbol{\omega}_1 + \boldsymbol{D}_{12}\boldsymbol{u} \\ \boldsymbol{z}_2 = \boldsymbol{C}_2 \boldsymbol{x}_g + \boldsymbol{D}_{21}\boldsymbol{\omega}_1 + \boldsymbol{D}_{22}\boldsymbol{u} \\ \boldsymbol{y} = \boldsymbol{C}_3 \boldsymbol{x}_g + \boldsymbol{D}_{31}\boldsymbol{\omega}_1 + D_{32} u \end{cases} \tag{6}$$

$\omega_1 = [p \quad \omega]^T$, $z_1 = q$, $\mathbf{z_2} = z$, x_g is general state variable, $\Delta_m(s)$ is the worst case uncertainty $\Delta(s)$, $\boldsymbol{\omega}$ is disturbance signal, u is control input signal, z is the evaluated output, y is the measured output, and q and p are input and output signals of $\Delta_m(s)$, respectively.

3 A Dynamical Incomplete Information Game

We formulate the trade-offs between robustness and fragility as a dynamical incomplete information game, and at the same time, choose channels $\mathbf{T_{qp}}$ 、 $\mathbf{T_{z\omega}}$ and $\mathbf{T_{u\omega}}$ as three players and eight control strategies as pure strategies, which are shown in Figs 1.

Three players could be constructed as follows: (1) Player1 refers to $\mathbf{T_{qp}}$. From equation (6), it can be seen that $\mathbf{T_{qp}}$ is the transfer function from p, which is the output signal of $\Delta_m(s)$ to q with the input signal of $\Delta_m(s)$. (2) Player2 refers to $\mathbf{T_{z\omega}}$. It can be seen that $\mathbf{T_{z\omega}}$ is the transfer function from $\boldsymbol{\omega}$, which is disturbance signal to z with the evaluated output signal. (3) Player3 refers to $\mathbf{T_{u\omega}}$. It can be readily seen that $\mathbf{T_{u\omega}}$ is the transfer function from $\boldsymbol{\omega}$, which is disturbance signal to u with the control input signal.

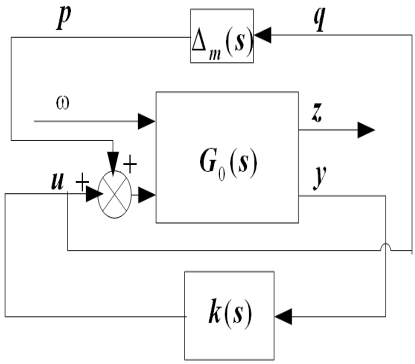

Fig. 1. Control of the generalized plant

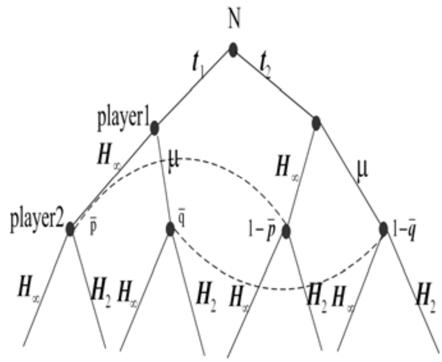

Fig. 2. The perfect Bayesian-Nash equilibrium

According to three controllers including μ、 H_2 and H_∞ control, three players could select each of three controllers and design eight control strategies. Thus, eight control strategies and norms can be described as follows:

A1) H_∞ control .

A2) Mixed H_∞ / H_2 control. Minimizing $\|T_{u\omega}\|_2$ and $\left\|\begin{bmatrix} T_{qp} \\ T_{z\omega} \end{bmatrix}\right\|_\infty < \gamma$

A3) Mixed H_∞ / H_2 control. Minimizing $\|T_{z\omega}\|_2$ and $\left\|\begin{bmatrix} T_{qp} \\ T_{u\omega} \end{bmatrix}\right\|_\infty < \gamma$

A4) Mixed H_∞ / H_2 control. Minimizing $a\|T_{qp}\|_\infty^2 + b\left\|\begin{bmatrix} T_{qp} \\ T_{u\omega} \end{bmatrix}\right\|_2^2$

A5) Mixed μ / H_∞ control. Minimizing $\|\boldsymbol{T}_{qp}\|_\mu$ and $\left\|\begin{matrix} \mathbf{T}_{z\omega} \\ \mathbf{T}_{u\omega} \end{matrix}\right\|_\infty$

A6) Mixed $\mu / H_\infty / H_2$ control. Minimizing $\|T_{qp}\|_\mu$ and $a\|T_{z\omega}\|_\infty^2 + b\|T_{u\omega}\|_2^2$

A7) Mixed $\mu / H_2 / H_\infty$ control. Minimizing $\|\boldsymbol{T}_{qp}\|_\mu$ and $a\|T_{z\omega}\|_2^2 + b\|T_{u\omega}\|_\infty^2$

A8) Mixed μ / H_2 control. Minimizing $\|\boldsymbol{T}_{qp}\|_\mu$ and $\left\|\begin{matrix} \mathbf{T}_{z\omega} \\ \mathbf{T}_{u\omega} \end{matrix}\right\|_2$

Generally, a payoff matrix is a table that describes the utility in a game for each possible combination of strategies. Therefore we obtain the payoff matrix of Tables I as follows. In the 3-person game, the row of a payoff matrix is player2's strategy and the column of a payoff matrix is player3's strategy when player1 chooses the strategy. For example, $\|\mathbf{T}_{z\omega}\|_\infty$ and $\|\mathbf{T}_{z\omega}\|_2$ are player2's strategy, meanwhile, $\|\mathbf{T}_{u\omega}\|_\infty$ and $\|\mathbf{T}_{u\omega}\|_2$ are player3's strategy from Table I. The values of matrix are the utility of player2、player1 and player3, which are the reciprocal of their own norms.

Table 1. The payoff matrix when player1 chooses $f^1=\{H_\infty \text{control}\}/f^2=\{\mu\text{control}\}$

$\|T_{qp}\|_\infty / \|T_{qp}\|_\mu$	$\|T_{u\omega}\|_\infty$	$\|T_{u\omega}\|_2$
$\|T_{z\omega}\|_\infty$	$(\frac{1}{b_{11}}\ \frac{1}{a_{11}}\ \frac{1}{c_{11}})/(\frac{1}{b_{21}}\ \frac{1}{a_{21}}\ \frac{1}{c_{21}})$	$(\frac{1}{b_{12}}\ \frac{1}{a_{12}}\ \frac{1}{c_{12}})/(\frac{1}{b_{22}}\ \frac{1}{a_{22}}\ \frac{1}{c_{22}})$
$\|\mathbf{T}_{z\omega}\|_2$	$(\frac{1}{b_{13}}\ \frac{1}{a_{13}}\ \frac{1}{c_{13}})/(\frac{1}{b_{23}}\ \frac{1}{a_{23}}\ \frac{1}{c_{23}})$	$(\frac{1}{b_{14}}\ \frac{1}{a_{14}}\ \frac{1}{c_{14}})/(\frac{1}{b_{24}}\ \frac{1}{a_{24}}\ \frac{1}{c_{24}})$

4 The Algorithms for Seeking Perfect Bayesian-Nash Equilibrium

We devise an algorithm to seek the perfect Bayesian-Nash equilibrium of a dynamical incomplete information game. In a cooperative dynamical incomplete information game, the utility depends on not only their own action, but the actions of others. Usually the perfect Bayesian-Nash equilibrium is the optimal strategy of players. No player can increase the system's utility by unilaterally deviating from the perfect Bayesian-Nash equilibrium. When seeking the perfect Bayesian-Nash equilibrium, we begin with 2-person game (player1 and player2), which can be described in Fig.2. When this game is finished, we can get the Bayesian-Nash equilibrium of 2-person game. Considering player3's strategy and 2-person Bayesian-Nash equilibrium we can obtain the Bayesian-Nash equilibrium of 3-person game.

Each player has its own strategy space $f^m=\{f_1^m, f_2^m\}$ which includes f_1^m and f_2^m .Therefore we can obtain strategy profiles, which include (f_1^m, f_1^m)、(f_1^m, f_2^m)、(f_2^m, f_1^m) and (f_2^m, f_1^m) (m=1,2,3). From Fig.2, it can be seen that $\bar{p}$ and $\bar{q}$ are player1's posterior probabilities with $\bar{p}=\bar{p}(t_1 \mid H_\infty)$ and $\bar{q}=\bar{p}(t_1 \mid \mu)$ respectively. Meanwhile, we can get $1-\bar{p}=\bar{p}(t_2 \mid H_\infty)$ and $1-\bar{q}=\bar{p}(t_2 \mid \mu)$. We also define probabilities $p(t_1)=p(t_2)=\frac{1}{2}$ when we consider equilibrium state of t_1 .and t_2 . $u_1(t_1,q_m,q_m)$ is player1's utility function, where $q_m=\{\mu,\ H_\infty,\ H_2\}$(m=1,2,3).

Algorithm 1. (Player 1 Selects $\{H_\infty control, H_\infty control\}$ or $\{\mu control, \mu control\}$)

Step 1: Posterior probabilities are defined as follows:

$$\bar{p}(t_1 \mid H_\infty) = \bar{p}(t_1 \mid \mu) = \frac{p(t_1)}{p(t_1)+p(t_2)}, \quad \bar{p}(t_2 \mid H_\infty) = \bar{p}(t_2 \mid \mu) = \frac{p(t_2)}{p(t_1)+p(t_2)}$$

Step 2: Judge the strategy of Player2.

Step2.1: Judge the strategy of Player2 when Playe1 selects $\{H_\infty control, H_\infty control\}$. $\sum_{t_k} \bar{p}(t_k \mid H_\infty) u_2(t_k, H_\infty, H_\infty)$ is the player2's probabilistic utility function when Player2 selects the strategy of H_∞ control. Meanwhile, $\sum_{t_k} \bar{p}(t_k \mid H_\infty) u_2(t_k, H_\infty, H_2)$ is the player2's probabilistic utility function when Player2 selects the strategy of H_2 control.

Step2.2: Judge the strategy of Player2 when Player1 selects $\{\mu control, \mu control\}$ $\sum_{t_k} \bar{p}(t_k \mid \mu) u_2(t_k, \mu, H_\infty)$ is the player2's probabilistic utility function when Player2 selects the strategy of H_∞ control. Meanwhile, $\sum_{t_k} \bar{p}(t_k \mid \mu) u_2(t_k, \mu, H_2)$ is the player2's probabilistic utility function when Player2 selects the strategy of H_2 control.

Rule1.1: If $\sum_{t_k} \bar{p}(t_K \mid H_\infty) u_2(t_K, H_\infty, H_\infty) > \sum_{t_k} \bar{p}(t_K \mid H_\infty) u_2(t_K, H_\infty, H_2)$, then Player2 selects H_∞ control; otherwise, Player 2 selects H_2 control.

Rule1.2: If $\sum_{t_k} \bar{p}(t_K \mid \mu) u_2(t_K, \mu, H_\infty) > \sum_{t_k} \bar{p}(t_K \mid \mu) u_2(t_K, \mu, H_2)$, then Player2 selects H_∞ control; otherwise, Player2 selects H_2 control.

Step 3: Judge the strategy of Player1 on account of Player2's strategy.

Rule1.3: If $u_1(t_1, H_\infty, H_\infty) > u_1(t_1, H_\infty, H_2)$ and $u_1(t_2, H_\infty, H_\infty) > u_1(t_2, H_\infty, H_2)$, then Player1 selects H_∞ control and Player2 selects H_∞ control.

Rule1.4: If $u_1(t_1, H_\infty, H_2) > u_1(t_1, H_\infty, H_\infty)$ and $u_1(t_2, H_\infty, H_2) > u_1(t_2, H_\infty, H_\infty)$, then Player1 selects H_∞ control, and Player2 selects H_2 control.

Rule1.5: If $u_1(t_1, \mu, H_\infty) > u_1(t_1, \mu, H_2)$ and $u_1(t_2, \mu, H_\infty) > u_1(t_2, \mu, H_2)$, then Player1 selects μ control and Player 2 selects H_∞ control.

Rule1.6: If $u_1(t_1,\mu,H_2) > u_1(t_1,\mu,H_\infty)$ and $u_1(t_2,\mu,H_2) > u_1(t_2,\mu,H_\infty)$, then Player1 selects μ control and Player2 selects H_2 control.

B. Algorithm 2 (Player1 Selects the Strategy of $\{\mu\text{control}, H_\infty\text{control}\}$). The implementation is just like *Algorithm 1*

C. Algorithm 3 (Player1 Selects the Strategy of $\{H_\infty\text{control}, \mu\text{control}\}$)

Step1: If H_∞ control is the optimal strategy of t_1, then H_∞ control is not the optimal strategy of. t_2. If μ control is the optimal strategy of t_2, then μ control is not the optimal strategy of t_1 .we can define $\bar{p}(t_1 | H_\infty) = \bar{p}(t_2 | \mu) = 1$ and $\bar{p}(t_2 | H_\infty) = \bar{p}(t_1 | \mu) = 0$ Steps 2 and 3 is like Steps 2 and 3 of Algorithm 1.

5 Experimental Results

Considering the glycolytic-glycogenolytic pathway in rat liver, the kinetic properties of the pathway can be described as shown in the following equations [18]:

$$\begin{aligned} \dot{x}_1 &= 0.077884314 x_4^{0.66} - 1.062708258 x_1^{1.53} x_2^{-0.59} x_7 \\ \dot{x}_2 &= 0.585012402 x_1^{0.95} x_2^{-0.41} x_5^{0.32} x_7^{0.62} x_{10}^{0.38} - 7.93456 \times 10^{-4} x_2^{3.97} x_3^{-3.06} x_8 \\ \dot{x}_3 &= 7.93456 \times 10^{-4} x_2^{3.97} x_3^{-3.06} x_8 - 1.05880847 x_3^{0.3} x_9 \end{aligned} \tag{7}$$

Diseases always alter the kinetic properties of a biochemical network. Suppose the pathway suffers from a parameter perturbation, which can be described as follows:

$$\begin{aligned} \dot{x}_1 &= 0.077884314 x_4^{0.66} - 1.062708258 x_1^{1.5135} x_2^{-0.6278} x_7 \\ \dot{x}_2 &= 0.585012402 x_1^{0.9133} x_2^{-0.437} x_5^{0.32} x_7^{0.62} x_{10}^{0.38} - 7.93456 \times 10^{-4} x_2^{3.9125} x_3^{-3.035} x_8 \\ \dot{x}_3 &= 7.93456 \times 10^{-4} x_2^{3.9125} x_3^{-3.035} x_8 - 1.05880847 x_3^{0.3825} x_9 \end{aligned} \tag{8}$$

$x_6 = 5.02$, $x_9 = 4909$, $x_{10} = 2.04 * 10^{-9}$ (**i.e.** $A = A_0 + \Delta A$, $\Delta_m(s) = \Delta A$)

Denoting $\gamma = 1$, a=0.5, b=0.5, and results is as follows: Player1 selects μ control, Player2 selects H_2 control and Player3 selects H_∞ control (2) Player1 selects H_∞ control, Player2 selects H_∞ control and Player3 selects H_∞ control.

It is shown that this system is stable and can converge to the steady state when there exists the uncertainty disturbance $\Delta_m(s)$ and noise disturbance ω from Fig. 3 to Fig. 5. The $\mu/H_2/H_\infty$ controller produces good robustness of the biochemical network

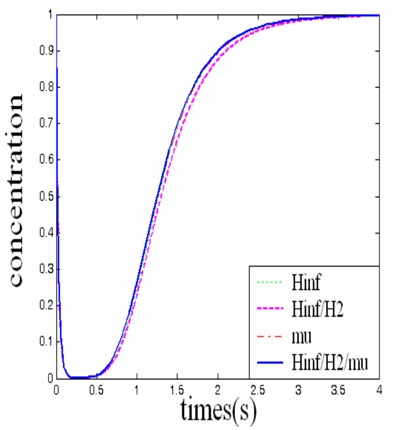

Fig. 3. The concentration of glucose-1-P

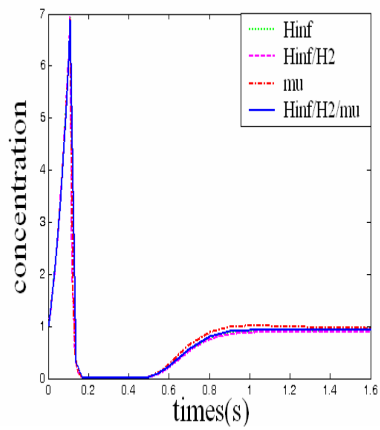

Fig. 4. The concentration of glucose-6-P

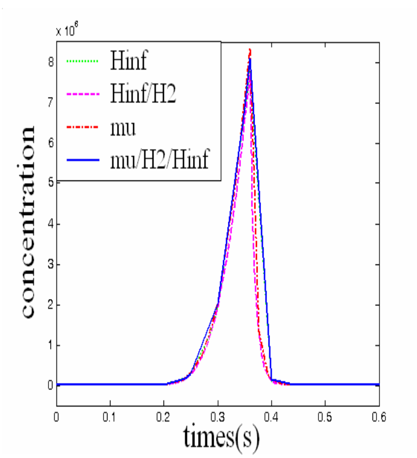

Fig. 5. The concentration of fructose-6-P

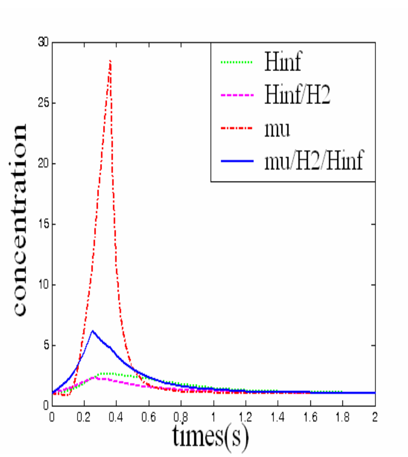

Fig. 6. The concentration of P_i

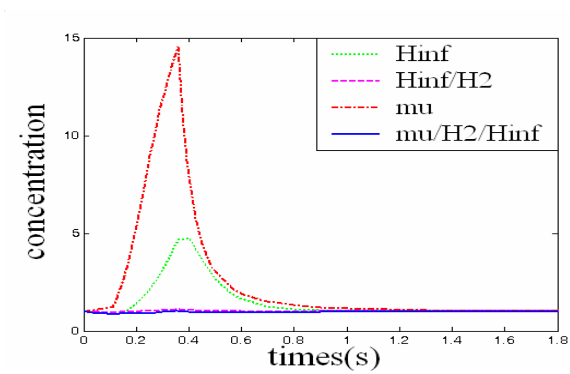

Fig. 7. The concentration of glucose

and robustness provides insensitivity to the parameter changes in this biochemical network. The poles of $\mu/H_2/H_\infty$ controller $K_{\mu/H_2/H_\infty}$ are –17.2360, -0.2518+3.0200i, and -0.2518-3.0200i, respectively, so the controller $K_{\mu/H_2/H_\infty}$ is a stable controller. The concentrations of glucose-1-P, glucose-6-P and fructose-6-P with $\mu/H_2/H_\infty$ controller achieve a better dynamical performance and the peak values of the concentration of glucose-1-P, glucose-6-P and fructose-6-P are lower than those of other controllers as shown from Fig 3 to Fig 5. Convergent rate is rapid and convergent time is short when we use $\mu/H_2/H_\infty$ controller. It is shown that mixed H_∞/H_2 control has the worst performance from Fig 3 to Fig 4 and μ control has the worst performance from Fig 5. From Fig 6, the biochemical network achieves better disturbance attenuation performance specification with mixed H_∞/H_2 control controller when the input value is identical. Also from Fig 7, it can be seen that the biochemical network achieves better disturbance attenuation performance specification with $\mu/H_2/H_\infty$ controller when the input value is identical. In conclusion, $\mu/H_2/H_\infty$ controller, which is Maximal-Robustness-Minimal-Fragility controller, outperforms other controllers and the biochemical network achieves a good balance between robust stability and dynamical performance. Maximal-Robustness-Minimal-Fragility negative feedback controller is helpful for maintaining stability margin and disturbance attenuation when uncertainty disturbance and noise disturbance are considered. This achievement is important to biochemical network, as errors in signal transduction can result in growth impairment or cancer [19].

6 Conclusions

Generally, S-system is a popular biochemical networks model, so we transform it into robust control model. The trade-offs between robustness and fragility is formulated as a dynamical incomplete information game model. We seek the perfect Bayesian-Nash equilibrium and devise the Maximal-Robustness-Minimal-Fragility controller when this control model has noise disturbance and uncertainty disturbance. Biochemical network needs to work in robust state against the various sources of inter- or intra-cellular perturbations. The biological robustness and dynamical performance provide general principle for understanding many biological phenomena and for constructing a system-level view of medical therapy and disease.

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References

1. Kitano, H.: Systems Biology: A Brief Overview. Science 295, 1662–1664 (2002)
2. Kitano, H.: Computational Systems Biology. Nature 420, 206–210 (2002)
3. Barkai, N.: Robust in Simple Biochemical Networks. Nature 387, 913–917 (1997)

4. Alon, U., Surette, M.G., Barkai, N., Leibler, S.: Robustness in Bacterial Chemotaxis. Nature 397, 168–171 (1999)
5. Yi, T.M., Huang, Y., Simon, M.I., Doyle, J.: Robust Perfect Adaptation in Bacterial Chemotaxis through Integral Feedback Control. PNAS 97, 4649–4653 (2000)
6. Csete, M.E., Doyle, J.: Reverse Engineering of Biological Complexity. Science 295, 1664–1669 (2000)
7. Angeli, D.: Detection of Multistability, Bifurcations, and Hysteresis in a Large Class of Biological Positive-Feedback Systems. PNAS 101, 1822–1827 (2004)
8. Kitano, H.: Biological Robustness. Nature 5, 826–837 (2004)
9. Carlson, J.M., Doyle, J.: Complexity and Robustness. PNAS 99, 2538–2545 (2002)
10. Basar, T., Olsder, G.J.: Dynamic NonCooperative Game Theory. Academic Press, New York (1982)
11. Fudenberg, D., Tirole, J.: Game Theory. MIT Press, Cambridge (1992)
12. Isidori, A.: Mixed H2 / H∞Control. Springer, Heidelberg (1995)
13. Bernsten, D.S., Hadded, W.M.: LQG Control with a H∞ Performance Bound: A Riccati Equation Approach. IEEE Transactions on Automatic Control 34, 293–305 (1989)
14. Zhou, K., Glover, K., Bodenheimer, B., Doyle, J.: Mixed H2 and H∞ Performance Objectives I: Robust Performance Analysis. IEEE Transactions on Automatic Control 39, 1564–1574 (1994)
15. Packard, A., Doyle, J.: The Complex Structured Singular Value. Automatica 29, 71–109 (1993)
16. Lin, J.L., Postlethwaite, I., Gu, D.W.: μ-K-Iteration for μ-Synthesis. Automatica 29, 219–224 (1993)
17. Balas, G.J., Doyle, J., Glover, K., Packard, A., Smith, R.: μ -Analysis and Synthesis Toolbox. Automatica 30, 733–735 (1994)
18. Voit, E.O.: Computational Analysis of Biochemical System. Cambridge University Press, Cambridge (2000)
19. Markus, K., Linda, L., Kilian, B., Jens, T., Victor, S.: Design Principles of a Bacterial Signaling Network. Nature 438, 504–507 (2005)
20. Chen, B.S., Wan, Y.C., Wu, W.S., Li, W.H.: A New Measure of the Robustness of Biochemical Networks. Bioinformatics 21, 2698–2705 (2005)