Time-Delayed Feedback Channel Design: Discrete Time H_{∞} Approach

Marcella M. Gomez*, Seungil You* and Richard M. Murray

Abstract—This paper proposes a method of improving performance of scalar discrete-time systems with substantial delay by adding additional delayed feedback channels (i.e. imposing a distributed delay feedback). The optimal weights for the added feedback channels are found using optimization techniques. In particular, we reduce the H_{∞} norm of the closed loop transfer function with multiple delayed feedback using techniques from static output feedback design. We impose constraints on the feedback gain in order to highlight the effectiveness of the distribution. In this manner, improvement on performance is a result of the distribution and not a change in the overall effective gain. The concept of applying a multiple delayed feedback channel is inspired by biological systems, where substantial delays can be present in feedback control. To show the effectiveness of this idea we apply our method to an example of a scalar genetic autoregulatory network. The constraint on the gain allows one to implement the feedback in a genetic regulatory network without having to change the reaction rates. A possible method of synthesizing such a system in a wet lab is explained in more detail. Finally, stability results indicate the possibility of stabilizing an unstable system with added delayed feedbacks (by adding larger delays). This approach may also be applicable to systems with large delays in which simple controllers are needed due to limitations in computational power. This paper motivates and provides preliminary results towards direct design of purely delay based controllers for network systems with large delays.

I. INTRODUCTION

Time delay in systems is an important uncertainty to consider and should be treated carefully. Much work has been done to deal with the existence of time delay in systems, from stability analysis to controller synthesis; see [1] and [2] for an excellent survey and references therein.

Although many tools exists for feedback controller design, such as PID, LQR, and H_{∞} [3], implementing such controllers in a synthetic biological network is not trivial, due to a lack of computational components in synthetic biology [4]. In addition, controller design for systems with inherently large delays is a relatively new problem brought about by synthetic biology and large network systems. Although, some processes in biology operate on fast time scales, some protein regulated networks can have substantial delays. For example, protein folding can impart significant delays, depending on its size [5].

We look to existing biological systems for a possible answer. Despite having delays and inherent stochastic processes, biological systems remain robust in the presence of noise. In particular, this paper is motivated by recent findings highlighting the positive impact of delays on system dynamics in biological systems. Authors Longo et al in [6] and Bhartiya et al in [7] demonstrate robust behavior of genetic regulatory networks with multiple delayed feedbacks.

In some biological systems, feedback loops exhibit a time delay through the involved chemical reactions that take time to synthesize the proteins that regulate or activate gene expression. Furthermore, additional delays can be artificially implemented in transcription and translation through placement of the gene with respect to the promotor region and secondary structure design respectively. Therefore, in order to avoid building complex synthetic networks, this paper aims to explore the possibility of implementing simple proportional feedback where the time delayed output signal is the only component used in the controller design. Multiple delayed feedback channels are added to improve performance of the system.

Previous work [8,9] shows that multiple delayed feedback channels can stabilize a system and [10] concentrates on the analysis of systems with stochastic delays whose mean dynamics resemble a distributed delay system. To some extent, we now address a synthesis problem for these biological systems with mean dynamics, where we design a optimal distribution function for stochastic delays.

As an example, a scalar genetic regulatory network is considered, which is described by a nonlinear dynamical system. Ideally, feedback controller design should be done in the continuous-time domain with the nonlinear dynamics. However even stability analysis of a linear system with time delays in the continuous-time domain remains a hard problem. Therefore we consider a multiple delayed feedback design for a discrete-time linear scalar system. To apply our method to a nonlinear dynamical system, we first linearize the system, and convert the continuous-time system to a discrete-time system by periodic sampling. We then implement this controller in the continuous-time domain with nonlinear dynamics to check the closed loop stability and performance.

This paper is organized as follows. Section II presents the multiple delayed feedback design problem for a discretetime scalar linear system. Section III introduces a cone complementarity linearization algorithm to get a suboptimal solution of the design problem. Section IV describes the method to convert a continuous-time system to a discrete time system, Section V contains an application to a scalar genetic regulatory network, and Section VI concludes the paper.

^{*}Authors made equal contributions

The authors are with the Control and Dynamical Systems, California Institute of Technology, Pasadena, CA 91125, USA {mgomez, syou, murray}@caltech.edu

II. PROBLEM FORMULATION

Consider a scalar discrete-time linear system with inherent delay $\tau \ge 1$,

$$x_{k+1} = a \, x_k + b \, x_{k-\tau}.\tag{1}$$

We would like to improve performance and robustness of the system by adding additional delayed feedbacks. The system becomes

$$x_{k+1} = a x_k + b \sum_{i=\tau}^{N} w_i x_{k-i},$$
(2)

where τ and $N \geq \tau$ are positive integers. In addition, we require $\sum_{i=\tau}^{N} w_i = 1$, and $w_i \geq 0$. Although, one can also consider negative gains, we only consider positive gains in order to demonstrate the effect of the delay distribution alone. Constraining the sum of the weights to be unity ensures no change in the overall effective feedback gain. Later, we demonstrate the implementation of such a controller in a genetic regulatory network. Although, negative weights can also be considered in the synthesis of these networks, they require a different set up since it involves a different nonlinearity.

Consider an input disturbance η_k such that

$$x_{k+1} = a x_k + b \sum_{i=\tau}^N w_i x_{k-i} + \eta_k.$$

Suppose we want to minimize the effect from the input disturbance to the state. The transfer function from the input disturbance to the state is given by

$$H_{\eta \to x}(z) = \frac{P}{1 + PC},\tag{3}$$

where P and C are the z-transforms of the plant and controller:

$$P = \frac{1}{z-a}$$
$$C = -b\sum_{i=\tau}^{N} w_i z^{-i}.$$

This results in the following transfer function,

$$H_{\eta \to x}(z) = \frac{1}{z - a - b \sum_{i=\tau}^{N} w_i \, z^{-i}}.$$
 (4)

Assuming unwanted disturbances reside in the higher frequency regime, we apply a weighting function [11], namely, a pre-determined filter F to ensure signals at higher frequencies are more greatly penalized. This is achieved with a first order high-pass filer

$$F(z) = \frac{(1+\alpha)z}{z-\alpha},$$

where $0 \le \alpha < 1$, resulting in the following problem:

$$\begin{array}{ll} \underset{w_{\tau}, \cdots, w_{N}}{\text{minimize}} & ||FH_{\eta \to x}||_{\infty} \\ \text{subject to} & \sum_{i=\tau}^{N} w_{i} = 1, w_{i} \ge 0. \end{array}$$
(5)

The objective function is the H_{∞} norm of the transfer function,

$$||FH_{\eta \to x}||_{\infty} = \sup_{||\eta||_2 \le 1} \frac{||\mathbf{x}||_2}{||\eta||_2},$$

which is the worst-case 2 norm of the state induced by the input disturbance with unit 2 norm. Since F is a high pass filter, the high frequency gain in the transfer function is attenuated by solving the optimization (5). Using the generalized plant model, we can convert the optimization (5) to a static output feedback H_{∞} problem with additional affine constraints on the gain. The state dynamics can be re-written as

$$\mathbf{x}_{k+1} = \mathbf{A}_0 \, \mathbf{x}_k + \mathbf{B}_1 \, \eta_k + \mathbf{B}_2 \, u_k$$
$$z_k = \mathbf{C}_1 \, \mathbf{x}_k + \mathbf{D}_{11} \, \eta_k + \mathbf{D}_{12} \, u_k$$
$$\mathbf{y}_k = \mathbf{C}_2 \, \mathbf{x}_k$$
$$u_k = \mathbf{w} \mathbf{y}_k, \tag{6}$$

where

$$\mathbf{A}_{0} = \begin{bmatrix} a & 0 & \cdots & 0 & 0 & 0 \\ 1 & 0 & \cdots & 0 & 0 & 0 \\ 0 & 1 & \cdots & 0 & 0 & 0 \\ \vdots & \vdots & \ddots & \vdots & \vdots & \vdots \\ 0 & 0 & \cdots & 1 & 0 & 0 \\ \alpha & 0 & \cdots & 0 & 0 & \alpha \end{bmatrix}, \\ \mathbf{B}_{1} = \begin{bmatrix} 1 & 0 & \cdots & 0 & 0 \end{bmatrix}^{T}, \\ \mathbf{B}_{2} = \begin{bmatrix} b & 0 & \cdots & 0 & 0 \end{bmatrix}^{T}, \\ \mathbf{C}_{1} = \begin{bmatrix} 1 + \alpha & \cdots & 0 & 1 + \alpha \end{bmatrix}, \\ \mathbf{D}_{11} = 0, \quad \mathbf{D}_{12} = 0, \\ \mathbf{C}_{2} = \begin{bmatrix} \mathbf{0}_{d \times \tau} & \mathbf{I}_{d \times d} & \mathbf{0}_{d \times 1} \end{bmatrix}, \\ \mathbf{w} = \begin{bmatrix} w_{\tau} & w_{\tau+1} & \cdots & w_{N} \end{bmatrix}, \end{bmatrix}$$

and $d = N - \tau + 1$. In addition, the state vector $\mathbf{x}_{k+1} = \begin{bmatrix} x_{k+1} & x_k & \cdots & x_{k-N+1} \end{bmatrix}^T \in \mathbb{R}^{N+1}$, $u \in \mathbb{R}$ and $\mathbf{y} \in \mathbb{R}^{N-\tau+1}$. The optimization problem is reformulated as

$$\begin{array}{ll}
\underset{w_{\tau},\cdots,w_{N}}{\text{minimize}} & \sup_{||\eta||_{2} \leq 1} \frac{||\mathbf{x}||_{2}}{||\eta||_{2}} \\
\text{subject to} & \mathbf{1}^{T} \mathbf{w} = 1, \mathbf{w}_{i} \geq 0.
\end{array}$$
(7)

We refer to the gain w as the delay distribution. The static output feedback H_{∞} design is well studied in the literature, see [12, 13]. This problem is known to be non-convex, and hard in some cases [14], however, in practice there exists a good solver which gives a reasonable solution in many cases.

The discrete-time KYP lemma [15] converts the H_{∞} norm minimization problem (7) into the following optimization problem with Linear Matrix Inequalities (LMI):

$$\begin{array}{l} \underset{\mathbf{w}, \mathbf{X}, \mathbf{Y}, \gamma}{\text{minimize}} & \gamma \\ \text{subject to} & \mathbf{1}^T \mathbf{w} = 1, \mathbf{w} \succeq \mathbf{0}, \\ & \mathbf{X} \mathbf{Y} = \mathbf{I}, \mathbf{X} \succ \mathbf{0}, \\ & T \prec \mathbf{0}, \end{array}$$
(8)

where

$$T = \begin{bmatrix} -\mathbf{Y} & \mathbf{A}_0 + \mathbf{B}_2 \mathbf{w} \mathbf{C}_2 & \mathbf{B}_1 & \mathbf{0} \\ * & -\mathbf{X} & \mathbf{0} & (\mathbf{C}_1 + \mathbf{D}_{12} \mathbf{w} \mathbf{C}_2)^T \\ * & * & -\gamma & \mathbf{D}_{11}^T \\ * & * & * & -\gamma \end{bmatrix}$$

For a review of LMI and convex optimization, see [16]. Notice that this problem is non-convex because of the nonaffine equality XY = I. In some cases, one can convert the non-convex problem (8) to a convex one through a change of variables [17]. However, (8) does not satisfy the necessary assumptions in [17]. Therefore, we use a cone complementarity linearization algorithm [18] to handle the bilinear matrix equality.

III. A CONE COMPLEMENTARITY LINEARIZATION ALGORITHM

Since the optimization (8) is not convex, we present an approximate semidefinite program which gives us a suboptimal solution of the problem (8). Let us start with following observation.

Proposition 1: The optimal solution of following problem, $(\mathbf{X}^*, \mathbf{Y}^*)$, satisfies $\mathbf{X}^*\mathbf{Y}^* = \mathbf{I}$.

$$\begin{array}{ll} \underset{\mathbf{X},\mathbf{Y}}{\text{minimize}} & \operatorname{Tr}(\mathbf{X}\mathbf{Y}) \\ \text{subject to} & \begin{bmatrix} \mathbf{X} & \mathbf{I} \\ \mathbf{I} & \mathbf{Y} \end{bmatrix} \succeq \mathbf{0} \\ & \mathbf{X} \succ \mathbf{0} \\ & \mathbf{Y} \succ \mathbf{0}. \end{array} \tag{9}$$

Proof: By taking Schur complement to the first LMI, we have, $\mathbf{Y} - \mathbf{X}^{-1} \succeq 0$. This is equivalent to $\mathbf{X}^{1/2}\mathbf{Y}\mathbf{X}^{1/2} \succeq$ I. Since $\text{Tr}(\mathbf{X}^{1/2}\mathbf{Y}\mathbf{X}^{1/2}) = \text{Tr}(\mathbf{X}\mathbf{Y})$, the minimum is achieved when $\mathbf{X}^{1/2}\mathbf{Y}\mathbf{X}^{1/2} = \mathbf{I}$. This implies $\mathbf{X}\mathbf{Y} = \mathbf{I}$.

Now for a given γ , consider the following optimization problem:

$$\begin{array}{ll} \underset{\mathbf{w},\mathbf{X},\mathbf{Y}}{\text{minimize}} & \operatorname{Tr}(\mathbf{X}\mathbf{Y}) \\ \text{subject to} & \mathbf{1}^{T}\mathbf{w} = 1, \mathbf{w} \succeq \mathbf{0}, \\ & \mathbf{X}, \mathbf{Y} \succeq \mathbf{0}, \\ & \begin{bmatrix} \mathbf{X} & \mathbf{I} \\ \mathbf{I} & \mathbf{Y} \end{bmatrix} \succeq 0 \qquad T \prec 0 \end{array}$$

where

$$T = \begin{bmatrix} -\mathbf{Y} & \mathbf{A}_0 + \mathbf{B}_2 \mathbf{w} \mathbf{C}_2 & \mathbf{B}_1 & \mathbf{0} \\ * & -\mathbf{X} & \mathbf{0} & (\mathbf{C}_1 + \mathbf{D}_{12} \mathbf{w} \mathbf{C}_2)^T \\ * & * & -\gamma & \mathbf{D}_{11}^T \\ * & * & * & -\gamma \end{bmatrix}$$

If there exists a triplet $(\mathbf{w}, \mathbf{X}, \mathbf{Y})$ that satisfies all the constraints and $\mathbf{X}\mathbf{Y} = \mathbf{I}$, then the above optimization problem recovers this triplet. Therefore, we can successfully construct a w such that the H_{∞} norm of the transfer function is less than γ . However, since the objective function is

not convex, we use a linearization technique to solve this problem, namely:

$$\begin{array}{ll} \underset{\mathbf{w},\mathbf{X},\mathbf{Y}}{\text{minimize}} & \operatorname{Tr}(\mathbf{X}_{k}\mathbf{Y} + \mathbf{X}\mathbf{Y}_{k}) \\ \text{subject to} & \mathbf{1}^{T}\mathbf{w} = 1, \mathbf{w} \succeq \mathbf{0}, \\ & \mathbf{X},\mathbf{Y} \succeq \mathbf{0}, \\ & \left[\begin{array}{c} \mathbf{X} & \mathbf{I} \\ \mathbf{I} & \mathbf{Y} \end{array} \right] \succeq 0 \\ & T \prec \mathbf{0}. \end{array}$$
(10)

Cone complementary solver:

- 1) Set k = 0, and $X_0 = Y_0 = I$.
- 2) Solve the optimization problem (10) to generate \mathbf{X}_{k+1} , \mathbf{Y}_{k+1} .
- 3) Set k = k + 1, and do step 2 until \mathbf{X}_k converges.

Note that if iterative procedure above finds $(\mathbf{w}, \mathbf{X}, \mathbf{Y})$ where $\mathbf{XY} = \mathbf{I}$, then this weight \mathbf{w} guarantees the stability of the closed loop system and the H_{∞} norm is less than γ . However, since the above procedure uses a linearized version of the true objective function, the procedure may fail to recover the solution $(\mathbf{w}, \mathbf{X}, \mathbf{X}^{-1})$ in some cases. In this sense, this procedure is only an approximate solver for the original problem. In practice, this approach works well.

Finally, since we can approximately solve the problem given γ , we now apply a bisection search to obtain the minimum γ .

Bisection search:

- 1) Set l = 0, and $\gamma = 1$.
- 2) Solve the optimization problem (10) for γ .
- 3) If (10) recovers $\mathbf{XY} = \mathbf{I}$, then set $u = \gamma$, otherwise $l = \gamma$.
- 4) Set $\gamma = \frac{1}{2}(l+u)$. Repeat step 2 until γ converges.

Again, since (10) is an approximate solver, the above bisection search can converge to a point which is not a true minimum.

IV. CONTINUOUS TIME CONVERSION

We briefly summarize a method used to convert a continuous-time linear system to a discrete-time linear system.

Suppose we have a continuous-time linear dynamical system,

$$\frac{d\mathbf{x}}{dt} = A\mathbf{x} + B\mathbf{u}.$$

Consider we sample x(t) with sampling period T, then, this system generates sequence $\mathbf{x}_k = \mathbf{x}(kT)$. The zero order hold (ZOH) method [19] assumes $\mathbf{u}(t)$ remains constant during the each sampling period [kT, (k+1)T]. Assuming $\mathbf{u}_k =$ $\mathbf{u}(kT)$, we can convert the above continuous-time system to the following discrete time system,

$$\mathbf{x}_{k+1} = e^{AT}\mathbf{x}_k + A^{-1}(e^{AT} - I)B\mathbf{u}_k$$

However, biological systems, which are a main target application, are usually described by nonlinear dynamical systems. Henceforth, we linearize the nonlinear dynamics and then apply the ZOH method to the linearized system. From the obtained delay distribution vector **w**, we appropriately incorporate the distributed delayed feedback into the original nonlinear dynamics. The full nonlinear dynamics are simulated to check performance and stability.

To draw a bode plot in *s*-domain from the data in the *z*-domain, we use the following method. Suppose one has a transfer function in the *z*-domain, H(z), then substitute $z = e^{jwT}$ to obtain a complex valued function $H(e^{jwT})$. Plot $|H(e^{jwT})|$ as a Bode magnitude plot by varying $w \in [0, \frac{\pi}{T}]$. For details, see [20].

V. APPLICATION TO A SCALAR GENETIC REGULATORY NETWORK

A. Basic Model



Fig. 1. Self regulating protein production.

In this section we apply the numerical method to the design of a scalar auto-regulatory genetic system. We take a scalar example from [21],

$$\dot{x} = \beta \frac{p_{tot}}{x/K_d + 1} - \delta x + \sqrt{\frac{\beta p_{tot}}{A_e/K_d + 1}} n_1 - \sqrt{\delta x} n_2,$$
(11)

where x represents the concentration of a self regulating protein. The rates β and δ are the production and degradation rates respectively. In addition, n_1 and n_2 represent the noises on production and decay respectively. An example of the system is shown in Fig. 1, where protein x inhibits further production of itself by not allowing the RNA polymerase to bind and, therefore, inhibiting initiation of transcription. The constants p_{tot} and K_d represent the total concentration of the DNA promotor and the ratio of dissociation to association rates.

We will consider only noise on protein production $(n_2 = 0)$. We modify the model to account for delays due to transcription and translation,

$$\dot{x} = \beta \frac{p_{tot}}{x(t-\tau)/K_d + 1} - \delta x + \sqrt{\frac{\beta p_{tot}}{A_e/K_d + 1}} n_1.$$

The system is then linearized around the equilibrium point $x_e = \frac{1}{2} \left(\sqrt{K_d^2 + 4\beta p_{tot} K_d / \delta} - K_d \right)$ by treating the delay channel as an input which gives

$$\dot{x} = -\delta x(t) + \kappa x(t-\tau) + b_1 n_1,$$

where $\kappa = -\beta \frac{p_{tot}/K_d}{(x_e/Kd+1)^2}$, $b_1 = \sqrt{\frac{\beta p_{tot}}{x_e/K_d+1}}$ and $b_2 = -\sqrt{\delta x_e}$. Applying the zero order hold method, an equivalent discrete time system is given by,

$$x(k+1) = d_2 x(k) + d_1 \kappa x(k-\tau) + d_1 b_1 n_1(k)$$

where $d_2 = e^{-T\delta}$ and $d_1 = \frac{1}{\delta}(1 - e^{-T\delta})$. By assuming that the delay is a multiple of the sampling time T, we can arrive at a discrete-time system with multiple delayed feedback channels:

$$x(k+1) = d_2 x(k) + d_1 \kappa \sum_{i=\tau}^N w_i x(k-i) + d_1 b_1 n_1(k).$$

We optimize over the weights and compare to the original system. The system parameters are partially taken from [21] and chosen to be $p_{tot} = 10$, $K_d = 10$, $\beta = .1$, and $\delta = .01$.

B. Design Results



Fig. 2. First order highpass filter, $\frac{(1+\alpha)z}{z-\alpha}$, with multiple α .

We first present various high pass filters, $\frac{(1+\alpha)z}{z-\alpha}$, by varying α in Fig. 2. Note, a larger α results in a smaller cut-off frequency. Therefore, depending on our assumption on the noise, we can choose α to obtain an appropriate sensitivity transfer function.

For the discretization, we use T = 60s (1 minute) as a sampling period, and assume the minimum time delay $\tau = 10$, which corresponds 10 minutes. For maximum delays, we test N = 10, 15, 20, 25 and 30 as an example, and set the filter parameter $\alpha = 0.99$.

Fig. 3 shows the bode magnitude pot of the transfer function for various maximum delays. A larger maximum delay N results in more degrees of freedom in the design stage, hence, we should expect better performance in the result. As we can see, when N = 30 the transfer function $H = \frac{P}{1+PC}$ shows better attenuation. Notice that we optimized the filtered version of the H_{∞} norm, $||FH||_{\infty}$ and



Fig. 3. Resulting transfer function $\frac{P}{1+PC}$ for multiple maximum delays N. The lower, the better.



Fig. 4. Resulting delay distribution for multiple maximum delays N.

not the unweighted one, so a direct numerical comparison of Bode magnitude plots should be considered carefully.

For the corresponding delay distribution vector see Fig. 4. Notice that the first and the last delay channels are most important, and other channels have similar weights to each other.

C. Time Simulation

We apply the results obtained to the original nonlinear equation (11) with $n_2 = 0$. For a general distributed delay representation, (11) can be re-written as

$$\dot{x} = \beta \frac{p_{tot}}{\tilde{x}/K_d + 1} - \delta x + \sqrt{\frac{\beta p_{tot}}{A_e/K_d + 1}} n_1$$
$$\tilde{x} = \int_0^\infty x(t - \tau)g(\tau)d\tau$$

where g(t) is the delay distribution function such that $\int_0^\infty g(\tau) d\tau = 1$, and $g(t) \ge 0$ for all t. In the discretization of the system, g(t) takes on the form

$$g(t) = \sum_{k=\tau}^{N} w_k \,\delta(\tau - kT)$$

where $\sum_{k=\tau}^{N} w_i = 1$, T is the sampling period, and δ is the Dirac delta function. The final model representing the modified network is described by

$$\dot{x}(t) = \beta \frac{p_{tot}}{\frac{\left(\sum_{k=\tau}^{N} w_k x(t-kT)\right)}{K_d} + 1} - \delta x(t) + \sqrt{\frac{\beta p_{tot}}{A_e/K_d + 1}} n_1.$$

One way the delays can be implemented is by adding "junk" DNA in between the promotor site and the gene to delay the initiation of transcription. The "junk" DNA would be a sequence of DNA strand that does not code for anything, but that the RNA polymerase would still need to transcribe before beginning transcription of the target gene. Since the overall gain remains unchanged there is no need to change any of the parameters in the system such as the production rate. This, in general, may be harder to do. However, one does need to consider how to account for the differences in the weights. This can possibly be implemented through proportions of various plasmids with the different delays implemented so that the ratios on concentrations correspond to the weights. A more challenging but possibly useful approach would be to apply competitive binding so that the weights correspond to the probability of each particular delayed state binding to the promotor site.

Before presenting simulations, the stability regions for the different sets of delays and their respective weights are considered. This is important to take note of when considering how the system stability may change with respect to uncertainty in the parameters of the system when adding delays. The stability region for the general system (2) is determined by the characteristic equation

$$z - a - b\sum_{i=\tau}^{N} w_i z^{-i} = 0$$

given by the denominator of the transfer function (4). For discrete-time systems, a system is unstable when $|z| \ge 1$, therefore, the characteristic equation is evaluated at |z| = 1to map out the curves on the (a, b) parameter space when an eigenvalue crosses the unit circle. These curves can be obtained by evaluating the characteristic equation at z = 1, z = -1, and $z = e^{i\theta}$ [22,23]. It is worth noting z = 1(black curve) gives a delay independent stability condition b = 1 - a. However, z = -1 (red curve) and $z = e^{i\theta}$ (blue curves) give

$$b = \frac{-(a+1)}{\sum_{i=\tau}^{N} w_i (-1)^i}$$

and

$$b(\theta) = -\sin(\theta) / \left(\sum_{i=\tau}^{N} w_i \sin(i\theta)\right)$$
$$a(\theta, b) = \cos(\theta) - b \left(\sum_{i=\tau}^{N} w_i \cos(i\theta)\right)$$

respectively.



Fig. 5. Stability plot for the system with a single delay $\tau = 10$. The black circle indicates the parameter values corresponding to the simulations.

Fig. 5 shows the stability region for the original system with a single delay. If the system parameters (a, b) are in the shaded region, then the system is stable. From our nominal parameter values, we obtain (a, b) = (0.5488, -0.3293), which is indicated by a circle marker in Fig. 5.

Fig. 6 shows the stability regions for the various distributed delayed systems. The overlaying green shaded region and grey curves correspond to the stability region for the original system shown in Fig. 5. One can see that the area of the stability region increases as the maximum delay N increases. There is also a notable difference in the robustness to uncertainty in parameter values.

Lastly, the nonlinear system with multiple delayed feedback is simulated in Fig. 7. The noise is modeled as a sum of periodic functions at various equally spaced frequencies beginning at 10^{-3} Hz. Notice that in Fig. 7, our designed multiple delayed feedback channels help to decrease the fluctuations in protein production.

VI. CONCLUSION

Inspired by biological applications, we consider the suboptimal multiple delayed feedback channel design for a scalar linear discrete-time system. We formulate a H_{∞}



Fig. 6. Stability plots for different delay ranges and distributions (blue). The shaded green region and grey lines correspond to the stability plot in Fig. 5. The black circle indicates the parameter values corresponding to the simulations.



Fig. 7. Simulations of nonlinear system with distributed delays.

design problem with multiple delayed feedback, and make a connection to a static output feedback H_{∞} with additional linear constraints on a static gain. We apply this design procedure to a sampled, linearized scalar auto-regulatory genetic system, and show that the effect from the input disturbance can be suppressed by adding appropriate multiple delays. Furthermore, we simulate an auto-regulatory genetic system with multiple delays, and show, indeed, the full nonlinear system has improved performance in the presence of stochastic protein production.

Notice, that even though adding additional delays decreases the H_{∞} norm from the input to the output, the waterbed affect can result in larger magnitudes at the higher frequencies. It appears as though the distribution which gives the smallest H_{∞} norm may not always be the best choice. One could imagine designing the weighting filter such that improvement is obtained where needed, based on knowledge of uncertainty.

In the future, we generalize this concept to a multi-state system. We would also like to explore removing the positive definite constraint on the weights in order to allow for design with a combination of positive and negative feedback loops. Another potential application to explore is that of achieving plant stability in a car following model with delays. Plant stability is achieved when the H_{∞} norm of the transfer functions from every possible source of input to output remain equal to or below unity. This method may provide a simpler method of improving performance with minimized computational cost.

VII. ACKNOWLEDGMENTS

The authors gratefully acknowledge the helpful discussions regarding genetic regulatory networks and biological process with the Murray lab, as well as Erin O'Brien and Andrew Hirning from the Bennett lab at Rice University. This work was supported in part by the TerraSwarm Research Center, one of six centers supported by the STARnet phase of the Focus Center Research Program (FCRP) a Semiconductor Research Corporation program sponsored by MARCO and DARPA, and the Kwanjeong Graduate Fellowship.

REFERENCES

- J.-P. Richard, "Time-delay systems: an overview of some recent advances and open problems," *automatica*, vol. 39, no. 10, pp. 1667– 1694, 2003.
- [2] R. Sipahi, S.-I. Niculescu, C. T. Abdallah, W. Michiels, and K. Gu, "Stability and stabilization of systems with time delay," *Control Systems, IEEE*, vol. 31, no. 1, pp. 38–65, 2011.
- [3] K. J. Aström and R. M. Murray, Feedback systems: an introduction for scientists and engineers. Princeton university press, 2010.
- [4] P. E. M. Purnick and R. Weiss, "The second wave of synthetic biology: from modules to systems," *Nature*, vol. 10, pp. 410–422, June 2009.
- [5] A. N. Naganathan and V. M. noz, "Scaling of folding times with protein size," *Journal of the American Chemical Society*, no. 127, pp. 480–481, 2005.
- [6] D. M. Longo, J. Selimkhanov, J. D. Kearns, J. Hasty, A. Hoffman, and L. S. Tsimring, "Dual delayed feedback provides sensitivity and robustness to the nf-κb signaling module," *PLoS Computational Biology*, vol. 9, no. 6, June 2013.
- [7] S. Bhartiya, N. Chaudhary, K. Venkatesh, and F. J. D. III, "Multiple feedback loop design in the tryptophan regulatory network of escherichia coli suggests a paradigm for robust regulation of processes in series," *Journal of The Royal Society Interface*, no. 3, pp. 383–391, 2006.
- [8] M. M. Gomez and R. M. Murray, "Stabilization of feedback systems via distribution of delays," in *IFAC Workshop on Time Delay Systems*, 2012.
- [9] G. Orosz, J. Moehlis, and R. M. Murray, "Controlling biological networks by time-delayed signals," *Philosophical Transactions of Royal Society A*, pp. 368,439–454, November 2010.
- [10] M. M. Gomez, G. Orosz, and R. M. Murray, "Stability of discrete time systems with stochastically delayed feedback," in *European Control Conference*, 2013.
- [11] J. C. Doyle, B. A. Francis, and A. Tannenbaum, *Feedback control theory*. Macmillan Publishing Company New York, 1992, vol. 1.

- [12] J. Gadewadikar, F. L. Lewis, and M. Abu-Khalaf, "Necessary and sufficient conditions for h-infinity static output-feedback control," *Journal of guidance, control, and dynamics*, vol. 29, no. 4, pp. 915– 920, 2006.
- [13] V. L. Syrmos, C. T. Abdallah, P. Dorato, and K. Grigoriadis, "Static output feedbacka survey," *Automatica*, vol. 33, no. 2, pp. 125–137, 1997.
- [14] V. Blondel and J. N. Tsitsiklis, "Np-hardness of some linear control design problems," *SIAM Journal on Control and Optimization*, vol. 35, no. 6, pp. 2118–2127, 1997.
- [15] G. E. Dullerud and F. Paganini, A course in robust control theory. Springer New York, 2000, vol. 6.
- [16] S. P. Boyd and L. Vandenberghe, *Convex optimization*. Cambridge university press, 2004.
- [17] C. W. Scherer, "An efficient solution to multi-objective control problems with lmi objectives," *Systems & control letters*, vol. 40, no. 1, pp. 43–57, 2000.
- [18] L. El Ghaoui, F. Oustry, and M. AitRami, "A cone complementarity linearization algorithm for static output-feedback and related problems," *Automatic Control, IEEE Transactions on*, vol. 42, no. 8, pp. 1171–1176, 1997.
- [19] G. F. Franklin, M. L. Workman, and D. Powell, *Digital control of dynamic systems*. Addison-Wesley Longman Publishing Co., Inc., 1997.
- [20] A. V. Oppenheim, A. S. Willsky, and S. H. Nawab, Signals & systems (2nd ed.). Upper Saddle River, NJ, USA: Prentice-Hall, Inc., 1996.
- [21] D. D. Vecchio and R. M. Murray, Biomolecular Feedback Systems, ser. DRAFT v0.4a. California Institute of Technology, 2011. http://www.cds.caltech.edu/murray/BFS.
- [22] J. Guckenheimer and P. Holmes, *Nonlinear Oscillations, Dynamical Systems, and Bifurcations of Vector Fields*, ser. Applied Mathematical Sciences. Springer, 1983, vol. 42.
- [23] Y. A. Kuznetsov, *Elements of Applied Bifurcation Theory*, 3rd ed., ser. Applied Mathematical Sciences. Springer, 2004, vol. 112.