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Predicting adaptation for uncertain systems with robust real plots

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***Abstract*— In systems biology, perfect adaptation (adaptation) denotes the property of a system reacting to a step input stimulus by completely (partially) restoring the pre-stimulus output value at steady state. We address the problem of predicting adaptation for uncertain dynamical systems. To this aim, we introduce a formal definition of adaptation tailored to the robust analysis of dynamical systems. Whilst the definition is more general and valid also for the step response analysis of nonlinear systems, in the linear case such a definition of adaptation reduces to the presence of a single real zero that dominates all poles. Based on this definition, we can assess robust adaptation by means of the *robust real plot*, which characterises the position of real zeros and poles for linear systems with parametric uncertainties.**

I. Introduction: Defining Robust Adaptation

An input-output dynamical system exhibits *adaptation to a persistent constant input* if the output initially increases and, after a transient, eventually decreases; this is a widespread concept in systems biology [1], [18]. Fig. 1 shows three output signals: the green one does not show adaptation, since it does not decrease asymptotically; the red one (first increasing and then decreasing) shows adaptation; the purple one shows over-adaptation, because the response first increases and then decreases so much that it changes sign. In the special case of *perfect adaptation*, the step response, starting from zero initial conditions, is zero at steady state; hence, asymptotically the output recovers the pre-stimulus value. This property, well studied for biological systems [11], [15], [20], can be characterised, robustly or even structurally [12], as the transfer function vanishing at the origin.

Adaptation includes perfect adaptation, but is broader. We require the step response to be *essentially* first increasing and then decreasing: it can exhibit temporary trend changes and oscillations during the transient, but it must be *predominantly* decreasing for large values of t.

Although the concept as used in the biological literature is intuitively clear, it is not easy to provide a formal definition, or a classification. For instance, the step response of externally positive linear systems [3], [6], i.e. systems with a positive impulse response (PIR) [8], [14], [16], including input-output monotone systems [17] and unimodal systems [13], is *necessarily* monotonically increasing, hence these

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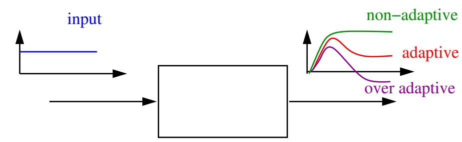

Fig. 1: System with adaptive, over-adaptive and non-adaptive responses.

systems cannot be adaptive. However, we cannot claim that non-PIR linear systems are adaptive in general, since they include, for instance, systems whose step response exhibits poorly damped oscillations, as well as spiking systems whose step response is eventually increasing (see the second and third case in Fig. 3). In particular, not all overshooting responses [19] can be considered adaptive.

Assessing adaptation becomes even more challenging for uncertain systems (such as biological systems) of the form

$$\dot{x}(t) = f(x(t), u(t), d), \quad y(t) = g(x(t)) \tag{1}$$

where $x(t) \in \mathbb{R}^n$, $u(t), y(t) \in \mathbb{R}$, and the origin is a steady state, $f(0,0,d) = 0$, for all values of the uncertain parameter vector $d \in \mathcal{D} \subsetneq \mathbb{R}^m$. The uncertain system (1) enjoys robust adaptation if it exhibits adaptation for any value of the uncertain parameter $d \in \mathcal{D}$. To enable a robust analysis of adaptation for uncertain systems, we need to introduce a new formal definition, based on an exponential weighting function. We work under the following assumption.

Assumption 1. *Given system* (1)*, and $d \in \mathcal{D}$, the step response $y_s(t)$ corresponding to the input $u(t) = \bar{u}$ is initially positive (i.e. $\exists\, \tau > 0$ such that $\dot{y}_s(t) \doteq \frac{d}{dt} y_s(t) > 0$ for $0 < t \leq \tau$) and $\lim_{t\to\infty} y_s(t)$ is finite.*

We assume that the sign of $\bar{u}$ is implicitly chosen so that $y_s(t)$ is initially positive. Then, the system is adaptive if $\dot{y}_s(t)$ is essentially positive at first and essentially negative in the long run. Formally, consider the weighted integral

$$I_a = \int_0^\infty e^{at} \dot{y}_s(t) dt \tag{2}$$

and define the abscissa of convergence, σ, as the largest value of a for which the integral in (2) is finite:

$$\sigma = \sup\{a : |I_a| < \infty\}. \tag{3}$$

For $a = 0$, the integral is equal to $y_s(\infty)$ in view of the Final Value Theorem, hence it is finite according to Assumption 1. Now we look for a value $\bar{a} < \sigma$ such that $I_a > 0$ for $a < \bar{a}$ and $I_a < 0$ for $a > \bar{a}$. If no such value exists, then the system is not adaptive. This leads to the next definition.

Definition 1. *Under Assumption 1, consider the weighted integral I_a defined in* (2)*. If there exists $\bar{a} < \sigma$ such that*

$$\begin{aligned} I_a > 0 \quad &\textit{for} \quad a < \bar{a}, \\ I_a < 0 \quad &\textit{for} \quad \bar{a} < a < \sigma, \end{aligned}$$

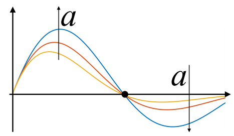

Fig. 2: Increasing (resp. decreasing) a gives more relative weight to the values of the function at later (resp. earlier) times.

then the step response, starting from zero initial conditions, is adaptive. *In particular, we have* partial adaptation *if* $\bar{a} > 0$*;* perfect adaptation *if* $\bar{a} = 0$*;* over-adaptation *if* $\bar{a} < 0$*. Moreover, for the uncertain system* (1)*, adaptation is robust if the previous property holds for any* $\bar{u}$ *and any* $d \in \mathcal{D}$*.*

Setting $a < 0$ weights more the values of $\dot{y}_s(t)$ at earlier times (mainly positive in an adaptive system), while setting $a > 0$ weights more the values of $\dot{y}_s(t)$ at later times (mainly negative in an adaptive system); the effect becomes more pronounced when increasing a, see Fig. 2. Observe that:

- Definition 1 does not require linearity of the system.
- In case of perfect adaptation, $\dot{y}_s(t)$ has zero mean on the interval $[0, \infty)$, i.e. $y_s(\infty) = I_0 = 0$.
- In case of partial (resp. over-) adaptation, $\dot{y}_s(t)$ has zero mean on the interval $[0, \infty)$ if weighted by an *increasing* (resp. *decreasing*) exponential $e^{\bar{a}t}$; namely, $y_s(\infty) = I_0 > 0$ (resp. $y_s(\infty) = I_0 < 0$).
- $\dot{y}_s(t)$ being sign definite (either positive or negative) implies non-adaptation, but not the other way round.

A. The linear system case

When considering Linear Time-Invariant (LTI) systems, Assumption 1 implies Bounded-Input Bounded-Output (BIBO) stability. In this case, adaptation and the parameter $\bar{a}$ introduced in Definition 1 have a simple characterisation.

Consider a LTI BIBO system with impulse response $f(t) = \dot{y}_s(t)$, for $\bar{u} = 1$, and rational transfer function $F(s)$. Then, σ, as defined in equation (3), is the abscissa of convergence of $F(s)$ and $-\sigma$ is the spectral abscissa, namely, the largest among the real parts of the poles of $F(s)$.

Given the complex numbers z and w, we say that z *dominates* w if $\mathrm{Re}(z) > \mathrm{Re}(w)$. Then, the following proposition states that adaptation, according to Definition 1, is characterised by the presence of a single dominant real zero, larger than the spectral abscissa.

Proposition 1. *Let* $F(s)$ *be the rational, strictly proper transfer function of a linear asymptotically stable system. Then, the step response is adaptive if and only if there exists precisely one real zero,* $-z$*, such that* $z < \sigma$*. We have partial adaptation if* $z > 0$*, perfect adaptation if* $z = 0$*, over-adaptation if* $z < 0$*.*

Proof. For $a < \sigma$, we have the equality

$$I_a = \int_0^\infty e^{at} f(t) dt = \lim_{s \to 0} F(s-a) = F(-a).$$

Then, the value $\bar{a}$ is exactly z, where $-z$ is a real zero, which must be the only zero in the open interval $(-\sigma, \infty)$ to prevent other sign changes. $\square$

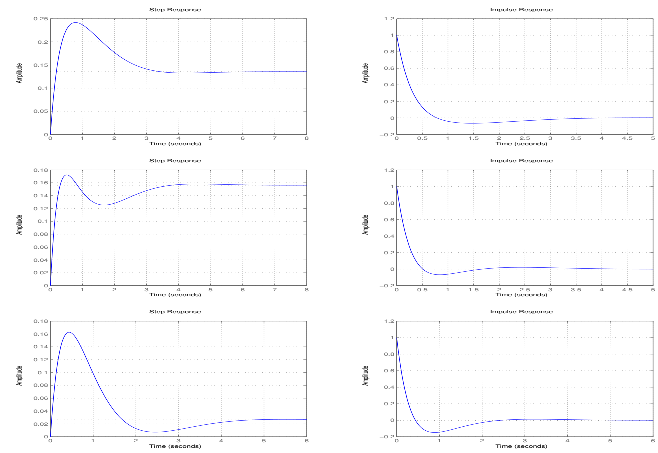

Fig. 3: Step response (left) and impulse response (right) for the transfer functions in (4), (5) and (6).

Example 1. *For the three systems with transfer functions*

$$F_A(s) = \frac{(s+0.5)[(s+1.5)^2+1]}{(s+2)(s+3)[(s+1)^2+1]}, \tag{4}$$

$$F_{NA1}(s) = \frac{(s+1.5)[(s+0.5)^2+1]}{(s+2)(s+3)[(s+1)^2+1]}, \tag{5}$$

$$F_{NA2}(s) = \frac{(s+1.5)(s+0.5)(s+0.3)}{(s+2)(s+3)[(s+1)^2+1]}, \tag{6}$$

having the same poles but different zeros, Fig. 3 reports the step response (left) and its derivative, the impulse response (right). The dominant poles are $-1 \pm j$*, hence* $\sigma = 1$*: the spectral abscissa is* -1*.*

$F_A(s)$ *has a dominant real zero at* -0.5 *and two complex zeros at* $-1.5 \pm j1$*. Hence, according to Proposition 1, it is adaptive. Indeed, the step response is initially increasing but* essentially decreasing *in the long run (it is not* strictly *decreasing because the dominant poles are complex).*

System $F_{NA1}(s)$ *has complex dominant zeros* $-0.5 \pm j$ *and a real zero at* -1.5*. It does not meet the criterion of Proposition 1. Indeed, it has an eventually increasing response, although there is an initial overshoot.*

System $F_{NA2}(s)$*, has two real zeros* -0.5 *and* -0.3 *dominating the spectral abscissa, and it is non-adaptive. The step response is spiking (with a strong overshoot), but not adaptive, because it is increasing in the long run (its value is more than doubled from time* $t = 3$ *to the end of the plot).*

Remark 1. *Externally positive systems, having a positive impulse response* $f(t)$*, clearly cannot be adaptive according to Definition 1. In fact, they must have a dominant real pole* $-p_1$ *that dominates all real zeros* $-z_k$ *[3], [14], [16].*

Remark 2. *For linear systems, the integral* I_a *has two additional interpretations. If* (A, E, H) *is a minimal realisation of* $F(s)$*, then* I_a *is the static gain of the modified system* $(aI + A, E, H)$*. Also,* I_a *describes the long term response to the input* $e^{-at}\bar{u}$*: for* t *large,* $y(t) \approx I_a\ e^{-at}\bar{u}$*. Hence, the system is adaptive if, when replacing the step* $e^{0t}\bar{u}$ *with the* decaying step $e^{-at}\bar{u}$*, the response becomes negative when* a *gets close to* σ*. For nonlinear systems, the proposed interpretations are not equivalent.*

II. Linear Uncertain Systems: Robust Adaptation

Consider a linear uncertain system of the form

$$\dot{x}(t) = A(d)x(t) + Eu(t), \quad y(t) = Hx(t), \tag{7}$$

with $A(d) = BD(d)C$, where $D(d) = \text{diag}\{d_1, d_2, \dots, d_m\}$, while matrices B and C have size $n \times m$ and $m \times n$, respectively. This class significantly includes chemical and biochemical reaction networks [2], [7], [10], [12]. The uncertain parameters d_k, $k = 1, \dots, m$, are subject to the interval bounds

$$d_k^- \le d_k \le d_k^+, \quad k = 1, \dots, m, \tag{8}$$

where d_k^- and d_k^+ are known. Henceforth we write $\hat{d}_k$ when the parameter lies on a vertex, $\hat{d}_k \in \{d_k^-, d_k^+\}$. We collect all the uncertain parameters in the vector $d = [d_1\ d_2 \dots d_m]^\top$.

Assumption 2. *The system's transfer function is rational and strictly proper, $F(s,d) = q(s,d)/p(s,d)$, and the coefficients of both the numerator and the denominator polynomials, $q_\ell(d)$ and $p_h(d)$, are multi-affine functions of the parameters d. The denominator $p(s,d)$ has order n, and it is monic ($p_n \equiv 1$) and Hurwitz for all values of d satisfying* (8)*.*

Remark 3. *Assumption 2 always holds for systems of the form* (7)*; our results are valid for generic linear systems with parametric uncertainties satisfying the assumption. Computing the polynomial coefficients may be cumbersome for large systems, but we do not need their explicit expressions. Numerically, we can exploit the expressions: $p(s,d) = \det\left[sI - BDC\right]$ and $q(s,d) = \det\begin{bmatrix} sI - BDC & -E \\ H & 0 \end{bmatrix}$.*

To check whether the uncertain system (7) exhibits adaptation, we need to assess for all admissible values of d:

- the position of its real zeros;
- the spectral abscissa $-\sigma$ (largest real part of all poles).

If, for all possible values of the uncertain parameters, there is a single real zero $-z$ with $z < \sigma$, this reveals *robust adaptation*. To solve the problem, we propose graphical methods inspired from the theory of parametric robustness [5], and we consider the *robust real plot*.

A. Evaluating σ

First, we discuss how to evaluate the spectral abscissa $-\sigma$. Given $s = j\omega - a$, we consider the polygon in the complex plane defined as the convex hull of the 2^m values of $p(s, \hat{d})$ obtained for $\hat{d}_k$ chosen at the extrema of the interval bounds:

$$\mathcal{C}(\omega, a) = \text{conv}\left\{p(j\omega - a, \hat{d}), \quad \hat{d}_k \in \{d_k^-, d_k^+\}\right\}.$$

Proposition 2. *Assume that, for a given value of a, the zero exclusion condition holds: $0 \notin \mathcal{C}(\omega, a)$, for all $\omega \ge 0$. Then, $-a$ is* a robust spectral abscissa*: $a < \sigma(d)$ for all d satisfying* (8)*, where $\sigma(d)$ is the abscissa of convergence associated with the transfer function $F(s,d)$.*

Proof. It is a consequence of the mapping theorem [5]. Indeed, the spectral abscissa $-\sigma$ is less than $-a$ iff all roots of $p(s,d)$ have real parts less than $-a$, equivalently, iff $p(s-a,d)$ is Hurwitz for all d satisfying (8). The remaining part follows from [5, Section 14.6]. □

The condition can be checked by fixing a and depicting via computer graphics the set $\mathcal{C}(\omega, a)$ for all frequencies (in practice, the frequency range can be chosen to be finite and sufficiently large), possibly iterating on a.

An alternative, non-conservative, but harder to implement, is to check whether $p(s-a,d)$ is Hurwitz, by solving a convex optimisation problem [9].

B. Robust Real Plot

Now, we consider the problem of locating the real zeros and poles. Consider the following functions of the real variable λ:

$$\begin{aligned}
\phi^-(\lambda) &= \min\left\{q(\lambda, \hat{d}), \quad \hat{d}_k \in \{d_k^-, d_k^+\}\right\}, \\
\phi^+(\lambda) &= \max\left\{q(\lambda, \hat{d}), \quad \hat{d}_k \in \{d_k^-, d_k^+\}\right\}, \\
\psi^-(\lambda) &= \min\left\{p(\lambda, \hat{d}), \quad \hat{d}_k \in \{d_k^-, d_k^+\}\right\}, \\
\psi^+(\lambda) &= \max\left\{p(\lambda, \hat{d}), \quad \hat{d}_k \in \{d_k^-, d_k^+\}\right\}.
\end{aligned}$$

Then, we can state the following result.

Theorem 1. *Under Assumption 2, the real λ is not a zero (resp. a pole) of the transfer function $F(s,d)$, i.e. $q(\lambda,d) \neq 0$ (resp. $p(\lambda,d) \neq 0$), for all d_k satisfying* (8) *iff functions $\phi^-(\lambda)$ and $\phi^+(\lambda)$ (resp. $\psi^-(\lambda)$ and $\psi^+(\lambda)$) have the same sign.*

Proof. For fixed λ, $q(\lambda,d)$ is multi-affine in d, so it achieves its minimum, $\phi^-(\lambda)$, and maximum, $\phi^+(\lambda)$, on a vertex of the box (8). So, if $\phi^-(\lambda)$ and $\phi^+(\lambda)$ have the same sign, also $q(\lambda,d)$ does. Conversely, if these extrema have different sign, i.e. $\phi^-(\lambda) \le 0 \le \phi^+(\lambda)$, then by continuity there exists d^* such that $q(\lambda, d^*) = 0$. The proof for the pole case is identical. □

Corollary 1. *The functions $\phi^-(\lambda)$ and $\phi^+(\lambda)$ ($\psi^-(\lambda)$ and $\psi^+(\lambda)$) are tight, namely, for each real λ they are the actual minimum and maximum of $q(\lambda,d)$ (resp. $p(\lambda,d)$) over d.*

Remark 4. *The previous corollary means that we can draw the exact envelope of the real plot (*robust real plot*) of polynomials $p(\lambda,d)$ and $q(\lambda,d)$. Conversely, robust adaptation cannot be assessed directly in the time domain, since the envelope of the step responses is not so easily characterised.*

Then, drawing the two functions $\phi^-(\lambda)$ and $\phi^+(\lambda)$ (resp. $\psi^-(\lambda)$ and $\psi^+(\lambda)$) is enough to locate the real zeros (resp. real poles) of the uncertain system.

Corollary 2. *The set of all zeros (poles) of the transfer function in Assumption 2 is the (possibly empty) union of a finite number of intervals. Denoting by n the degree of the denominator and by r the relative degree, there are at most $n-r$ disjoint intervals for the zeros, at most n for the poles.*

Proof. The set $\{\lambda \in \mathbb{R} : \phi^-(\lambda) \le 0 \le \phi^+(\lambda)\}$ of all zeros is the union of a finite number of intervals in view of

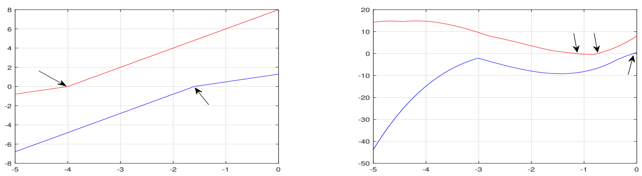

Fig. 4: Robust real plot with lower and upper bounding functions for the numerator (left) and the denominator (right) in Example 2. The arrows indicate the intersections with the real line, i.e. the extrema of the intervals where real zeros and real poles can lie.

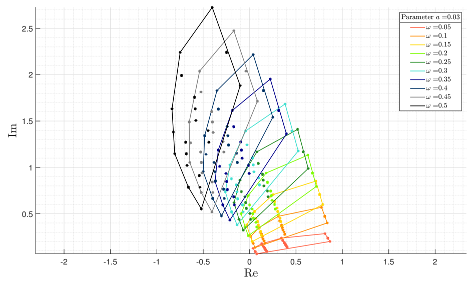

Fig. 5: The set $\mathcal{C}(\omega, a)$ for $a = 0.03$ and $\omega \in [0.05, 0.5]$ in Example 2. For each ω, stars denote the 2^m values of $p(s, \hat{d})$ obtained for $\hat{d}_k \in \{d_k^-, d_k^+\}$, while the straight line polygon denotes their convex hull.

continuity and of the fact that both $\phi^-(\lambda)$ and $\phi^+(\lambda)$ have a finite number of intersections with the real line. The same argument applies to the pole case. Now, assume that $[c_k^L, c_k^R]$ is an isolated interval for the roots. Then, by continuity, for each d as in (8) there is a root in this interval. Hence there can be at most $n-r$ (resp. n) disjoint intervals for the zeros (resp. poles). $\square$

Example 2. *Consider the (bio)chemical reaction network* $\emptyset \xrightarrow{u_1} X_1$, $\emptyset \xrightarrow{u_2} X_2$, $X_1 \xrightarrow{g_1} X_3$, $X_1 + X_2 \xrightarrow{g_{12}} \emptyset$, $X_3 \xrightarrow{g_3} X_1$, $X_2 \xrightarrow{g_2} \emptyset$, *and denote by* $x = \begin{bmatrix} x_1 & x_2 & x_3 \end{bmatrix}^\top$ *the corresponding state vector. Linearisation yields a system of the form* (7) *with*

$$D = \mathrm{diag}\{\partial g_1/\partial x_1, \partial g_{12}/\partial x_1, \partial g_{12}/\partial x_2, \partial g_3/\partial x_3, \partial g_2/\partial x_2\},$$

$$B = \begin{bmatrix} -1 & -1 & -1 & 1 & 0 \\ 0 & -1 & -1 & 0 & -1 \\ 1 & 0 & 0 & -1 & 0 \end{bmatrix}, \; C = \begin{bmatrix} 1 & 1 & 0 & 0 & 0 \\ 0 & 0 & 1 & 0 & 1 \\ 0 & 0 & 0 & 1 & 0 \end{bmatrix}^\top$$

and with bounds $0.5 \le d_k \le 1$. *Let* $E = \begin{bmatrix} 1 & 0 & 0 \end{bmatrix}^\top$ *and* $H = \begin{bmatrix} 0 & 0 & 1 \end{bmatrix}$ *be the input and output vectors, respectively, and consider a perturbation* u *on the input* u_1, *i.e.,* $u_1 + u$. *The system has one zero (which is real) and three poles (of which either one or three are real). The bounding functions for numerator and denominator are reported in Fig. 4. Then, for all possible values of the uncertain parameters, the zero can only lie in the interval* $[-4.0, -1.6]$ *and the real pole(s) can only lie within the union of the intervals* $[-6.49, -1.14]$ *and* $[-0.75, -0.058]$. *Hence, the system is not robustly adaptive (rather, it is robustly non-adaptive): the real zero is robustly dominated by a real pole. Moreover, to assess that the abscissa of convergence of the system is larger than* $a = 0.03$, *Fig. 5 illustrates the set* $\mathcal{C}(\omega, a)$ *for the frequency range* $\omega \in [0.05, 0.5]$. *In view of Proposition 2, since* $\mathcal{C}(\omega, a)$ *does not include the origin, then* $-a = -0.03$ *is a robust spectral abscissa.*

III. Assessing Robust Adaptation

To investigate whether an uncertain system has a real dominant zero for all possible values of the uncertain parameters we need to preliminarily check Assumption 1.

Lemma 1. *Assumption 1 is verified for all* d *satisfying* (8) *iff the leading coefficient of* $q(s,d)$ *is positive for all* $d_k \in \{d_k^-, d_k^+\}$.

Proof. The step response is positive in a right neighbourhood of 0 due to Assumption 1. Hence, the first non-zero derivative of $f(t)$, which is the rth order derivative (where r is the relative degree of $F(s,d)$), must be positive. Then, by applying the initial value theorem, $\lim_{t\to 0} f^{(r)}(t) = \lim_{s\to\infty} s^r F(s,d) > 0$, hence the leading coefficient $q_{n-r}(d)$ of $q(s,d)$ must be positive for all $d_k \in [d_k^-, d_k^+]$. In view of Assumption 2, $q_{n-r}(d)$ is a multi-affine function, hence its minimum is achieved on the vertices $d_k \in \{d_k^-, d_k^+\}$. Then, it is necessary and sufficient that the 2^m values at the vertices are all positive. $\square$

Definition 2. *The transfer function in Assumption 2 has the* weakly robust real zero dominance *property if, for each* d *satisfying* (8)*, there exists a real zero that dominates* $-\sigma$. *Furthermore, if* $-\sigma < 0$ *is a robust spectral abscissa (i.e. it dominates all poles for all* d *satisfying* (8)*), the system has the* strongly robust real zero dominance *property if, for all* d *satisfying* (8)*, there exists a real zero that dominates* $-\sigma$.

The strong property implies the weak property (which is in general harder to check), but not the other way round. Strongly robust real zero dominance can be checked as follows.

Proposition 3. *Let* $-\sigma$ *be a robust spectral abscissa for the transfer function in Assumption 2. Under Assumption 1, the system has the strongly robust real zero dominance property if* $\phi^+(-\sigma) < 0$. *Furthermore, the real dominant zero is unique if* $q'(\lambda, d)$*, the derivative of* $q(\lambda, d)$ *with respect to* λ*, is positive for all* $\hat{d}_k \in \{d_k^-, d_k^+\}$ *and for all* $\lambda \in [-\sigma, \infty)$.

Proof. The leading coefficient of $q(s,d)$ is positive under Assumption 1, hence $q(\lambda, d)$ converges to $+\infty$ as $\lambda \to +\infty$. If $\phi^+(-\sigma) < 0$, then $q(-\sigma, d) < 0$ for all d, hence there is at least one real root to the right of $-\sigma$, i.e. a dominant real zero. The root is unique if, for all $\lambda \in [-\sigma, \infty)$, $q'(\lambda, d) > 0$ for all d, which is implied by $q'(\lambda, \hat{d}) > 0$ for all $\hat{d}_k \in \{d_k^-, d_k^+\}$ due to the multi-affinity of the derivative. $\square$

The presence of at least one dominant real zero suggests that there is adaptation, but is not enough: the dominant real zero must be unique in view of Proposition 1. In general, to establish *robust uniqueness*, we can exploit the next result.

Proposition 4. *Let* $[c^L, c^R]$ *be an interval where* ϕ^- *and* ϕ^+ *have opposite sign and* $\phi^+(c^L) = 0$ *and* $\phi^-(c^R) = 0$ *(or the other way round). Each point in the interval is a root of* $q(s,d)$ *for some* d *satisfying* (8). *The root is unique for all* d *satisfying* (8) *if all the* 2^m *derivative polynomials* $q'(s, \hat{d})$, $\hat{d}_k \in \{d_k^-, d_k^+\}$, *have the same sign (either positive or negative) in this interval.*

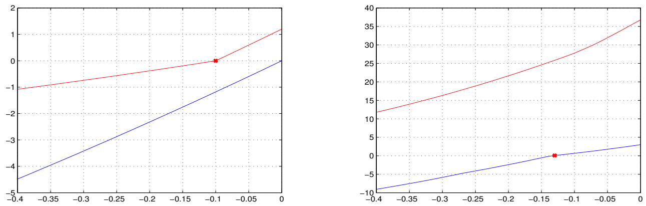

Fig. 6: Robust real plot with lower and upper bounding functions for the numerator (left) and the denominator (right) in Example 3. The real pole and zero intervals are disjoint and the zero dominates the pole.

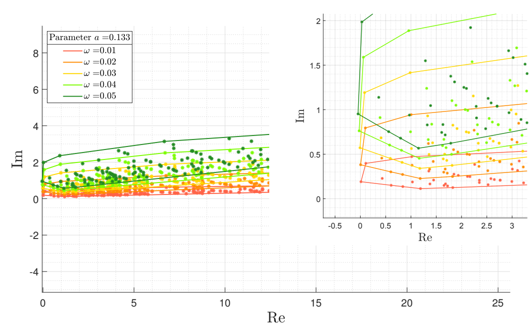

Fig. 7: The set $\mathcal{C}(\omega, a)$ for $a = 0.133$ and $\omega \in [0.01, 0.05]$ in Example 3.

Proof. The intersection of $q(s,d)$ with the interval $[c^L, c^R]$ is unique for all d satisfying (8) if the derivative $q'(s,d)$ does not change sign in the interval for all d satisfying (8). Since the derivative $q'(s,d)$ is a multi-affine function of d, its maximum and minimum value are on the extrema $\hat{d}_k \in \{d_k^-, d_k^+\}$. $\square$

Example 3. *Consider the (bio)chemical reaction network* $\emptyset \xrightarrow{u_1} X_1$, $\emptyset \xrightarrow{u_2} X_2$, $X_1 + X_2 \xrightarrow{g_{12}} X_3 \xrightarrow{g_3} X_4$, $X_1 + X_4 \xrightarrow{g_{14}} \emptyset$, $X_2 \xrightarrow{g_2} \emptyset$, $X_4 \xrightarrow{g_4} \emptyset$, *with* $x = \begin{bmatrix} x_1 & x_2 & x_3 & x_4 \end{bmatrix}^\top$ *the associated state vector. Linearisation yields a system of the form* (7) *with* $D = diag\{\frac{\partial g_{12}}{\partial x_1}, \frac{\partial g_{12}}{\partial x_2}, \frac{\partial g_3}{\partial x_3}, \frac{\partial g_{14}}{\partial x_1}, \frac{\partial g_{14}}{\partial x_4}, \frac{\partial g_2}{\partial x_2}, \frac{\partial g_4}{\partial x_4}\}$,

$$B = \begin{bmatrix} -1 & -1 & 0 & -1 & -1 & 0 & 0 \\ -1 & -1 & 0 & 0 & 0 & -1 & 0 \\ 1 & 1 & -1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 1 & -1 & -1 & 0 & -1 \end{bmatrix},$$
$$C = \begin{bmatrix} 1 & 0 & 0 & 1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 1 & 0 & 0 & 0 & 0 \\ 0 & 0 & 0 & 0 & 1 & 0 & 1 \end{bmatrix}^\top.$$

Consider an additive input on x_1 and take x_3 as output, namely $E = [1\ 0\ 0\ 0]^\top$ and $H = [0\ 0\ 1\ 0]$. Let the bounds on d be $d^- = [1\ 1\ 1\ 1\ 1\ 0.0\ 3]$ and $d^+ = [2\ 2\ 2\ 2\ 2\ 0.1\ 4]$. For $d_6 = 0$, the system has perfect adaptation. Is adaptation maintained, although non-perfect, for small values of d_6? The real plot in Fig. 6 shows that the dominant zero interval $[-0.1, -0.0]$ is to the right of the dominant pole interval, $[-0.79, -0.133]$. Therefore, we have strongly robust real zero dominance. The same conclusion can be drawn by noticing that $-a = -0.133$ is a robust spectral abscissa (since the origin does not belong to the set $\mathcal{C}(\omega, a)$, see Fig. 7), and that $\psi^+(-a) < 0$.

A. Systems with All-Real or Dominant-Real Poles

If the system has only real poles, or a dominant real pole, assessing robust adaptation boils down to checking whether a single real zero robustly dominates the dominant pole. The problem is easy to solve if the dominant poles and the dominant zeros are confined in disjoint intervals, as in Example 2 where the zero dominates. Conversely, if the dominant zero and the dominant pole have overlapping intervals, then the next robustness result comes into play.

Proposition 5. *Consider a transfer function as in Assumption 2 whose dominant pole is real and lies in an interval $[c^L, c^R]$. Assume that, for an arbitrary choice $\bar{d}$ of the parameters d, the dominant zero is to the right (resp. left) of the dominant pole. Then, the dominant zero is to the right (resp. left) of the dominant pole for all values of d satisfying* (8) *iff there are no real zero-pole cancellations in $[c^L, c^R]$.*

Proof. Sufficiency. By contradiction, if there exists $\tilde{d}$ such that the dominant root of $q(\lambda, \tilde{d})$ is less than the dominant root of $p(\lambda, \tilde{d})$, then, by continuity of the roots of a polynomial, there must exist $\bar{d}$ and $\bar{\lambda}$ for which $q(\bar{\lambda}, \bar{d}) = p(\bar{\lambda}, \bar{d}) = 0$, hence a cancellation occurs. *Necessity.* If there is a cancellation, the dominant zero does not fulfill the condition of dominance, because $z < \sigma$ is not strict. $\square$

Then, we propose a numerical test to check weak robust real zero dominance.

Proposition 6. *Let $[c^L, c^R]$ be an interval where both $p(s,d)$ and $q(s,d)$ have (dominant) real roots. Assume that, for some $\hat{d}$, each root of $p(s, \hat{d})$ in the interval is dominated by some root of $q(s, \hat{d})$ in the interval. Then, the roots of $q(s,d)$ dominate the roots of $p(s,d)$ in $[c^L, c^R]$ for all d if there exists a multiplier $\theta > 0$ such that the 2^m polynomial inequalities*

$$\theta p(\lambda, \hat{d}) - q(\lambda, \hat{d}) > 0, \quad \hat{d}_k \in \{d_k^-, d_k^+\},$$

are satisfied for all $\lambda \in [c^L, c^R]$.

Proof. In view of multi-affinity of $\theta p(\lambda, d) - q(\lambda, d)$, the condition on the vertices $\hat{d}_k \in \{d_k^-, d_k^+\}$ implies the same conditions for all $d_k \in [d_k^-, d_k^+]$, i.e. $\theta p(\lambda, d) - q(\lambda, d) > 0$. Then, no cancellations are possible, since p and q cannot be both zero, and the proof follows from Proposition 5. $\square$

Example 4. *Reconsider Example 3 with bounds $d^- = [1\ 1\ 1\ 1\ 1\ 0.0\ 3]$ and $d^+ = [2\ 2\ 2\ 2\ 2\ 0.3\ 4]$. Since the set $\mathcal{C}(\omega, a)$ does not include the origin, see Fig. 8, $-a = -0.1$ is a robust spectral abscissa. The dominant zero interval is $[-0.3\ 0.0]$, while the dominant pole interval is $[-0.89\ -0.13]$: the intervals have the intersection $[-0.3\ \ -0.13]$. Hence, there is no strongly robust real zero dominance. However, for $\theta = 0.4$, the polynomial $\theta p(\lambda, \hat{d}) - q(\lambda, \hat{d})$ is positive on $[-0.3\ -0.13]$: we have weakly robust real zero dominance.*

B. Parallel of Systems: the Incoherent Feed-Forward Loop

We consider here the composition of systems in parallel.

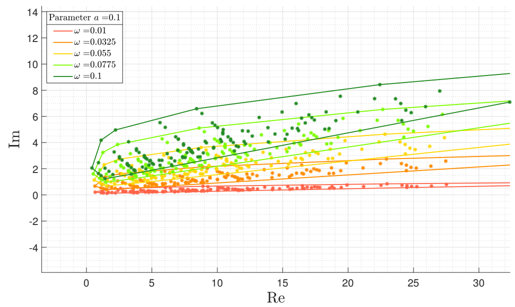

Fig. 8: The set $\mathcal{C}(\omega, a)$ for $a = 0.1$ and $\omega \in [0.01, 0.1]$ in Example 4.

Proposition 7. (Parallel). *Consider the transfer function*

$$F(s, p_i^{(k)}, \delta^{(k)}) = \sum_{k=1}^{M} F_k(s, p_i^{(k)}, \delta^{(k)}) = \sum_{k=1}^{M} \frac{q^{(k)}(s, \delta^{(k)})}{\prod_{i=1}^{n_k}(s + p_i^{(k)})}$$

with $q^{(k)}(s, \delta^{(k)})$ multi-affine in the parameter vector $\delta^{(k)}$. Assume that: there exists a real zero $-z_1$ for all values of the parameters; all poles lie in intervals $p_i^{(k)} \in [p_i^{(k)-}, p_i^{(k)+}]$; there is no intersection between the intervals corresponding to the poles of different transfer functions. Then, either
1) the dominant zero $-z_1$ dominates the poles for all d; or
2) the dominant zero $-z_1$ is dominated by a pole for all d.

Proof. Consider minimal realisations of the transfer functions F_k. The parallel of reachable and observable SISO systems is reachable and observable iff the systems have no common poles, and the result follows from Proposition 5. $\square$

We can apply Proposition 7 to the Incoherent Feed-Forward Loop (IFFL), a widespread fundamental motif recurring in biological systems [1], described by the transfer function $F(s) = F_1(s) + F_2(s) = \frac{\alpha}{(s+p_1)} - \frac{\beta}{(s+p_2)(s+p_3)} = \frac{\alpha s^2+[\alpha(p_2+p_3)-\beta]s+(\alpha p_2 p_3-\beta p_1)}{(s+p_1)(s+p_2)(s+p_3)}$. Take for instance $1 \leq \alpha \leq 2$, $3 \leq \beta \leq 4$, $3 \leq p_1 \leq 4$, $1 \leq p_2 \leq 3$ and $6 \leq p_3 \leq 7$. The numerator leading coefficient is positive. The pole intervals are disjoint. The robust real plot of the numerator, in Fig. 9, shows the two disjoint zero intervals $[-6.16, -3.78]$ and $[-1.47, 2.87]$, which overlap with the pole intervals. However, for some parameter values there is a zero that dominates all the poles; therefore, according to Proposition 7, the zero is dominant for all parameter values.

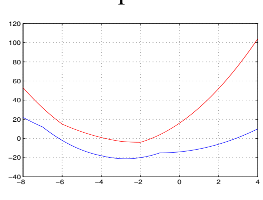

Fig. 9: Lower and upper bounding functions for the numerator of the IFFL.

If the interval of p_1 overlaps with the intervals of p_2 or p_3, a cancellation can occur, so we need to check that the dominant zero is not cancelled. Assume for instance that $p_1 = p_3$, then $F(s) = \frac{\alpha s+\alpha p_2-\beta}{(s+p_1)(s+p_2)}$ and the zero dominance condition is $\beta - \alpha p_2 > -\alpha p_i$, $i = 1, 2$, hence $\beta > 0$ (always true) and $\beta - \alpha(p_2 - p_1) > 0$, which is robustly satisfied if $\beta^- > \alpha^+(p_2^+ - p_1^-)$.

IV. Conclusions and Future Work

A novel notion of adaptation for linear systems has been associated with the presence of a single real dominant zero. The *robust real plot* allows to robustly assess adaptation for systems with parametric uncertainties [5], by identifying the intervals where real zeros and poles can lie. Future research aims at extending this analysis to nonlinear systems by adopting the technique of model matching [4]. Our novel tools to robustly assess adaptation can ensure that an uncertain model always exhibits adaptation, and can help falsify models (when the model is adaptive for all possible parameter values, but absence of adaptation is experimentally observed at least once, then the model is not well suited to describe the phenomenon), particularly in systems biology.

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