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Quality-by-design by skewed spherical structured singular value

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Abstract: This study develops numerical algorithms to compute an ellipsoidal set of input parameters, called a design space, that ensures that the system outputs lie within a set of design specifications in *quality-by-design*. The algorithm is based on a proposed *skewed spherical structured singular value* ν_s, for which this study derives upper bounds and proves the (scaled) main loop theorems and small-gain theorem for the Frobenius norm. Three examples are included to illustrate applications of the numerical algorithms.

1 Introduction

One of the tenets of quality-by-design (QbD) initiatives is the determination of a set of input parameters, called a *design space*, that ensures that the system outputs lie within a set of design specifications in spite of perturbations in the manufacturing process [1].

A common industrial practice for the construction of a design space is to collect data from a large number of time-consuming and expensive experiments (e.g. see [2] for a description of the state-of-the-art in industrial practice in the pharmaceutical industry). Some companies take a more sophisticated approach, in which a first-principles, grey-box, or black-box model of the manufacturing process is constructed, the parameter space is gridded, and a large number of simulations are run to determine parameter values that satisfy the output specifications. While this latter approach requires fewer experiments, gridding is a computationally expensive approach for constructing a design space. A grid of 100 values for each of the n parameters, for example requires running 100^n simulations, which becomes infeasible when n is large and the simulation time is long. In addition, gridding does not theoretically guarantee accurate characterisation of the design space due to non-linearities and non-convexities in the full set of allowable parameters that satisfy the output specifications. In particular, defining a set around parameter vectors that satisfy the output specifications does not ensure that every parameter within the box satisfies the output specifications. It is certainly preferable to have rigorous assurances that all parameters within a design space are valid indicators of output performance, as well as to reduce the computational cost from exponential to polynomial time.

Existing methods for the construction of design spaces for non-linear systems are described by box constraints on the input parameters, which can limit the sizes of the design space specifications [3]. On the other hand, there is a strong motivation to continue using a convex set to characterise a design space, so that the set can be directly inserted into monitoring and feedback control algorithms with minor increases in computational cost. Motivated by this observation, as well as by the plotting of many input spaces that are consistent with specified target regions, this paper considers the characterisation of an ellipsoidal design space, which can be a better representation for a design space than a box set [4].

For this purpose, this paper introduces the *skewed spherical structured singular value*, ν_s, which is a generalisation of both the skewed structured singular value [5] and the spherical structured singular value [6], and allows the box set to be replaced by an ellipsoidal set. The structured singular value [7–9] has been used to analyse the performance and robustness properties of linear feedback systems. Although the computation of the structured singular value is known to be NP-hard [10], various methods have been developed to compute tight upper and lower bounds with a computationally tractable cost, i.e. in polynomial time [11–14]. Later, a family of structured singular values, such as the skewed structured singular value and the spherical structured singular value, were introduced (see Section 3 for relevant definitions), which allows different scalings of the perturbations and different uncertainty descriptions, respectively. The skewed spherical structured singular value treats the spherical (ellipsoidal) uncertainty defined by the Frobenius norm, similarly to how the skewed structured singular value is defined from the structured singular value.

The main loop theorem [12, 15, 16] and the scaled main loop theorem [5, 17, 18] form the basis for the use of the structured singular value for the analysis and design of controllers for uncertain linear systems. To the authors' knowledge, all the main loop theorems in the existing literature employ the maximum singular value norm (i.e. the matrix norm induced by Euclidean norms on the input and output). However, the Frobenius norm must be used in the analysis of systems with ellipsoidal uncertainty. Therefore, this paper also discusses a variation of the main loop theorem and the scaled main loop theorem for the Frobenius norm, which are then used in the development of a numerical algorithm for QbD.

The organisation of this paper is as follows. Section 2 covers the requisite preliminary mathematical background. Section 3 introduces the skewed spherical structured singular value ν_s and derives an upper bound on ν_s. Section 4 discusses the scaled main loop theorem and the main loop theorem for the Frobenius norm. Section 5 presents an algorithm for the construction of an ellipsoidal design space by using ν_s. Section 6 proposes extensions to more general cases. Section 7 presents three numerical examples that apply the proposed algorithm and theorems. Section 8 concludes the paper.

2 Mathematical preliminaries

The set of real numbers, real vectors of length n, and real matrices of size $n \times m$ are denoted by $\mathbb{R}$, $\mathbb{R}^n$, and $\mathbb{R}^{n\times m}$, respectively. The set of complex numbers, real vectors of length n, and real matrices of size $n \times m$ are denoted by $\mathbb{C}$, $\mathbb{C}^n$, and $\mathbb{C}^{n\times m}$, respectively. For a vector $v \in \mathbb{R}^n$, v^{T} denotes the transpose of the vector v, v_i denotes the ith element of v, and $\|v\|_2 = \sqrt{v^{\mathrm{T}}v}$. For a matrix $M \in \mathbb{R}^{n\times m}$, M^{T} denotes the transpose of the matrix M, for a matrix

$M \in \mathbb{C}^{n\times m}$, M^* denotes the conjugate transpose of the matrix M, and m_{ij} denotes the i,j-element of M. The $n \times 1$ vector of ones is denoted by $\mathbf{1}_n$, the $n \times n$ identity matrix is denoted by I_n, the $n \times n$ zero matrix is denoted by 0_n and the subscripts n are dropped when the dimensions are clear from the context. diag[v] for some vector v is a diagonal matrix with v_i on the diagonal and diag$[A_1, \ldots, A_n]$ for some matrices A_i is a block-diagonal matrix with A_i on the diagonal. $\det(M)$ is the determinant of M and $\mathrm{tr}(M)$ is the trace of M. The maximum singular value norm of a matrix M is denoted by $\|M\|_2$. The Frobenius norm of a matrix $M \in \mathbb{R}^{n\times m}$ is defined as $\|M\|_F = \sqrt{\mathrm{tr}(M^{\mathrm{T}}M)}$.

For a given matrix block structure $\mathcal{K} = (r_1, \ldots, r_n)$, let

$$\boldsymbol{\Delta}_{\mathcal{K},F} := \left\{\Delta = \mathrm{diag}\left[\frac{1}{\sqrt{r_1}}\delta_1 I_{r_1}, \ldots, \frac{1}{\sqrt{r_n}}\delta_n I_{r_n}\right] : \ \delta_i \in \mathbb{R}\right\},$$

$$\mathbf{B}\boldsymbol{\Delta}_{\mathcal{K},F} := \left\{\Delta = \mathrm{diag}\left[\frac{1}{\sqrt{r_1}}\delta_1 I_{r_1}, \ldots, \frac{1}{\sqrt{r_n}}\delta_n I_{r_n}\right] : \ \delta_i \in \mathbb{R}, \ \|\Delta\|_F \le 1\right\}$$

and

$$k\mathbf{B}\boldsymbol{\Delta}_{\mathcal{K},F} := \left\{\Delta = \mathrm{diag}\left[\frac{1}{\sqrt{r_1}}\delta_1 I_{r_1}, \ldots, \frac{1}{\sqrt{r_n}}\delta_n I_{r_n}\right] : \ \delta_i \in \mathbb{R}, \ \|\Delta\|_F \le k\right\},$$

where $1/\sqrt{r_i}$ are normalising factors. In fact, $\|\Delta\|_F \le 1$ holds if and only if $\delta^{\mathrm{T}}\delta \le 1$ and similarly $\|\Delta\|_F \le k$ holds if and only if $\delta^{\mathrm{T}}\delta \le k$.

For matrices

$$M = \begin{bmatrix} M_{11} & M_{12} \\ M_{21} & M_{22} \end{bmatrix}$$

and Δ of compatible dimensions, the upper linear fractional transform (LFT) is

$$F_u(M, \Delta) := M_{22} + M_{21}\Delta(I - M_{11}\Delta)^{-1}M_{12},$$

and the lower LFT is

$$F_l(M, \Delta) := M_{11} + M_{12}\Delta(I - M_{22}\Delta)^{-1}M_{21}.$$

A non-invertible $I - M_{11}\Delta$ or $I - M_{22}\Delta$ occurs for some perturbation Δ of interest if and only if the LFT is ill-posed. The well-posedness of the LFT with Δ under consideration can be evaluated using the structured singular value (e.g. [16]). To simplify the presentation, this paper assumes that this verification is carried out before applying the algorithms. Note that the LFT for any particular function is not unique.

A set of equalities utilised throughout this paper are obtained by considering determinants for block matrices [19] for $\Delta = \mathrm{diag}[\Delta_1, \ \Delta_2]$ with compatible dimensions:

$$\begin{aligned} &\text{For non-singular } I - M_{22}\Delta_2 : \\ &\qquad \det(I - M\Delta) = \det(I - M_{22}\Delta_2)\det(I - F_l(M, \Delta_2)\Delta_1), \\ &\text{For non-singular } I - M_{11}\Delta_1 : \\ &\qquad \det(I - M\Delta) = \det(I - M_{11}\Delta_1)\det(I - F_u(M, \Delta_1)\Delta_2). \end{aligned} \tag{1}$$

Remark 1: Any well-posed rational function can be written in the LFT form by using block-diagram algebra (e.g. [16]) or through the application of multidimensional realisation algorithms (e.g. [20]). Multidimensional model reduction algorithms (e.g. see [21] and references cited therein) can also be applied to an LFT to reduce its dimensions.

Lemma 1 (*Sylvester's determinant*)*:* If A is an $n \times m$ matrix and B is an $m \times n$ matrix, then $\det(I + AB) = \det(I + BA)$.

Lemma 2 [22]: A matrix family $\mathcal{A}$ is non-singular if there exists another matrix C (multiplier) such that the $AC + C^{\mathrm{T}}A^{\mathrm{T}} > 0$ for all $A \in \mathcal{A}$.

Lemma 3 (*Schur product [23]*)*:* If $X_i \ge 0$ and $X = X_1 \circ X_2$, then $X \ge 0$.

Lemma 4 [24]: For vectors a and b of the same length, if $A = \mathrm{diag}[a]$ and $B = \mathrm{diag}[b]$, then $AXB = X \circ (ab^{\mathrm{T}})$.

Lemma 5 (*Schur complement [25]*)*:* Suppose $A = A^*$ and $C = C^*$. Then

- $\begin{bmatrix} A & B \\ B^* & C \end{bmatrix} \ge 0$ iff $C > 0$ and $A - BC^{-1}B^* \ge 0$,
- $\begin{bmatrix} A & B \\ B^* & C \end{bmatrix} \ge 0$ iff $A > 0$ and $C - B^*A^{-1}B \ge 0$.

Proposition 1 (*Application of Schur complement*)*:* For a vector $v \in \mathbb{R}^n$, $1 - v^{\mathrm{T}}v \ge 0$ if and only if $I - vv^{\mathrm{T}} \ge 0$.

Proof: Use Lemma 5 for

$$\begin{bmatrix} I & v \\ v^{\mathrm{T}} & 1 \end{bmatrix}.$$

□

3 Skewed spherical structured singular value

Definition 1 (*Spherical structured singular value [6]*)*:* For $M \in \mathbb{C}^{m\times m}$ and $\mathcal{K}$, the *spherical structured singular value* is defined by

$$\mu_{s,\mathcal{K}}(M) = \frac{1}{\min\{k \ge 0 : \det(I - kM\Delta) = 0, \ \ \Delta \in \mathbf{B}\boldsymbol{\Delta}_{\mathcal{K},F}\}}$$

unless no k exists that makes $I - kM\Delta$ singular for any $\Delta \in \mathbf{B}\boldsymbol{\Delta}_{\mathcal{K},F}$, in which case $\mu_{s,\mathcal{K}}(M) = 0$.

Definition 2 (*Skewed spherical structured singular value*)*:* For $M \in \mathbb{R}^{m\times m}$ and $\mathcal{K}_1$, $\mathcal{K}_2$, the *skewed spherical structured singular value* is defined by

$$\nu_{s,\mathcal{K}_1,\mathcal{K}_2}(M) = \frac{1}{\min\left\{\begin{matrix} k \ge 0 : \det(I - M\Delta) = 0, \ \ \Delta = \mathrm{diag}[\Delta_1, k\Delta_2], \\ \Delta_1 \in \mathbf{B}\boldsymbol{\Delta}_{\mathcal{K}_1,F}, \ \ \Delta_2 \in \mathbf{B}\boldsymbol{\Delta}_{\mathcal{K}_2,F} \end{matrix}\right\}}$$

unless no k exists that makes $I - M\Delta$ singular for any $\Delta_1 \in \mathbf{B}\boldsymbol{\Delta}_{\mathcal{K}_1,F}$ and $\Delta_2 \in \mathbf{B}\boldsymbol{\Delta}_{\mathcal{K}_2,F}$, in which case $\nu_{s,\mathcal{K}_1,\mathcal{K}_2}(M) = 0$.

The skewed spherical structured singular value is a natural generalisation of the skewed structured singular value [5] to the Frobenius norm on the perturbation matrix, and a direct generalisation of the spherical structured singular value [6] to have a different scaling on two sets of perturbations.

Theorem 1 (*Upper bound for $\nu_{s,\mathcal{K}_1,\mathcal{K}_2}(M)$*)*:*

$$\nu_{s,\mathcal{K}_1,\mathcal{K}_2}(M) \le \inf_{D_i \in \mathcal{D}_{\mathcal{K}_i}, G \in \mathcal{G}_{\mathcal{K}}} \{\gamma > 0 : M^{\mathrm{T}}((D_1 + D_2) \circ I)M - D_1 + j(GM - M^{\mathrm{T}}G) - \gamma^2 D_2 < 0\},$$

where

$$\mathcal{K}_1 = (r_{1,1}, \ldots, r_{1,n}),$$
$$\mathcal{K}_2 = (r_{2,1}, \ldots, r_{2,m}),$$
$$\mathcal{D}_{\mathcal{K}_1} = \left\{ \mathrm{diag}[\underline{D}_1, 0_q] : \underline{D}_1 \in \mathbb{R}^{p\times p},\ \underline{D}_1 = \underline{D}_1^{\mathrm{T}} > 0 \right\},$$
$$p = \sum r_{1,i},$$
$$\mathcal{D}_{\mathcal{K}_2} = \left\{ \mathrm{diag}[0_p, \underline{D}_2] : \underline{D}_2 \in \mathbb{R}^{q\times q},\ \underline{D}_2 = \underline{D}_2^{\mathrm{T}} > 0 \right\},$$
$$q = \sum r_{2,i},$$
$$\mathcal{G}_{\mathcal{K}} = \left\{ \mathrm{diag}[G_{1,1}, \ldots, G_{1,n}, G_{2,1}, \ldots, G_{2,m}] : G_i = G_i^*,\ jG_i \in \mathbb{R}^{r_i\times r_i} \right\}.$$

Proof: The proof is similar to the proofs for the upper bound for the spherical structured singular value [24, 26, 27]. First, consider the conversion between the scalar uncertainty and structured uncertainty. Let

$$\Delta_1 = \mathrm{diag}\left[\frac{1}{\sqrt{r_{1,1}}}\delta_{1,1} I_{r_{1,1}}, \ldots, \frac{1}{\sqrt{r_{1,n}}}\delta_{1,n} I_{r_{1,n}} \right],$$
$$\delta_1 = [\delta_{1,1}, \ldots, \delta_{1,n}],$$
$$Q_1 = \mathrm{diag}\left[\frac{1}{\sqrt{r_{1,1}}}\delta_{1,1} \mathbf{1}_{r_{1,1}}, \ldots, \frac{1}{\sqrt{r_{1,n}}}\delta_{1,n} \mathbf{1}_{r_{1,n}} \right],$$

then

$$\Delta_1 = \mathrm{diag}[Q_1\delta_1]. \tag{2}$$

Similarly, for

$$\Delta_2 = \mathrm{diag}\left[\frac{1}{\sqrt{r_{2,1}}}\delta_{2,1} I_{r_{2,1}}, \ldots, \frac{1}{\sqrt{r_{2,m}}}\delta_{2,m} I_{r_{2,m}} \right],$$
$$\delta_2 = [\delta_{2,1}, \ldots, \delta_{2,m}],$$
$$Q_2 = \mathrm{diag}\left[\frac{1}{\sqrt{r_{2,1}}}\delta_{2,1} \mathbf{1}_{r_{2,1}}, \ldots, \frac{1}{\sqrt{r_{2,m}}}\delta_{2,m} \mathbf{1}_{r_{2,m}} \right],$$

it holds that

$$\Delta_2 = \mathrm{diag}[Q_2\delta_2]. \tag{3}$$

To prove the upper bound, use that $\det(I - M\Delta) \neq 0$ if and only if $\det(I - \Delta M) \neq 0$ (from Lemma 1), and a sufficient condition for $\det(I - \Delta M) \neq 0$ is that there exists C such that $C(I - \Delta M) + (I - \Delta M)^{\mathrm{T}} C^*$ is non-singular (from Lemma 2).

Let

$$C = D_1 + \gamma^2 D_2 + jM^{\mathrm{T}} G$$

for some $\gamma > 0$, $D_i \in \mathcal{D}_{\mathcal{K}_i}$ and $G \in \mathcal{G}_{\mathcal{K}}$. Then, by using Lemma 4, (2), and (3), (see (4))

where

$$\Psi(D_1, D_2, G) = M^{\mathrm{T}}((D_1 + D_2)\circ I)M - D_1 + j(GM - M^{\mathrm{T}}G) - \gamma^2 D_2.$$

Therefore, if (4) is positive definite, then $\det(I - M\Delta) \neq 0$. The second term of (4) is non-negative because it is a squared form with $D_i \geq 0$. The last term of (4) is also non-negative because the following equivalences hold

$$\|\Delta_1\|_F \leq 1 \text{ and } \|\Delta_2\|_F \leq \gamma^{-1}$$
$$\Leftrightarrow (Q_1\delta_1)^{\mathrm{T}}(Q_1\delta_1) \leq 1 \text{ and } (Q_2\delta_2)^{\mathrm{T}}(Q_2\delta_2) \leq \gamma^{-2}$$
$$[\because (2) \text{ and } (3)]$$
$$\Leftrightarrow I - (Q_1\delta_1)(Q_1\delta_1)^{\mathrm{T}} \geq 0 \text{ and } I - \gamma^2 (Q_2\delta_2)(Q_2\delta_2)^{\mathrm{T}} \geq 0$$
$$(\because \text{Proposition } 1)$$
$$\Leftrightarrow I - \begin{bmatrix} (Q_1\delta_1)(Q_1\delta_1)^{\mathrm{T}} & \\ & \gamma^2(Q_2\delta_2)(Q_2\delta_2)^{\mathrm{T}} \end{bmatrix} \geq 0.$$

Lemma 3 implies that, for $D_1 + D_2 > 0$

$$(D_1 + D_2)\circ\left(I - \begin{bmatrix} (Q_1\delta_1)(Q_1\delta_1)^{\mathrm{T}} & \\ & \gamma^2(Q_2\delta_2)(Q_2\delta_2)^{\mathrm{T}} \end{bmatrix} \right) \geq 0.$$

Thus, the last term of (4) is non-negative. Hence, if $\Psi(D_1, D_2, G) < 0$, then $\det(I - M\Delta) \neq 0$ for all $\|\Delta_1\|_F \leq 1$ and $\|\Delta_2\|_F \leq \gamma^{-1}$. Therefore, an upper bound on ν can be obtained by minimising γ, while satisfying $\Psi(D_1, D_2, G) < 0$. □

4 Scaled main loop theorem

The main loop theorem [16] does not hold if bounds on the mixed structured perturbation are given in terms of the Frobenius norm (usually the maximum singular value norm is used), because the main loop theorem relies on the equivalence

$$\|\Delta_1\|_2 \leq 1 \text{ and } \|\Delta_2\|_2 \leq 1 \Leftrightarrow \|\Delta\|_2 \leq 1 \text{ for } \Delta = \begin{bmatrix} \Delta_1 & 0 \\ 0 & \Delta_2 \end{bmatrix}, \tag{5}$$

which *does not hold* for the Frobenius norm. Instead

$$\|\Delta\|_F^2 = \|\Delta_1\|_F^2 + \|\Delta_2\|_F^2;$$

therefore, it holds that (see (6))

Equation (5) is critical in the original proof of the main loop theorem, hence modifications are required in order to apply the main loop theorem to the Frobenius norm. The modification utilises (6).

On the other hand, the invalidity of (5) does not pose any problems in our statement of the scaled main loop theorem, because the combined mixed structured uncertainty matrix Δ never appears; instead, each mixed structured uncertainty is treated separately. This section carefully investigates how the (scaled) main loop theorems differ for the Frobenius norm.

The following two theorems are revisions to the main loop theorem so as to be applicable to the Frobenius norm.

$$C(I - \Delta M) + (I - \Delta M)^{\mathrm{T}} C^* = -\Psi(D_1, D_2, G) + (I - \Delta M)^{\mathrm{T}}(D_1 + \gamma^2 D_2)(I - \Delta M) + M^{\mathrm{T}}\left((D_1 + D_2)\circ\left(I - \begin{bmatrix} (Q_1\delta_1)(Q_1\delta_1)^{\mathrm{T}} & \\ & \gamma^2(Q_2\delta_2)(Q_2\delta_2)^{\mathrm{T}} \end{bmatrix} \right) \right) M, \tag{4}$$

$$\left\{ \Delta : \Delta = \begin{bmatrix} \Delta_1 & 0 \\ 0 & \Delta_2 \end{bmatrix},\ \|\Delta\|_F \leq 1 \right\} = \left\{ \Delta : \Delta = \begin{bmatrix} \Delta_1 & 0 \\ 0 & \Delta_2 \end{bmatrix},\ \|\Delta_1\|_F \leq \epsilon,\ \|\Delta_2\|_F \leq \sqrt{1-\epsilon^2},\ \forall\epsilon \in [0, 1] \right\}. \tag{6}$$

Theorem 2 (*A variation on the main loop theorem*):

$$\mu_{s,\mathcal{K}}(M) < 1 \Rightarrow \begin{cases} \mu_{s,\mathcal{K}_2}(M_{22}) < 1, \\ \epsilon\left(\max_{\Delta_2 \in \sqrt{1-\epsilon^2}\mathbf{B\Delta}_{\mathcal{K}_2,F}} \mu_{s,\mathcal{K}_1}(F_l(M,\Delta_2))\right) < 1, \ \forall \epsilon \in [0,1], \end{cases}$$

where $\mathcal{K}_1$ and $\mathcal{K}_2$ are the uncertain structures for $\Delta = \text{diag}[\Delta_1, \Delta_2]$ with $\Delta_i \in \mathbf{\Delta}_{\mathcal{K}_i,F}$ for given $\mathcal{K}$.

Proof: $\mu_{s,\mathcal{K}}(M) < 1$ implies that

$$\det\left(I - M\begin{bmatrix}\Delta_1 & 0 \\ 0 & \Delta_2\end{bmatrix}\right) \neq 0, \ \forall \Delta = \text{diag}[\Delta_1, \Delta_2] \in \mathbf{B\Delta}_{\mathcal{K},F}. \tag{7}$$

This equation must hold for $\Delta_1 = 0 \in \mathbf{B\Delta}_{\mathcal{K}_1,F}$, which implies that

$$\det(I - M_{22}\Delta_2) \neq 0, \ \forall \Delta_2 \in \mathbf{B\Delta}_{\mathcal{K}_2,F}$$

and

$$\mu_{s,\mathcal{K}_2}(M_{22}) < 1, \tag{8}$$

which guarantees the well-posedness of $F_l(N, \Delta_2)$ for $\Delta_2 \in \mathbf{B\Delta}_{\mathcal{K}_2,F}$ and hence for $\Delta_2 \in \sqrt{1-\epsilon^2}\,\mathbf{B\Delta}_{\mathcal{K}_2,F}$ for any $\epsilon \in [0,1]$. Equations (7) and (8) with (1) imply that

$$\det(I - F_l(N,\Delta_2)\Delta_1) \neq 0,$$
$$\forall \Delta_1 \in \epsilon\mathbf{B\Delta}_{\mathcal{K}_1,F}, \ \forall \Delta_2 \in \sqrt{1-\epsilon^2}\,\mathbf{B\Delta}_{\mathcal{K}_2,F}$$

for any $\epsilon \in [0,1]$. Therefore

$$\epsilon\left(\max_{\Delta_2 \in \sqrt{1-\epsilon^2}\mathbf{B\Delta}_{\mathcal{K}_2,F}} \mu_{s,\mathcal{K}_1}(F_l(M,\Delta_2))\right) < 1, \ \forall \epsilon \in [0,1].$$

□

Theorem 3 (*A variation on the main loop theorem*):

$$\mu_{s,\mathcal{K}}(M) < 1 \Leftarrow \begin{cases} \mu_{s,\mathcal{K}_2}(M_{22}) < 1, \\ \max_{\Delta_2 \in \mathbf{B\Delta}_{\mathcal{K}_2,F}} \mu_{s,\mathcal{K}_1}(F_l(M,\Delta_2)) < 1, \end{cases}$$

where $\mathcal{K}$ is the uncertain structure for $\Delta = \text{diag}[\Delta_1, \Delta_2]$ with $\Delta_1 \in \mathbf{\Delta}_{\mathcal{K}_1,F}$ and $\Delta_2 \in \mathbf{\Delta}_{\mathcal{K}_2,F}$, for given $\mathcal{K}_1$ and $\mathcal{K}_2$.

Proof: The inequality $\mu_{s,\mathcal{K}_2}(M_{22}) < 1$ implies that

$$\det(I - M_{22}\Delta_2) \neq 0, \ \forall \Delta_2 \in \mathbf{B\Delta}_{\mathcal{K}_2,F}. \tag{9}$$

Similarly, the inequality $\max_{\Delta_2 \in \mathbf{B\Delta}_{\mathcal{K},F}} \mu_{s,\mathcal{K}_1}(F_l(M,\Delta_2)) < 1$ implies that

$$\det(I - F_l(M,\Delta_2)\Delta_1) \neq 0, \ \forall \Delta_1 \in \mathbf{B\Delta}_{\mathcal{K}_1,F}, \ \forall \Delta_2 \in \mathbf{B\Delta}_{\mathcal{K}_2,F}. \tag{10}$$

With (1), (9) and (10) imply that

$$\det(I - M\Delta) \neq 0, \ \forall \Delta = \text{diag}\,[\Delta_1, \Delta_2],$$
$$\Delta_1 \in \mathbf{B\Delta}_{\mathcal{K}_1,F}, \Delta_2 \in \mathbf{B\Delta}_{\mathcal{K}_2,F}. \tag{11}$$

Since $\mathbf{B\Delta}_{\mathcal{K},F} \subset \{\Delta = \text{diag}[\Delta_1, \Delta_2] : \Delta_1 \in \mathbf{B\Delta}_{\mathcal{K}_1,F}, \Delta_2 \in \mathbf{B\Delta}_{\mathcal{K}_2,F}\}$, (11) implies that $\det(I - M\Delta) \neq 0$ for all $\Delta \in \mathbf{B\Delta}_{\mathcal{K},F}$. Therefore, $\mu_{s,\mathcal{K}}(M) < 1$. □

The scaled main loop theorem for spherical uncertainties, which is one of the main results of this paper, is stated below.

Theorem 4 (*Scaled main loop theorem for* $\nu_{s,\mathcal{K}_1,\mathcal{K}_2}(M)$):

$$\nu_{s,\mathcal{K}_1,\mathcal{K}_2}(M) < \alpha \Leftrightarrow \begin{cases} \mu_{s,\mathcal{K}_2}(M_{22}) < \alpha, \\ \max_{\Delta_2 \in \frac{1}{\alpha}\mathbf{B\Delta}_{\mathcal{K}_2,F}} \mu_{s,\mathcal{K}_1}(F_l(M,\Delta_2)) < 1. \end{cases}$$

Proof: The proof is similar to those of the main loop theorem [16] and the scaled main loop theorem [18] for the skewed structured singular value.

($\Leftarrow$) The inequality $\mu_{s,\mathcal{K}_2}(M_{22}) < \alpha$ implies that

$$\det(I - M_{22}\Delta_2) \neq 0, \quad \forall \Delta_2 \in \frac{1}{\alpha}\mathbf{B\Delta}_{\mathcal{K}_2,F}. \tag{12}$$

Similarly, the inequality $\max_{\Delta_2 \in \frac{1}{\alpha}\mathbf{B\Delta}_{\mathcal{K},F}} \mu_{s,\mathcal{K}_1}(F_l(M,\Delta_2)) < 1$ implies that

$$\det(I - F_l(M,\Delta_2)\Delta_1) \neq 0, \quad \forall \Delta_1 \in \mathbf{B\Delta}_{\mathcal{K}_1,F}, \quad \forall \Delta_2 \in \frac{1}{\alpha}\mathbf{B\Delta}_{\mathcal{K}_2,F}. \tag{13}$$

With (1), (12) and (13) imply that

$$\det(I - M\Delta) \neq 0, \quad \forall \Delta = \text{diag}[\Delta_1, \Delta_2],$$
$$\Delta_1 \in \mathbf{B\Delta}_{\mathcal{K}_1,F},$$
$$\Delta_2 \in \frac{1}{\alpha}\mathbf{B\Delta}_{\mathcal{K}_2,F}.$$

Therefore,

$$\det\left(I - M\begin{bmatrix}\Delta_1 & 0 \\ 0 & \frac{1}{\alpha}\Delta_2\end{bmatrix}\right) \neq 0, \ \forall \Delta_1 \in \mathbf{B\Delta}_{\mathcal{K}_1,F}, \ \forall \Delta_2 \in \mathbf{B\Delta}_{\mathcal{K}_2,F},$$

which implies that $\nu_{s,\mathcal{K}_1,\mathcal{K}_2}(M) < \alpha$.

($\Rightarrow$) $\nu_{s,\mathcal{K}_1,\mathcal{K}_2}(M) < \alpha$ implies that

$$\det\left(I - M\begin{bmatrix}\Delta_1 & 0 \\ 0 & \Delta_2\end{bmatrix}\right) \neq 0, \ \forall \Delta_1 \in \mathbf{B\Delta}_{\mathcal{K}_1,F}, \ \forall \Delta_2 \in \frac{1}{\alpha}\mathbf{B\Delta}_{\mathcal{K}_2,F}. \tag{14}$$

Equation (14) must hold for $\Delta_1 = 0 \in \mathbf{B\Delta}_{\mathcal{K}_1,F}$ and hence

$$\det(I - M_{22}\Delta_2) \neq 0, \quad \forall \Delta_2 \in \frac{1}{\alpha}\mathbf{B\Delta}_{\mathcal{K}_2,F}$$

and

$$\mu_{s,\mathcal{K}_2}(M_{22}) < \alpha, \tag{15}$$

which guarantees the well-posedness of $F_l(N, \Delta_2)$. Equations (14) and (15) with (1) imply that

$$\det(I - F_l(N,\Delta_2)\Delta_1) \neq 0, \quad \forall \Delta_1 \in \mathbf{B\Delta}_{\mathcal{K}_1,F}, \quad \forall \Delta_2 \in \frac{1}{\alpha}\mathbf{B\Delta}_{\mathcal{K}_2,F}$$

and

$$\max_{\Delta_2 \in \frac{1}{\alpha}\mathbf{B\Delta}_{\mathcal{K}_2,F}} \mu_{s,\mathcal{K}_1}(F_l(M,\Delta_2)) < 1.$$

□

The well-known small-gain theorem also holds with the Frobenius norm.

Theorem 5 (*Small gain theorem with Frobenius norm [28]*): For the matrix $M \in \mathbb{R}^{m\times m}$,

$$\|M\|_2 \min_{\Delta \in \mathbb{R}^{m\times m}} \{\|\Delta\|_F : \det(I - M\Delta) = 0\} = 1.$$

Proof: For any square matrices Δ and M, if $\det(I - M\Delta) = 0$ then there exists $x \neq 0$ such that $(I - M\Delta)x = 0$, which implies that

$$\begin{aligned} \|x\|_2 &= \|M\Delta x\|_2 \le \|M\|_2 \|\Delta x\|_2 \\ &\Rightarrow 1 \le \|M\|_2 \frac{\|\Delta x\|_2}{\|x\|_2} \\ &\le \|M\|_2 \|\Delta\|_2 \le \|M\|_2 \|\Delta\|_F. \end{aligned}$$

Completing the proof just requires showing that there exists a Δ in the set that shows that the latter inequality can be replaced by an equality. Choose

$$\Delta = \frac{1}{\|M\|_2} v u^{\mathrm{T}},$$

where a singular value decomposition of M is $M = U\Sigma V^{\mathrm{T}}$ and v and u are columns of U and V that correspond to the maximum singular value. Then Δ is a matrix of rank one with $\|\Delta\|_F = 1/\|M\|_2$ that satisfies

$$(I - M\Delta)u = u - U\Sigma V^{\mathrm{T}} \frac{1}{\|M\|_2} v u^{\mathrm{T}} u = u - u = 0,$$

so $I - M\Delta$ has a non-trivial null space and $\det(I - M\Delta) = 0$. Hence the inequality holds as an equality and the proof is complete. □

The next theorem is used when developing the proposed QbD algorithm.

Theorem 6 (A variation on the small-gain theorem for $\nu_{s,\Delta_1,\Delta_2}$): For $\mathcal{K}_2 = (r_1)$,

$$\max_{\Delta_1 \in \mathbf{B\Delta}_{\mathcal{K}_1,F}} \|F_u(M, \Delta_1)\|_2 = \sqrt{r_1}\, \nu_{s,\mathcal{K}_1,\mathcal{K}_2}(M).$$

Proof: For the right-hand side of Theorem 4, the following statements are equivalent.

$$\begin{aligned} &\nu_{s,\mathcal{K}_1,\mathcal{K}_2}(M) < \alpha \\ &\Leftrightarrow \begin{cases} \mu_{s,\mathcal{K}_2}(M_{22}) < \alpha, \\ \max_{\Delta_2 \in \frac{1}{\alpha}\mathbf{B\Delta}_{\mathcal{K}_2,F}} \mu_{s,\mathcal{K}_1}(F_l(M, \Delta_2)) < 1 \end{cases} \\ &\Leftrightarrow \begin{cases} \det(I - M_{22}\Delta_2) \neq 0, \ \det(I - F_l(M, \Delta_2)\Delta_1) \neq 0, \\ \forall \Delta_1 \in \mathbf{B\Delta}_{\mathcal{K}_1,F}, \ \forall \Delta_2 \in \frac{1}{\alpha}\mathbf{B\Delta}_{\mathcal{K}_2,F} \end{cases} \\ &\overset{(*)}{\Leftrightarrow} \begin{cases} \det(I - M_{11}\Delta_1) \neq 0, \ \det(I - F_u(M, \Delta_1)\Delta_2) \neq 0, \\ \forall \Delta_1 \in \mathbf{B\Delta}_{\mathcal{K}_1,F}, \ \forall \Delta_2 \in \frac{1}{\alpha}\mathbf{B\Delta}_{\mathcal{K}_2,F} \end{cases} \\ &\Leftrightarrow \begin{cases} \det(I - M_{11}\Delta_1) \neq 0, \ \forall \Delta_1 \in \mathbf{B\Delta}_{\mathcal{K}_1,F}, \\ \max_{\Delta_1 \in \mathbf{B\Delta}_{\mathcal{K}_1,F}} \|F_u(M, \Delta_1)\|_2 < \sqrt{r_1}\alpha, \end{cases} \end{aligned}$$

where $(*)$ is from (1) and $\mu_{s,\mathcal{K}_1}(M_{11}) < 1$, which can be shown in a similar manner as in (8). Therefore, from Theorem 4, it must hold

$$\nu_{s,\mathcal{K}_1,\mathcal{K}_2}(M) = \frac{1}{\sqrt{r_1}} \max_{\Delta_1 \in \mathbf{B\Delta}_{\mathcal{K}_1,F}} \|F_u(M, \Delta_1)\|_2.$$

□

5 Application to QbD

This section develops a numerical algorithm to determine a set of input parameters that ensures that the system output lies within a set of specifications. Functions relating the input and output of the system are assumed to be rational, so that an LFT can be constructed using multidimensional realisation algorithms.

Other non-linearities can be approximated with an LFT, by first expanding the system output by a multivariate polynomial or rational function of perturbations of the real parameters, which is then written as an LFT (see [3] for a detailed discussion). Tight bounds can be computed on the approximation error, which can be introduced as an additional perturbation in the analysis to ensure that all parameters in the constructed design space are valid for the original non-linearity.

5.1 Problem setup

Problem 1: Consider a system described by a rational map $y : \mathbb{R}^n \mapsto \mathbb{R}$, that maps a parameter vector $p \in \mathbb{R}^n$ to an output $y(p) \in \mathbb{R}$. Suppose that bounds $y_{\min}$ and $y_{\max}$ on $y(p)$ are given such that there exists at least one parameter vector p_0 that satisfies $y_{\min} \le y(p_0) \le y_{\max}$. The objective of the QbD analysis problem is to determine a matrix $E = E^{\mathrm{T}} > 0$ and a vector p_c such that an ellipsoid in the parameter space expressed by

$$\mathcal{E} = \{p : (p - p_c)^{\mathrm{T}} E (p - p_c) \le 1\}$$

has the maximum volume among all the ellipsoids in the parameter space whose elements consist only of model parameters p satisfying

$$y_{\min} \le y(p) \le y_{\max}. \tag{16}$$

The matrix E determines the shape of the ellipsoid and the vector p_c is the centre of the ellipsoid.

Due to the non-linearity in $y(p)$, it is straightforward to modify the proof of the NP-hardness of the μ analysis in [10] to show that the exact calculation of this design space $\mathcal{E}$ is NP-hard. The following subsection proposes a method for approximating the solution to Problem 1 with skewed spherical structured singular values.

5.2 Approach

The proposed approach to Problem 1 considers two subproblems.

5.2.1 Approximation problem: Determine a target shape of the uncertainty ellipsoid $\hat{E} = \hat{E}^{\mathrm{T}} > 0$ and the centre of the ellipsoid p_c for an initial estimate of a set

$$\hat{\mathcal{E}} = \{p : (p - p_c)^{\mathrm{T}} \hat{E} (p - p_c) \le 1\},$$

for which the most elements of $\hat{\mathcal{E}}$ satisfy (16) and the most parameters p satisfying (16) are in $\hat{\mathcal{E}}$.

This approximation problem can be skipped, if the nominal parameter vector p_c is known and the objective is to find a design space centred at the nominal parameter vector with a specified shape of the ellipsoid, such as a sphere.

5.2.2 Tuning problem: By scaling the initially estimated set $\hat{\mathcal{E}}$, find the maximum-volume ellipsoid of the form

$$\mathcal{E} = \{p : (p - p_c)^{\mathrm{T}} E (p - p_c) \le 1, \text{ where } E = \alpha^2 \hat{E} \text{ for some } \alpha \in \mathbb{R}\} \tag{17}$$

such that $\forall p \in \mathcal{E}$ satisfies (16).

Here p_c and $\hat{E}$ are known from the approximation problem and α is a tuning parameter that is used to maximise the volume of the ellipsoid.

This problem can be further simplified by using a unit ball, instead of an ellipsoid, by noting that the parameter set $\mathcal{E}$ defined in (17) can also be expressed by

$$\mathcal{E} = \{p : p = p_c + \alpha^{-1}\sqrt{\hat{E}}^{-1} \delta q, \ \|\delta q\|_2 \le 1, \ \alpha \in \mathbb{R}\}, \tag{18}$$

where p_c, $\hat{E}$, and α are the same as in (17). With δq in (18), the output of the system can be expressed using a different map $\hat{y} : \mathbb{R}^n \mapsto \mathbb{R}$ and the revised tuning problem is below.

5.2.3 Tuning problem′ (revised): Since the map is rational, it can be written in the form of an LFT. Suppose that the LFT has minimal dimension of Δ, so as to minimise the computational cost.

Find the smallest α for $M(\alpha)$ such that

$$y_{\min} \le F_u(M(\alpha), \Delta_1) \le y_{\max}, \tag{19}$$

where

$$y(p) = \hat{y}(\delta q) = F_u(M(\alpha), \Delta_1) \tag{20}$$

and $M(\alpha)$ takes the form of

$$M(\alpha) = \begin{bmatrix} \alpha^{-1}M_{11} & M_{12} \\ \alpha^{-1}M_{21} & M_{22} \end{bmatrix},$$

and

$$\Delta_1 = \operatorname{diag}\left[\frac{1}{\sqrt{r_1}}\delta q_1 I_{r_1}, \frac{1}{\sqrt{r_2}}\delta q_2 I_{r_2}, \ldots, \frac{1}{\sqrt{r_n}}\delta q_n I_{r_n} \right]$$

satisfies $\Delta_1 \in \mathbf{B\Delta}_{\mathcal{K}_1,F}$ given that $\|\delta q\|_2 \le 1$.

5.2.4 Algorithm for the approximation problem: *Step 1:* Approximate the region of p that satisfies (16) using a polytope $\mathcal{P} = \{p | a_i^{\mathrm{T}} p \le b_i, i = 1, \ldots, n\}$, which is used to obtain a better approximate solution to the problem in Step 2. The set $\mathcal{P}$ depends on n and a_i, which can be determined by the first-order Taylor series approximation of the system $y(p)$, or alternatively, some points on the boundary (namely, several p that satisfy $y(p) = y_{\min}$ or $y(p) = y_{\max}$) can be chosen as vertices. If $y(p)$ is polynomial in p, then finding the extreme values of $y(p)$ on the *boundary* of a given ellipsoid can be formulated in terms of linear matrix inequalities [29].

Step 2: With a fixed $\mathcal{P}$, find a maximum-volume ellipsoid

$$\hat{\mathcal{E}} = \{p : (p - p_c)^{\mathrm{T}} \hat{E}(p - p_c) \le 1\}$$

inside the polytope $\mathcal{P}$.

This problem of finding p_c and $\hat{E}$ can be written as (e.g. [30])

$$\max_{\hat{E}, p_c} \log\det \hat{E}^{-1}$$
$$\text{such that } \hat{E} = \hat{E}^{\mathrm{T}} > 0,$$
$$\mathcal{E} \subset \mathcal{P},$$

which can be cast as the max-det problem

$$\max_{\hat{E}, p_c} \log\det \hat{E}^{-1}$$

such that $\hat{E} = \hat{E}^{\mathrm{T}} > 0$

$$\begin{bmatrix} (b_i - a_i^{\mathrm{T}} p_c)I & \sqrt{\hat{E}}^{-1} a_i \\ a_i^{\mathrm{T}} \sqrt{\hat{E}}^{-1} & b_i - a_i^{\mathrm{T}} p_c \end{bmatrix} \ge 0, \quad i = 1, \ldots n.$$

This max-det problem can be solved by using algorithms given in [31, 32].

5.2.5 Algorithm for the tuning problem: The tuning problem scales the initially estimated ellipsoid by iteratively applying bisections and the main loop theorem for the skewed spherical structured singular value. The steps and pseudocode are given below in Algorithm 1 (see, Fig. 1).

Algorithm 1 :

Input: $y_{\max}$, $y_{\min}$, $\hat{E}$, p_c, $\epsilon > 0$ (tolerance)
Output: E

Step 1 (Initialisation):
  Choose $\alpha_1 > 0$ and $\alpha_2 > 0$ such that α_1 satisfies (19) and α_2 does not satisfy (19).[1]
Step 2 (Bisection):
while $\alpha_1 - \alpha_2 > \epsilon$ **do**
  $\alpha_c := (\alpha_1 + \alpha_2)/2$
  Step 2-1 (write in shifted forms):
  Choose large enough $c > 0$ and write

$$\begin{aligned} y &= F_u(M(\alpha_c), \Delta_1) \\ &= \underbrace{F_u(M(\alpha_c), \Delta_1) + c}_{:=F_u(M_{\max}(\alpha_c), \Delta_1)} - c \\ &= \underbrace{F_u(M(\alpha_c), \Delta_1) - c}_{:=F_u(M_{\min}(\alpha_c), \Delta_1)} + c \end{aligned}$$

  Step 2-2 (apply the skewed structured singular value to compute bounds with unstructured $\mathcal{K}_2$):

$$\bar{y} = \nu_{s,\mathcal{K}_1,\mathcal{K}_2}(M_{\max}(\alpha_c)) - c,$$
$$\underline{y} = -\nu_{s,\mathcal{K}_1,\mathcal{K}_2}(M_{\min}(\alpha_c)) + c$$

  Step 2-3 (update bisection parameters):
  if $y_{\min} \le \underline{y}$ and $\bar{y} \le y_{\max}$, **then**
    replace α_1 by α_c
  else
    replace α_2 by α_c
  end if
end while

Fig. 1 *Algorithm for the tuning problem*
Compute a maximum-volume uncertainty ellipsoid

Step 1: Prepare to apply the bisection algorithm by choosing two appropriate ellipsoids, one small and one large such that any p in the small ellipsoid satisfies (16), but the larger ellipsoid contains a p that does not satisfy (16).

Step 2: Apply the bisection algorithm. The values of the maximum and minimum of $F_u(M(\alpha_c), \Delta_1)$ need to be computed to continue the bisection algorithm.

Step 2-1: For a sufficiently large $c > 0$, $F_u(M(\alpha_c), \Delta_1) + c = F_u(M_{\max}(\alpha_c), \Delta_1) > 0$ for any $\Delta_1 \in \mathbf{B\Delta}_{\mathcal{K}_1,F}$, and

$$\begin{aligned} \max_{\Delta_1 \in \mathbf{B\Delta}_{\mathcal{K}_1,F}} F_u(M(\alpha_c), \Delta_1) &= \max_{\Delta_1 \in \mathbf{B\Delta}_{\mathcal{K}_1,F}} F_u(M_{\max}(\alpha_c), \Delta_1) - c \\ &= \max_{\Delta_1 \in \mathbf{B\Delta}_{\mathcal{K}_1,F}} |F_u(M_{\max}(\alpha_c), \Delta_1)| - c. \end{aligned}$$

Note that, for a scalar y, $\|y\|_2 = |y|$. Similarly

$$\begin{aligned} \min_{\Delta_1 \in \mathbf{B\Delta}_{\mathcal{K}_1,F}} F_u(M(\alpha_c), \Delta_1) &= \min_{\Delta_1 \in \mathbf{B\Delta}_{\mathcal{K}_1,F}} F_u(M_{\min}(\alpha_c), \Delta_1) + c \\ &= -\max_{\Delta_1 \in \mathbf{B\Delta}_{\mathcal{K}_1,F}} |F_u(M_{\min}(\alpha_c), \Delta_1)| + c. \end{aligned}$$

Step 2-2: By using Theorem 6, the maximum and minimum of the output range with parameter α_c can be found by

$$\max_{\Delta_1 \in \mathbf{B\Delta}_{\mathcal{K}_1,F}} F_u(M(\alpha_c), \Delta_1) = \nu_{s,\mathcal{K}_1,\mathcal{K}_2}(M_{\max}(\alpha_c)) - c,$$
$$\min_{\Delta_1 \in \mathbf{B\Delta}_{\mathcal{K}_1,F}} F_u(M(\alpha_c), \Delta_1) = -\nu_{s,\mathcal{K}_1,\mathcal{K}_2}(M_{\min}(\alpha_c)) + c.$$

Step 2-3: By using Step 2-2, determine if $F_u(M(\alpha_c), \Delta_1)$ remains inside the given bounds for any $\Delta_1 \in \mathbf{B\Delta}_{\mathcal{K}_1,F}$ and update the bisection parameters.

6 Extensions

Some extensions to multiple outputs are described in this section.

6.1 Box bounds on multiple outputs

Suppose that a system is described by a non-linear map $y : \mathbb{R}^n \mapsto \mathbb{R}^n$ in the form of an LFT that, for a parameter vector p, yields an output vector $y(p) \in \mathbb{R}^n$, and that vectors $y_{\min}$ and $y_{\max}$ are given as bounds on the output vector, such that $y_{\min} \le y(p) \le y_{\max}$. Then, the same analysis can be applied to each output, and the final allowable set of parameters is the intersection of the n allowable sets for each output. This proposed method can be applied to any type of mathematical model in which the output is a continuous function of the model parameters, including grey- and black-box models, as well as first-principles models.

6.2 Ellipsoidal bound on multiple outputs

Suppose that the bound on the output is given in the form of a hyperellipsoid

$$y(p)^{\mathrm{T}} A y(p) \le 1$$

for some matrix $A = A^{\mathrm{T}} > 0$, instead of bounds on each output $y_{\min} \le y(p) \le y_{\max}$. With (20), this constraint can be written as

$$\|\sqrt{A} F_u(M(\alpha), \Delta_1)\|_2 = \|F_u(M'(\alpha), \Delta_1)\|_2 \le 1, \qquad (21)$$

where

$$M'(\alpha) = \mathrm{diag}\left[\sqrt{A},\ I\right] M(\alpha).$$

This ellipsoidal bound on a vector output can be handled by replacing Step 2 of the tuning problem with checking whether

$$\|F_u(M'(\alpha_c), \Delta_1)\|_2 \le 1$$

for a given α_c.

7 Numerical examples

Three examples are presented in this section. The first example is somewhat artificial, while the second example is to determine a possible parameter range for a nasal spray so that the plume width is in a desirable range. The last example considers conditions for avoiding the occurrence of bifurcations, which corresponds to the case of box bounds on multiple outputs as discussed in Section 6.

In each example, four sets are compared

B: a box set computed by (non-spherical) ν upper bounds, as proposed in [3],
Eg: an ellipsoidal set computed by bisection with spherical μ gridding,
Eμ: an ellipsoidal set computed by bisection with spherical μ upper bound, and
Eν: an ellipsoidal set computed by spherical ν upper bound using Theorem 1.

In the computations of **Eg** and **Eμ**, Algorithm 2 (see Fig. 3) in the appendix is used.

Example 1: Possible parameter values for x and y

An output is given by

$$f = -\frac{10\bar{x}\bar{y}}{3\bar{x} - 10},$$

where $\bar{x}$ and $\bar{y}$ are scaled factor values of two parameters x and y, respectively, with

$$\bar{x} = \frac{2(x - 20)}{30 - 10}, \quad \bar{y} = \frac{2(y - 5)}{7 - 3}.$$

It is desired to keep $-0.2 \le f \le 0.2$.

Example 2: Possible parameter values for V and C.

A model for the plume width R of a nasal spray given by Guo *et al.* [33] is

$$R = 26.71 + 8.32V - 8.13C - 4.34V^2 + 4.34C^2,$$

where V and C are the scaled factor values for velocity and carboxymethylcellulose (CMC) concentration, respectively, defined by

$$V = \frac{2(\text{velocity} - 50)}{70 - 30}, \quad C = \frac{2(\text{CMC concentration} - 1\%)}{2\% - 0\%}.$$

It is desired that the nasal spray has a plume width of $15 \le R \le 30$. See [3] for the construction of an LFT for this example.

Example 3: Possible parameter values for p_1, p_2, and p_3 (a higher-dimensional case)

A predator-prey model is given by [34, 35]

$$\dot{x}_1 = x_1(1 - x_1) - \frac{p_1 x_1 x_2}{p_3 + x_1},$$
$$\dot{x}_2 = -p_2 x_2 + \frac{p_1 x_1 x_2}{p_3 + x_1},$$

where x_1 and x_2 are scaled population numbers, and p_1, p_2, p_3 are parameters that characterise the behaviour of the system. For this system to avoid bifurcations, the parameters must satisfy two conditions: one to avoid a steady-state bifurcation and one to avoid a Hopf bifurcation; these conditions can be simplified to two scalar conditions [36].

7.1 Discussion

Figs. 2*a–c* show the sets of allowable parameters.

For a fair comparison of box and ellipsoidal sets, the simulations are performed with fixed nominal parameters, which are denoted by a red dot in each figure. It is possible to scale and/or change the centre location of the square box to obtain a larger box; however, such a framework may require more computational effort (see [37] for a description of how to optimise the centre location).

To solve approximation problem, an initial estimate of a polytope is obtained from four vertices on the boundary in Example 1, three vertices on the boundary in Example 2, and two faces by linearising the bifurcation conditions around the nominal parameters $p_c = [9, 2, 2]^{\mathrm{T}}$ and four planes by forcing $7 \le p_1 \le 11$ and $0 \le p_2 \le 4$ in Example 3.

In all the figures, the ellipsoidal set covers a larger region than a box; nevertheless, both the set based on the known spherical μ upper bound [26] (**Eμ**) and the set based on the derived spherical ν upper bound (**Eν**) are conservative. The upper bound in Theorem 1, **Eν**, is less conservative than **Eμ** in Example 1, but vice versa in Example 2. The conservativeness comes from the conservativeness of LMI upper bounds for spherical uncertainties, as **Eg**, which replaces the LMI upper bounds by gridding, gives tight results in all examples.

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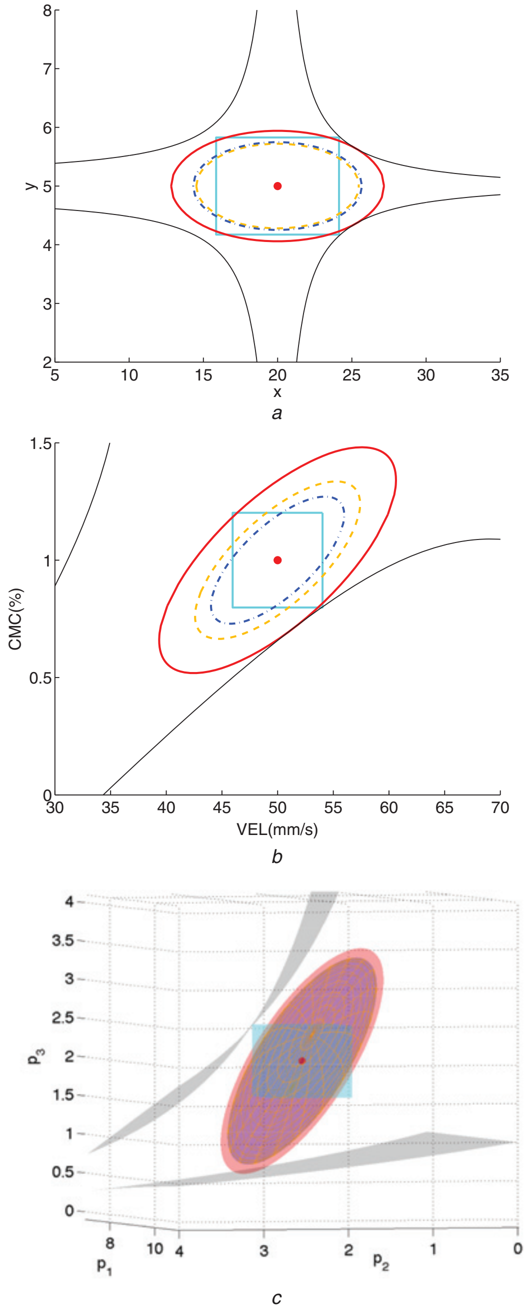

Fig. 2 *Allowable parameter sets: nominal parameters (red dot), exact set (between the two solid black curves),* **B** *(solid cyan),* **Eg** *(solid red),* **Eμ** *(yellow dashed/wire), and* **Eν** *(blue dasheddot/surface)*

a Example 1
b Example 2
c Example 3

8 Conclusions

This paper introduces the skewed spherical structured singular value and describes its use in a numerical algorithm to construct design spaces in QbD. In particular, an upper bound, the scaled main loop theorem, and the small-gain theorem for the skewed spherical structured singular value are derived for the algorithm.

Numerical examples show that an ellipsoidal design space can produce a larger region than a box design space; while motivating further research toward the development of better algorithms for computing polynomial-time upper and lower bounds on the spherical structured singular value.

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10 References

1 Juran, J.M.: ‘Juran on quality by design: the new steps for planning quality into goods and services’ (The Free Press, New York, 1992)
2 Garcia-Munoz, S., Dolph, S., Ward, H.W.: ‘Handling uncertainty in the establishment of a design space for the manufacture of a pharmaceutical product’, *Comput. Chem. Eng.*, 2010, **34**, pp. 1098–1107
3 Kishida, M., Braatz, R.D.: ‘A skewed structured singular value based approach for the construction of design spaces: theory and applications’, *IET Control Theory Appl.*, 2014, **8**, pp. 1321–1327
4 Kishida, M., Braatz, R.D.: ‘Ellipsoidal bounds on state trajectories for discrete-time systems with linear fractional uncertainties’, *Opt. Eng.*, 2014, pp. 1–17 http://dx.doi.org/10.1007/s11081-014-9255-9
5 Smith, R.S.R.: ‘Model validation for uncertain systems’. PhD thesis, California Institute of Technology, Pasadena, California, 1990
6 Khatri, S., Parrilo, P.A.: ‘Spherical μ’. Proc. of the American Control Conf., 1998, pp. 2314–2318
7 Doyle, J.C.: ‘Analysis of feedback systems with structured uncertainty’, *IEE Proc. D Control Theory Appl.*, 1982, **129**, pp. 242–250
8 Safonov, M.G.: ‘Stability margins of diagonally perturbed multivariable feedback systems’, *IEE Proc. D Control Theory Appl.*, 1982, **129**, pp. 251–256
9 Safonov, M.G., Doyle, J.C.: ‘Minimizing conservativeness of robustness singular values’, in Tzafestas S.G. (Ed.): ‘Multivariable control’, (Springer, Dordrecht, Netherlands, 1984), pp. 197–207
10 Braatz, R.D., Young, P.M., Doyle, J.C., Morari, M.: ‘Computational complexity of μ calculation’, *IEEE Trans. Autom. Control*, 1994, **39**, pp. 1000–1002
11 Fan, M., Tits, A.: ‘Characterization and efficient computation of the structured singular value’, *IEEE Trans. Autom. Control*, 1986, **31**, pp. 734–743
12 Packard, A., Doyle, J.: ‘The complex structured singular value’, *Automatica*, 1993, **29**, pp. 71–109
13 Packard, A., Fan, M., K.H., Doyle, J.: ‘A power method for the structured singular value’. Proc. of the IEEE Conf. on Decision and Control, 1988, pp. 2132–2137
14 Young, P.M., Doyle, J.C.: ‘A lower bound for the mixed μ problem’, *IEEE Trans. Autom. Control*, 1997, **42**, pp. 123–128
15 Doyle, J., Packard, A., Zhou, K.: ‘Review of LFTs, LMIs, and μ’. Proc. of the IEEE Conf. on Decision and Control, 1991, pp. 1227–1232
16 Zhou, K., Doyle, J.C., Glover, K.: ‘Robust and optimal control’ (Prentice-Hall, Upper Saddle River, New Jersey, 1995)
17 Fan, M.K.H., Tits, A.: ‘A measure of worst-case H_∞ performance and of largest acceptable uncertainty’, *Syst. Control Lett.*, 1992, **18**, pp. 409–421
18 Ferreres, G., Fromion, V.: ‘A new upper bound for the skewed structured singular value’, *Int. J. Robust Nonlinear Control*, 1999, **9**, pp. 33–49
19 Andreescu, T.: ‘Essential linear algebra with applications: a problem-solving approach’ (Birkhäuser, Basel, 2014)
20 Russell, E.L., Power, C.P.H., Braatz, R.D.: ‘Multidimensional realizations of large scale uncertain systems for multivariable stability margin computation’, *Int. J. Robust Nonlinear Control*, 1997, **7**, pp. 113–125
21 Russell, E.L., Braatz, R.D.: ‘Model reduction for the robustness margin computation of large scale uncertain systems’, *Comput. Chem. Eng.*, 1998, **22**, pp. 913–926
22 Fu, M., Barabanov, N.E.: ‘Improved upper bounds for the mixed structured singular value’, *IEEE Trans. Autom. Control*, 1997, **42**, pp. 1447–1452
23 Horn, R.A., Johnson, C.R.: ‘Matrix analysis’ (Cambridge University Press, New York, NY, 1990)
24 Khatri, S.: ‘Extensions to the structured singular value’. PhD thesis, California Institute of Technology, Pasadena, California, 1999
25 Boyd, S., El Ghaoui, L., Feron, E., Balakrishnan, V.: ‘Linear matrix inequalities in system and control theory’ (SIAM, Philadelphia, 1994)
26 Ishimoto, S., Terui, F.: ‘Spherical μ with application to flight control analysis’, *J. Guid. Control, Dyn.*, 2002, **25**, pp. 1021–1028
27 Zhu, X., Khatri, S., Parrilo, P.A.: ‘μ with linear cuts: Upper bound computation’. Proc. of the American Control Conf., 1999, pp. 2370–2374
28 Frazzoli, E.: ‘Lecture note of 6.241 on February 16, 2011, 2011, Available at http://ocw.mit.edu/courses/electrical-engineering-and-computer-science/6-241j-dynamic-systems-and-control-spring-2011/lecture-notes/
29 Chesi, G.: ‘LMI techniques for optimization over polynomials in control: a survey’, *IEEE Trans. Autom. Control*, 2010, **55**, pp. 2500–2510
30 Vandenberghe, L., Boyd, S., Wu, S.-P.: ‘Determinant maximization with linear matrix inequality constraints’, *SIAM J. Matrix Anal. Appl.*, 1998, **19**, pp. 499–533
31 Khachiyan, L.G., Todd, M.J.: ‘On the complexity of approximating the maximal inscribed ellipsoid for a polytope’, *Math. Program.*, 1993, **61**, pp. 137–159
32 Nesterov, Y., Nemirovskii, A.: ‘Interior-point polynomial algorithms in convex programming’ (SIAM, Philadelphia, Pennsylvania, 1994)
33 Guo, C., Stine, K.J., Kauffman, J.F., Doub, W.H.: ‘Assessment of the influence factors on in vitro testing of nasal sprays using Box–Behnken experimental design’, *Eur. J. Pharm. Sci.*, 2008, **35**, pp. 417–426
34 Holling, C.S.: ‘The functional response of predators to prey density and its role in mimicry and population regulation’, *Memoirs of the Entomological Society of Canada*, 1965, **97**, Supplement S45, pp. 5–60

35 Kuznetsov, Y.: 'Elements of applied bifurcation theory' (Springer, New York, 2004, 3rd edn.)

36 Kishida, M., Braatz, R.D.: 'Non-existence conditions of local bifurcations for rational systems with structured uncertainties'. Proc. of the American Control Conf., 2014, pp. 5085–5090

37 Kishida, M., Braatz, R.D.: 'Volume maximization of consistent parameter sets for linear fractional models'. Proc. of the IEEE Conf. on Decision and Control, 2014, pp. 1905–1910

38 Kishida, M., Braatz, R.D.: 'Quality-by-design by using the skewed spherical structured singular value'. Proc. of the American Control Conf., 2013, pp. 6673–6678

39 Ferreres, G., Fromion, V.: 'Computation of the robustness margin with the skewed μ tool', *Syst. Control Lett.*, 1997, **32**, pp. 193–202

11 Appendix

A regular (non-spherical) skewed structured singular value can be obtained from a regular structured singular value using fixed point iteration [39]. However, this approach is not straightforward from the spherical structured singular value to the skewed spherical structured singular value. An approach that uses bisection is described in Algorithm 2 (see Fig. 3).

This algorithm utilises the fact that the second uncertainty block is scalar for the examples. The initial value $\alpha_1 = 0$ comes from $k > 0$ in Definition 2, and $\alpha_2 = 1/|M_{22}|$ comes from $\det(I - M_{22}\Delta_2) \neq 0$ from (1). $\max\{\mu_{s,\mathcal{K}}(M1), \mu_{s,\mathcal{K}}(M2)\} < 1$ is the condition that $\nu_{s,\mathcal{K}_1,\mathcal{K}_2}(M)$ is greater that k_c.

Algorithm 2 :

Input: M, $\mathcal{K}_1$,$\mathcal{K}_2$, ϵ

Output: $\nu_{s,\mathcal{K}_1,\mathcal{K}_2}(M)$

(Initialisation): $k_1 = 0$ and $k_2 = 1/|M_{22}|$.
(Bisection):
while $|1 - k_1/k_2| > \epsilon$ **do**
  $k_c := (k_1 + k_2)/2$

$$M1 = (M_{11} + k_c M_{12}/(1 - k_c M_{22}) M_{21})$$
$$M2 = (M_{11} - k_c M_{12}/(1 + k_c M_{22}) M_{21})$$

  if $\max\{\mu_{s,\mathcal{K}}(M1), \mu_{s,\mathcal{K}}(M2)\} < 1$, **then**
    replace k_1 by k_c
  else
    replace k_2 by k_c
  end if
end while
$\nu_{s,\mathcal{K}_1,\mathcal{K}_2}(M) = 1/k_c$

Fig. 3 *Compute spherical ν using spherical μ*