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Systematizing product design by latent-variable modeling – A unifying framework for the formulation and solution of PLS model inversion problems

Elia Arnese-Feffin [a,b,*], Pierantonio Facco [a], Fabrizio Bezzo [a], Massimiliano Barolo [a]

[a] CAPE-Lab – Computer-Aided Process Engineering Laboratory, Department of Industrial Engineering, University of Padova, via Marzolo 9, 35131 Padova PD, Italy
[b] INSTM – Consorzio Interuniversitario Nazionale per la Scienza e Tecnologia dei Materiali, via Giusti 5, 50121 Firenze FI, Italy

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ABSTRACT

Data-driven modeling has significantly transformed problem-solving in the process industry, especially in designing new products digitally by finding the process conditions that are required to manufacture a product with assigned quality. This can be achieved by utilizing historical process data via latent-variable model inversion, notably through the extensively used partial least-squares (PLS) regression model. Despite the development of numerous PLS model-inversion techniques, from straightforward algebraic manipulation of the model equations to the formulation and solution of complex nonlinear optimization problems, there lacks a comprehensive discussion on their comparative benefits and limitations. This paper offers a systematic analysis of PLS model inversion strategies, especially those based on optimization problems. We delve into aspects such as optimization in the latent or input variable spaces, the nature of constraints (soft vs. hard), and the feasibility of analytical solutions. We outline a clear hierarchical structure of the available methods based on the successive inclusion of constraints, and propose a general formulation of the PLS model inversion by optimization problem that encompasses all available methods. We support our theoretical analysis with a numerical case study, and provide the code to reproduce it and to solve general latent-variable model inversion problems according to the proposed formulation.

1. Introduction

Data-driven modeling has become a valuable asset in the toolbox of process systems engineers due to the ever-growing availability of data from manufacturing processes, computational infrastructures, and efficient data analytics methods (Reis and Saraiva, 2021). Latent-variable models, such as principal component analysis (PCA; Wise and Gallagher, 1996; Wold et al., 1987) and partial least-squares (PLS) regression (Geladi and Kowalski, 1986; Wold et al., 2001), are attractive modeling platforms due to their architectural simplicity, ability to deal with a massive number of (possibly strongly correlated) variables, computational efficiency, and straightforward interpretability. These features make latent-variable models particularly attractive to tackle industry-relevant problems regarding, e.g., process understanding (Camacho et al., 2010; García-Muñoz et al., 2003; Kosanovich et al., 1996; Vitale et al., 2021), soft sensing (Arnese-Feffin et al., 2024; Philippe et al., 2013), and process monitoring (Kourti and MacGregor, 1995; Qin, 2003; Reis and Gins, 2017).

PLS is used to build a regression model between a set of input variables (e.g., those representing process operating conditions and/or raw materials properties) and a set of output variables (e.g., those quantifying the product quality), while simultaneously providing models for the spaces of input and output variables. The model is calibrated using historical data and can be applied to a given set of new process conditions to predict the product quality. However, it can also be used "in reverse mode" to address product design problems, i.e., to estimate the process conditions that are required to manufacture a product with an assigned target quality. This is the principle of latent-variable model inversion (LVMI; Ferrer, 2021; Jaeckle and MacGregor, 2000; Tomba et al., 2012). A schematic representation of LVMI is illustrated in Fig. 1.

LVMI was first proposed based on algebraic manipulation of the PLS model equations, also referred to as direct inversion (DI; Jaeckle and

* Corresponding author at: CAPE-Lab – Computer-Aided Process Engineering Laboratory, Department of Industrial Engineering, University of Padova, via Marzolo 9, 35131 Padova PD, Italy.
E-mail address: elia.arnesefeffin@phd.unipd.it (E. Arnese-Feffin).

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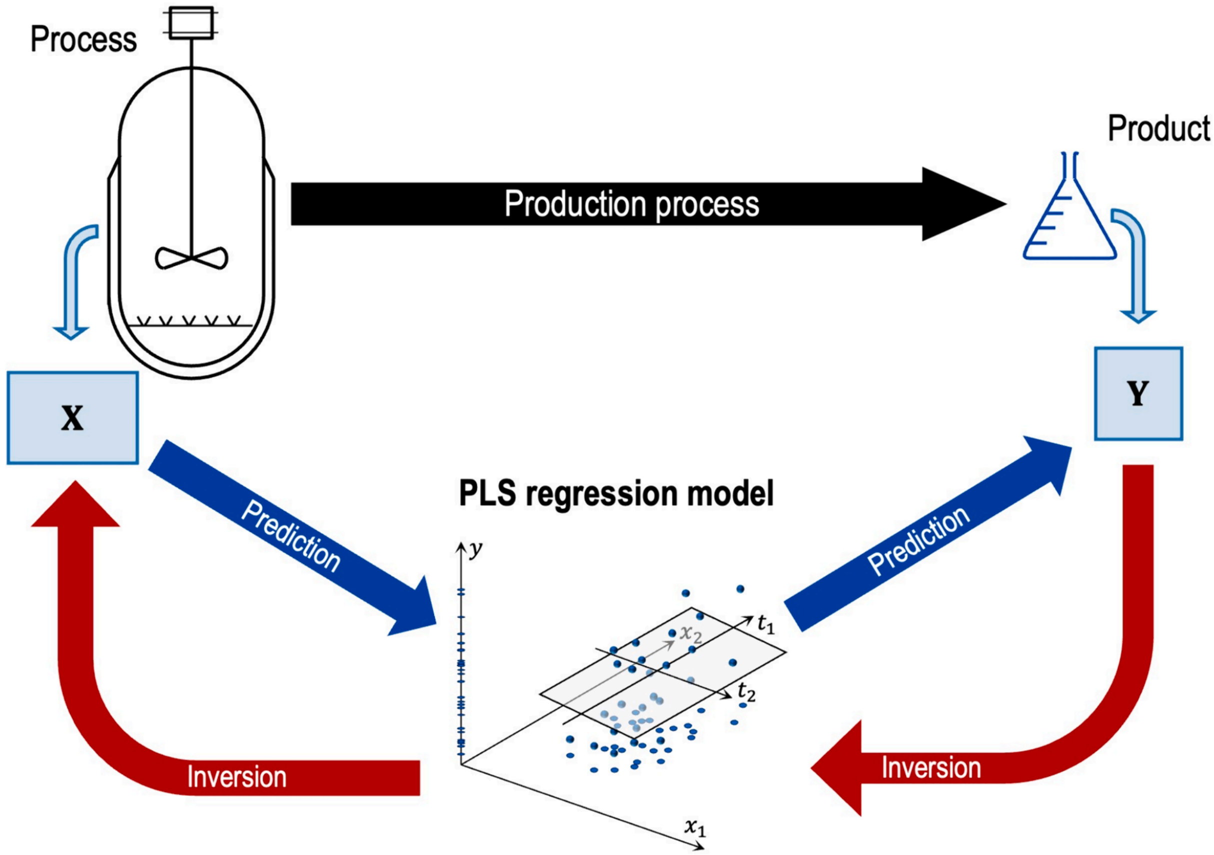

Fig. 1. Schematic workflow of latent-variable model inversion. Process conditions (**X**) are used in the prediction path to estimate the product quality (**Y**). In the inversion path, a target quality is set, and the model is inverted to find the process conditions that allow one to manufacture a product with the desired quality.

MacGregor, 2000, 1998). Shortly thereafter, PLS model inversion was re-formulated as an optimization problem (inversion by optimization, IbO; Yacoub and MacGregor, 2004). In IbO, the optimization problem is formulated in the space of latent variables, which offers advantages in that the optimization variables are few in number and independent (Ferrer, 2020); furthermore, IbO allows one to set soft and hard constraints on latent and output variables (García-Muñoz et al., 2006). To set hard constraints on the designed process conditions, IbO was generalized by formulating the optimization problem in the space of input variables by a two-step optimization strategy (García-Muñoz et al., 2008). The method was later extended to a single-step optimization problem (Tomba et al., 2012), which allows one to handle cases in which not all output variables have an assigned target. In a further generalization, LVMI was re-formulated as a multi-objective optimization problem, which is referred to as inversion by multi-objective optimization (Arce et al., 2021; Ruiz et al., 2018); however, this latter approach is not addressed by this study.

Besides the main developments described above, the research on LVMI focused also on the extension of DI to specific cases, e.g., targets set on linear combinations of the quality variables (Palací-López et al., 2019) and existence of correlated output variables (Arnese-Feffin et al., 2022). Finally, LVMI has been extended to other PLS-based methods, e.g., joint-Y PLS (García-Muñoz et al., 2005), total PLS (Zhao et al., 2019), kernel PLS (Zhu et al., 2021), and sequential-multiblock PLS (Borràs-Ferrís et al., 2023). Reported applications of LVMI are numerous, and the interested reader may find details elsewhere (Arnese-Feffin et al., 2022).

Although various seemingly alternative versions of LVMI exist in the literature, there is no systematic discussion regarding their merits and limitations. There is also a lack of clarity on whether to use soft or hard constraints, or whether to formulate the optimization problem in the latent space or the input variables space. While a recent discussion of inverse design using PLS modeling by Palací-López et al. (2024) touches on these points, it does not provide detailed guidance. Additionally, the extent to which DI can be considered a special case of IbO remains unclear. Finally, there are no clear guidelines for formulating the optimization problem.

This study provides a systematic analysis of the existing approaches for the formulation of latent-variable model-inversion problems. We discuss the merits and drawbacks of formulating the model-inversion problem in the space of latent variables or in the space of inputs. We show how the solution of the IbO problem can be obtained by computationally efficient methods, sometimes even in analytical form, by properly formulating the constraints on the model validity region. We outline a well-defined hierarchical structure in the formulation of the LVMI problem based on the successive inclusion of constraints, which results in clear guidelines for the solution algorithm to be used and, consequently, determines the computational demand of the solution. We finally identify a general form of the LVMI problem and highlight how all the cases in the proposed hierarchical structure can be derived from such general problem. Our reasoning is supported by subsequent simulations on a case study, which is used throughout the entire discussion to support our theoretical derivations.

The rest of this paper is organized as follows. We describe the mathematical background used in this study in Section 2, introducing PLS modeling, the algebraic formulations of LVMI, and the formalism of optimization we adopt; we provide further details on mathematical methods relevant to the discussion in Appendix A, Appendix B, and Appendix C. In Section 3 we introduce the case study, which we use to illustrate our theoretical analysis throughout Section 4, where we discuss several properties of IbO and develop a clear hierarchical structure, highlighting the consistency of the simplest cases with algebraic solution methods. In Section 5 we propose a general formulation for the IbO problem, which encompasses all cases investigated in Section 4. We draw the conclusions of this study in Section 6.

2. Mathematical background

In this section, we introduce the mathematical methods used in this study. We first describe PLS model regression, then introducing the algebraic methods for PLS model inversion. Finally, we describe the general form of the optimization problem we will refer to throughout our analysis of IbO. Upright bold uppercase symbols indicate matrices, upright bold lowercase symbols denote vectors, and symbols in italics refer to scalars. Vectors are arranged column-wise.

2.1. Partial-least squares regression

PLS regression (Geladi and Kowalski, 1986; Wold et al., 2001) is typically described based on a matrix $\mathbf{X} \in \mathbb{R}^N \times \mathbb{R}^{V_X}$, collecting N observations of V_X input (predictor) variables, and a matrix $\mathbf{Y} \in \mathbb{R}^N \times \mathbb{R}^{V_Y}$, gathering corresponding observations of V_Y output (response) variables. However, for the purpose of the theoretical analysis to be outlined in Section 4, it is convenient to adopt an alternative description of the PLS model, namely, based on random vectors of input and output variables, $\mathbf{x} \in \mathbb{R}^{V_X}$ and $\mathbf{y} \in \mathbb{R}^{V_Y}$, respectively, which offers a more straightforward interpretation of the PLS model in terms of linear operators. We describe the random-vector form of PLS in this Section, referring the readers to the literature for the classical sample form (Geladi and Kowalski, 1986; Wold et al., 2001).

PLS regression establishes a linear regression model between the spaces of input and output variables, while at the same time providing models for the spaces themselves. This is done by identifying two sequences of $A \ll V_X$ mutually orthogonal latent variables (LVs), one for the inputs and one for the outputs, defined as linear combinations of the input and output variables, respectively. LVs are formulated to maximize the modeled cross-covariance between $\mathbf{x}$ and $\mathbf{y}$, while at the same time retaining as much of the variances of $\mathbf{x}$ and $\mathbf{y}$ as possible.

Under the assumption that $\mathbf{x}$ and $\mathbf{y}$ follow multivariate standard normal distributions (i.e., their means are null vectors, and their covariance matrices are identity matrices), the models for input and output spaces are provided as:

$$\mathbf{x} = \mathbf{P}\cdot\mathbf{t} + \mathbf{e}, \tag{1}$$

$$\mathbf{y} = \mathbf{Q}\cdot\mathbf{u} + \mathbf{f}, \tag{2}$$

where $\mathbf{t} \in \mathbb{R}^A$ and $\mathbf{u} \in \mathbb{R}^A$ are the vectors of input and output LVs, respectively, i.e., the projections of input and output vectors onto the spaces of input and output LVs, respectively; matrices $\mathbf{P} \in \mathbb{R}^{V_X} \times \mathbb{R}^A$ and $\mathbf{Q} \in \mathbb{R}^{V_Y} \times \mathbb{R}^A$ (typically called loading matrices) are linear reduced-rank projection operators from the spaces of input and output LVs, respectively, to the spaces of input and output variables, respectively; $\mathbf{e} \in \mathbb{R}^{V_X}$ and $\mathbf{f} \in \mathbb{R}^{V_Y}$ are the vectors of projection residuals of $\mathbf{x}$ and $\mathbf{y}$. The symbol $\cdot$ is the row-by-column matrix product.

Concerning the PLS regression model, input LVs can be computed from the input variables as:

$$\mathbf{t} = (\mathbf{W}^*)^\top\cdot\mathbf{x}. \tag{3}$$

where $^\top$ denotes the matrix transpose operator. Matrix $\mathbf{W}^* \in \mathbb{R}^{V_X} \times \mathbb{R}^A$ is a linear reduced-rank projection operator from the space of input variables to the space of input LVs (also called the matrix of corrected, or rotated, input weights), which is related to the model of the input space as:

$$\mathbf{W}^* = \mathbf{W}\cdot(\mathbf{P}^\top\cdot\mathbf{W})^{-1}. \tag{4}$$

Matrix $\mathbf{W} \in \mathbb{R}^{V_X} \times \mathbb{R}^A$ is the input weight matrix, the columns of which are computed one at the time in PLS calibration to maximize cross-covariance between $\mathbf{x}$ and $\mathbf{y}$ retained by the model[1] (Wold et al., 2001). This operation results in the input and output LVs being as linearly correlated as possible, while at the same time maximizing the variances of input and output variables retained by the PLS model (i.e., the variances of input and output LVs, respectively). Input and output LVs are connected by a sequence of A additive linear regression models between pairs of corresponding LVs, expressed in compact notation as:

$$\mathbf{u} = \mathrm{diag}(\mathbf{b})\cdot\mathbf{t} + \mathbf{v}, \tag{5}$$

where vector $\mathbf{b} \in \mathbb{R}^A$, the PLS inner regression coefficients, lays on the diagonal of matrix $\mathrm{diag}(\mathbf{b}) \in \mathbb{R}^A \times \mathbb{R}^A$, acting as a linear projection model between the spaces of input and output LVs; $\mathbf{v} \in \mathbb{R}^A$ is the vector of inner regression residuals.

The number A of LVs is usually set to maximize the predictive performance of the PLS model, e.g., by cross-validation (Bro et al., 2008; Louwerse et al., 1999). All the operators in the PLS model ($\mathbf{P}$, $\mathbf{Q}$, $\mathbf{W}$, and $\mathbf{b}$) can be computed by any PLS calibration algorithm to satisfy all model equations. Readers are referred to literature resources for additional information (Geladi and Kowalski, 1986; Wold et al., 2001).

Once calibrated using historical data on $\mathbf{x}$ and $\mathbf{y}$, the PLS model can be applied to a new input vector $\mathbf{x}_{\mathrm{new}} \in \mathbb{R}^{V_X}$ (assumed to follow the same distribution as $\mathbf{x}$) to obtain $\widehat{\mathbf{y}}_{\mathrm{new}}$, an estimate of the corresponding (unknown) true output vector $\mathbf{y}_{\mathrm{new}} \in \mathbb{R}^{V_Y}$. The input vector is first projected onto the space of input LVs by (3):

$$\mathbf{t}_{\mathrm{new}} = (\mathbf{W}^*)^\top\cdot\mathbf{x}_{\mathrm{new}}, \tag{6}$$

Upon definition of a modified output loading matrix:

$$\widetilde{\mathbf{Q}} = \mathbf{Q}\cdot\mathrm{diag}(\mathbf{b}). \tag{7}$$

the estimate of the output observation is computed according to the output space model, (2):

$$\widehat{\mathbf{y}}_{\mathrm{new}} = \widetilde{\mathbf{Q}}\cdot\mathbf{t}_{\mathrm{new}}. \tag{8}$$

Equations (6) and (8) can be summarized in a single equation directly relating $\mathbf{x}_{\mathrm{new}}$ and $\widehat{\mathbf{y}}_{\mathrm{new}}$:

$$\widehat{\mathbf{y}}_{\mathrm{new}} = \left(\widetilde{\mathbf{Q}}\cdot(\mathbf{W}^*)^\top\right)\cdot\mathbf{x}_{\mathrm{new}} = \mathbf{B}^\top\cdot\mathbf{x}_{\mathrm{new}}, \tag{9}$$

where $\mathbf{B} \in \mathbb{R}^{V_X} \times \mathbb{R}^{V_Y}$ is the matrix of PLS (outer) regression coefficients.

If $\mathbf{y}_{\mathrm{new}}$ is unknown, the principle of the PLS model can be leveraged to define statistics to assess the reliability of predictions:

$$T^2 = \mathbf{t}_{\mathrm{new}}^\top\cdot\mathbf{\Lambda}^{-1}\cdot\mathbf{t}_{\mathrm{new}} = \mathbf{x}_{\mathrm{new}}^\top\cdot\mathbf{W}^*\cdot\mathbf{\Lambda}^{-1}\cdot(\mathbf{W}^*)^\top\cdot\mathbf{x}_{\mathrm{new}}, \tag{10}$$

$$Q = \mathbf{e}_{\mathrm{new}}^\top\cdot\mathbf{e}_{\mathrm{new}} = \mathbf{x}_{\mathrm{new}}^\top\cdot(\mathbf{I}_{V_X} - \mathbf{P}\cdot(\mathbf{W}^*)^\top)^\top\cdot(\mathbf{I}_{V_X} - \mathbf{P}\cdot(\mathbf{W}^*)^\top)\cdot\mathbf{x}_{\mathrm{new}}, \tag{11}$$

where T^2 measures the squared distance of the projection of $\mathbf{x}_{\mathrm{new}}$ from the center of the space of input LVs, $\mathbf{\Lambda}$ being a diagonal matrix containing unscaled variances of the LVs from the calibration dataset defined as $\mathbf{\Lambda} = \mathbf{T}^\top\cdot\mathbf{T}$, while Q measures the squared orthogonal distance between $\mathbf{x}_{\mathrm{new}}$ and the space of input LVs, being defined based on $\mathbf{e}_{\mathrm{new}} \in \mathbb{R}^{V_X}$, i.e., the reconstruction residual of $\mathbf{x}_{\mathrm{new}}$ based on the model of the input space, (1). The prediction of the PLS model is deemed

[1] Note that, in the matrix-based description of PLS, this operation amounts to the solution of an eigenvalue problem: the first column of $\mathbf{W}$ is the eigenvector of the cross-covariance matrix $\mathbf{X}\cdot\mathbf{Y}^\top\cdot\mathbf{Y}\cdot\mathbf{X}^\top$ corresponding to the largest eigenvalue of the same matrix.

reliable (and the model is deemed valid for the given $\mathbf{x}_{\text{new}}$) if both statistics fall below appropriate confidence limits (Jackson, 1959; Jackson and Mudholkar, 1979; Martin and Morris, 1996; Nomikos and MacGregor, 1995a; Qin, 2003; Tracy et al., 1992). We provide details on estimators for the confidence limits of T^2 and Q in Appendix A.

The reliability of the PLS predictions can be assessed also considering the uncertainty in the estimated $\widehat{\mathbf{y}}_{\text{new}}$ (Faber and Kowalski, 1997; Nomikos and MacGregor, 1995b; Zhang and García Muñoz, 2009). Details on the estimation of PLS prediction uncertainty are provided in Appendix B.

2.2. Algebraic inversion of PLS models

The rationale of PLS model inversion is to set a vector $\mathbf{y}_{\text{des}} \in \mathbb{R}^{V_Y}$ of desired output variables (i.e., the inversion target), and to estimate the vector $\widehat{\mathbf{x}}_{\text{des}}$ of input variables that allows one to obtain the given target by PLS regression. The simplest way to achieve such an objective is to algebraically manipulate the equations of the PLS model, which is the principle of DI (Jaeckle and MacGregor, 2000, 1998). Note that we will consider only input LVs when describing PLS model inversion, therefore we will refer to $\mathbf{t}$ simply as to LVs.

Once the target $\mathbf{y}_{\text{des}}$ has been set, the first step in DI is to invert (8), setting $\widehat{\mathbf{y}}_{\text{new}} = \mathbf{y}_{\text{des}}$, to estimate $\widehat{\mathbf{t}}_{\text{des}}$, i.e., the vector of LVs corresponding to the output target. We note that this operation is equivalent to solve the linear system defined by (8), where the vector of LVs is the unknown. Three cases may arise (Jaeckle and MacGregor, 1998) depending on the relative dimensions of the spaces on LVs and output variables.

1. If $A < V_Y$, no exact solution exists, but an optimal solution (in the least-squares sense) can be obtained by inverting (8) using the left generalized inverse of $\widetilde{\mathbf{Q}}$ (Rao and Mitra, 1971):

$$\widehat{\mathbf{t}}_{\text{des}} = \left(\widetilde{\mathbf{Q}}^{\top} \cdot \widetilde{\mathbf{Q}}\right)^{-1} \cdot \widetilde{\mathbf{Q}}^{\top} \cdot \mathbf{y}_{\text{des}}. \tag{12}$$

2. If $A = V_Y$, matrix $\widetilde{\mathbf{Q}}$ is square and a unique solution to the inversion of (8) exists:

$$\widehat{\mathbf{t}}_{\text{des}} = \widetilde{\mathbf{Q}}^{-1} \cdot \mathbf{y}_{\text{des}}. \tag{13}$$

3. If $A > V_Y$, an infinite number of solutions to the inversion of (8) exists. A particular solution (i.e., the one with the minimum Euclidean norm) can be obtained using the right generalized inverse of $\widetilde{\mathbf{Q}}$ (Rao and Mitra, 1971):

$$\widehat{\mathbf{t}}_{\text{des,p}} = \widetilde{\mathbf{Q}}^{\top} \cdot \left(\widetilde{\mathbf{Q}} \cdot \widetilde{\mathbf{Q}}^{\top}\right)^{-1} \cdot \mathbf{y}_{\text{des}}. \tag{14}$$

while the complete set of solutions can be obtained considering the null space of $\widetilde{\mathbf{Q}}$, i.e., its kernel. The kernel of $\widetilde{\mathbf{Q}}$ is implicitly defined as the subspace of LVs which projection through $\widetilde{\mathbf{Q}}$ is the null vector:

$$\widetilde{\mathbf{Q}} \cdot \widehat{\mathbf{t}}_{\text{des,n}} = \mathbf{0}_{V_Y}, \tag{15}$$

where $\mathbf{0}_{V_Y} \in \mathbb{R}^{V_Y}$ is the null vector and $\widehat{\mathbf{t}}_{\text{des,n}}$ represents the null space. We note that:

$$\widetilde{\mathbf{Q}} \cdot \left(\widehat{\mathbf{t}}_{\text{des,p}} + \widehat{\mathbf{t}}_{\text{des,n}}\right) = \mathbf{y}_{\text{des}}, \tag{16}$$

therefore, the complete set of solutions to the inversion of (8) in the case $A > V_Y$ can be expressed as:

$$\widehat{\mathbf{t}}_{\text{des}} = \widehat{\mathbf{t}}_{\text{des,p}} + \widehat{\mathbf{t}}_{\text{des,n}}. \tag{17}$$

We remark that the DI equations rely on the assumption that the covariance matrix of the distribution $\mathbf{y}$ is drawn from is diagonally dominant, i.e., the output variables are independent or barely correlated. If this condition is not met, matrix inversion operations in (12), (13), and (14) might not be possible due to rank deficiency of the matrices therein. Such an issue can be addressed by regularizing the inversion (Arnese-Feffin et al., 2022).

Regardless of the relationship between A and V_Y, the second step of DI is to project $\widehat{\mathbf{t}}_{\text{des}}$ back onto the space of input variables by means of (1) to obtain $\widehat{\mathbf{x}}_{\text{des}}$:

$$\widehat{\mathbf{x}}_{\text{des}} = \mathbf{P} \cdot \widehat{\mathbf{t}}_{\text{des}}, \tag{18}$$

where $\widehat{\mathbf{x}}_{\text{des}}$ is clearly a unique solution if $A \leq V_Y$, while it is an $(A - V_Y)$-dimensional subspace of the space of input variables if $A > V_Y$.

The reliability of the PLS model inversion solution can be evaluated in the same way as for regression, i.e., by computing the T^2 and Q statistics based on $\widehat{\mathbf{t}}_{\text{des}}$ and $\widehat{\mathbf{x}}_{\text{des}}$, respectively. However, note that in DI $\widehat{\mathbf{x}}_{\text{des}}$ is a rank-A reconstruction of the "true" $\mathbf{x}_{\text{des}}$, being derived based a reduced-rank linear projection operator from the space of LVs. This implies that $\widehat{\mathbf{x}}_{\text{des}}$ is perfectly compliant with the correlation structure of the input variables modeled by PLS; therefore, its Q statistic is null.

2.3. The null space

The concept of null space is particularly important when LVMI is used to design process conditions to achieve a given target quality (i.e., in product design). In fact, any feasible $\widehat{\mathbf{x}}_{\text{des}}$ (or $\widehat{\mathbf{t}}_{\text{des}}$) falling on the null space should yield the same product quality according to the model (Jaeckle and MacGregor, 1998), a property of the null space that has been demonstrated also experimentally (Tomba et al., 2014). In this context, the null space constitutes a degree of freedom to tune the PLS model inversion solution in such a way as to satisfy additionally constraints (e.g., minimization of the processing cost) while still achieving the desired product quality (Jaeckle and MacGregor, 2000). However, one must bear in mind that the estimated null space gets more and more uncertain when moving away from the center of space of LVs, i.e., the region wherein the calibration data used to build the PLS model are available (Tomba et al., 2014). Therefore, it is crucial to account for the null space uncertainty when performing such an additional fine tuning of the PLS model inversion solution. We provide details of analytical approaches to estimate the null space uncertainty (Facco et al., 2015; Palací-López et al., 2019) in Appendix C.

2.4. Formalism of a general optimization problem

In this study, we will adopt the following a general formalism to formulate an optimization problem:

$$\widehat{\mathbf{z}} = \underset{\mathbf{z}}{\operatorname{argmin}}[J(\mathbf{z})], \tag{19}$$

subject to:

$$\mathbf{z}_{\text{LB}} \leq \mathbf{z} \leq \mathbf{z}_{\text{UB}}, \tag{20}$$

$$\mathbf{A} \cdot \mathbf{z} \leq \mathbf{b}, \tag{21}$$

$$\mathbf{A}_{\text{eq}} \cdot \mathbf{z} = \mathbf{b}_{\text{eq}}, \tag{22}$$

$$C(\mathbf{z}) \leq 0, \tag{23}$$

$$C_{\mathrm{eq}}(\mathbf{z}) = 0, \tag{24}$$

where J is the objective function to be minimized, which depends on the vector of optimization variables, $\mathbf{z}$. The optimization problem might be subject to several hard constraints; namely: $\mathbf{z}_{\mathrm{LB}}$ and $\mathbf{z}_{\mathrm{UB}}$ are the lower bounds and the upper bounds, respectively, for the optimization variables; $\mathbf{A}$ and $\mathbf{b}$ are (respectively) the matrix and vector of linear inequality constraints; $\mathbf{A}_{\mathrm{eq}}$ and $\mathbf{b}_{\mathrm{eq}}$ are (respectively) the matrix and vector of linear equality constraints; $C(\mathbf{z})$ is the nonlinear inequality constraint function; and $C_{\mathrm{eq}}(\mathbf{z})$ is the nonlinear equality constraint function. The solution of the problem is denoted as $\widehat{\mathbf{z}}$, i.e., the vector of variables minimizing the objective function while simultaneously satisfying all the hard constraints.

In the following, we will assume that $J(\mathbf{z})$ is formulated as a standard quadratic function (Flores-Cerrillo and MacGregor, 2004):

$$J(\mathbf{z}) = \frac{1}{2}\mathbf{z}^{\top}\cdot\mathbf{H}\cdot\mathbf{z} + \mathbf{f}^{\top}\cdot\mathbf{z} + c, \tag{25}$$

where $\mathbf{H}$ is the matrix of the quadratic term (i.e., the Hessian matrix of $J(\mathbf{z})$), $\mathbf{f}$ is the vector of the linear term, and c is the constant term; however, since c is irrelevant for the optimization, it will be neglected in the following. Note that the use of (25) implies that (19) is a quadratic programming (QP) problem if nonlinear constraints are omitted, while it is a nonlinear programming (NLP) problem otherwise.

Matrix $\mathbf{H}$ is assumed to be symmetric and at least positive-semidefinite. If $\mathbf{H}$ is positive definite, $J(\mathbf{z})$ is a strictly convex function of $\mathbf{z}$ and the problem admits a unique global minimum (Bard, 1974; Rao, 2009). We also note that if no constraint is set in (19), the problem is an unconstrained QP and admits an analytical solution. The gradient $\nabla_{\mathbf{z}}$ of the objective function (25) is:

$$\nabla_{\mathbf{z}}[J(\mathbf{z})] = \mathbf{z}^{\top}\cdot\mathbf{H} + \mathbf{f}^{\top}, \tag{26}$$

which can be nulled to obtain the solution:

$$\widehat{\mathbf{z}} = \mathbf{H}^{-1}\cdot(-\mathbf{f}). \tag{27}$$

On the other hand, if $\mathbf{H}$ is positive-semidefinite, then $J(\mathbf{z})$ is still convex, although not strictly, therefore the problem admits an indefinite number of equivalent global minima (an infinite number, in principle). It can be proved (Nocedal and Wright, 2006) that a positive-semidefinite matrix features at least one null eigenvalue, therefore it is rank-deficient. Matrix $\mathbf{H}$ is thus non-invertible, and the problem does not admit an analytical solution in the form of (27). Analytical solution methods exist nonetheless (Nocedal and Wright, 2006), for example based on matrix factorization of $\mathbf{H}$.

Finally, we remark the difference between soft and hard constraints. Soft constraints are additional terms included in the objective function $J(\mathbf{z})$ and are satisfied by compromising the achievement of the target on the optimization variables with the minimization of the soft constraint function. Hard constraints are limits sets on the optimization problem to restrict the feasible space, i.e., the portion of the domain of the optimization variables in which the solution is deemed feasible.

3. Illustrative case study

To support our theoretical analysis in Section 4, we discuss a numerical case study alongside the derivation. We use MATLAB R2022a (The Mathworks, 2022) to carry out all the computations to follow, using a set of functions for PLS modeling and inversion developed in-house. The code is freely available for download and use (see the Data availability statement).

We use the "Example dataset" provided by Palací-López et al. (2019). Namely, we consider a dataset comprising $N = 6$ old (historical) products; each product is characterized by $V_Y = 1$ single quality attribute, and the historical products were obtained using different combinations of $V_X = 5$ process variables. Our purpose is to find the combination of process variables that returns a new product, i.e., one that was not manufactured in previous production campaigns.

Table 1
Example dataset from Palací-López et al. (2019). The data comprise $N = 6$ observations of $V_X = 5$ input variables (x_1, x_2, x_3, x_4, and x_5) and $V_Y = 1$ output variable (y).

Observation	x_1	x_2	x_3	x_4	x_5	y
1	5.43	7.54	125.64	58.51	50.49	61.85
2	5.43	15.97	126.20	258.48	74.44	278.99
3	99.23	7.54	9893.38	59.29	737.15	307.89
4	99.23	15.97	9765.16	254.11	1576.28	436.40
5	52.33	11.76	2787.64	139.21	583.76	266.08
6	52.33	11.76	2849.95	135.67	630.73	260.52

Table 2
Performance of the PLS model. EV_X and EV_Y are the explained variances of input and output variables, respectively.

LV	EV_X	EV_Y
1	0.5670	0.9223
2	0.4044	0.0136
Total	0.9174	0.9359

The input (process) and output (quality) variables are related by the following true model (Facco et al., 2015):

$$y = -21 + 4.3x_1 + 0.022x_2 - 0.0064x_3 + 1.1x_4 - 0.012x_5, \tag{28}$$

where x_1 and x_2 are the independent inputs obtained by a two-level full factorial design with two replicates of the center point, while:

$$x_3 = x_1^2, \tag{29}$$

$$x_4 = x_2^2, \tag{30}$$

$$x_5 = x_1x_2, \tag{31}$$

are the dependent inputs. After data generation, x_3, x_4, x_5, and y are each corrupted with independent Gaussian noise with zero mean and standard deviation equal to 5% of the one of the uncorrupted variable. The dataset is reported in Table 1.

Note that the relationship among input variables, e.g., (29), introduces correlation between them. Furthermore, nonlinear relationships are introduced to mimic a typical real-world scenario in which the underlying process is nonlinear, but it is modeled by a linear model (namely, the PLS model). This implies that part of the variability of the data cannot be explained by the model, thus will be left in the Q statistic; this is relevant for the discussion in Section 4.2.

A PLS model with $A = 2$ LVs is calibrated on the dataset in Table 1 after autoscaling the data (i.e., variables are centered on zero mean and scaled to unit variance). The performance of the PLS model in terms of explained variances of the input and output spaces are reported in Table 2.

We define a target output by setting $(x_1 \quad x_2) = (10 \quad 10)$, which yields $\mathbf{y}_{\mathrm{des}} = 119.58$; no Gaussian noise is added in this case. Note that, having assigned the target output based on a known set of independent inputs, we can compute the true vector of input variables corresponding to $\mathbf{y}_{\mathrm{des}}$, therefore the true vector of LVs, by (6). These vectors can be used as references in evaluating the results of PLS model inversion. We will label such vectors as "Target" in the following. The DI solution is computed for reference and comparison against the IbO solutions in our analysis (note that $\mathbf{y}_{\mathrm{des}}$ must be scaled on the means and standard deviations of the columns of the calibration matrix $\mathbf{Y}$, and that $\widehat{\mathbf{x}}_{\mathrm{des}}$ is returned as scaled on the means and standard deviations of the columns

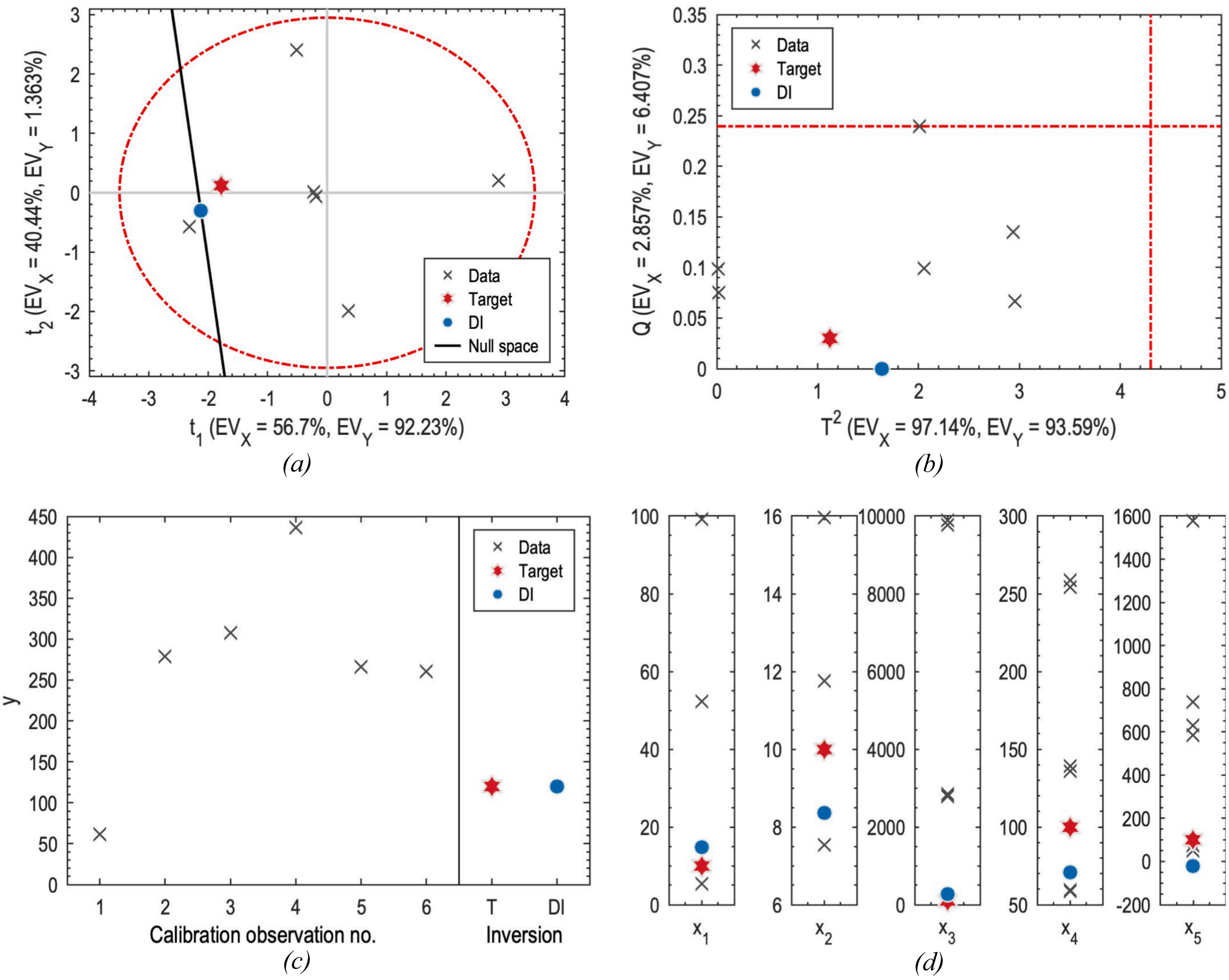

Fig. 2. Results of the PLS model inversion by DI: (a) space of LVs; (b) diagnostic plot; (c) space of output variables; (d) space of input variables. In all plots, the crosses represent the calibration data, the red star identifies the true solution, and the blue circle is the DI solution. The black solid line in (a) is the null space; the red dash-dotted lines in (a) and (b) delimit the validity region of the PLS model based on χ^2 confidence limits of T^2 and Q.

of the calibration matrix $\mathbf{X}$). A 1-dimensional null space exists (recall that $A = 2$ and $V_Y = 1$). The results of DI are illustrated in Fig. 2.

Fig. 2(a) highlights that the DI solution matches quite well the true vector of LVs. The solution is fully within the model validity region, as observed in Fig. 2(b); we can also see that Q is null for the DI solution, as expected. Being a purely algebraic procedure, the DI solution can match the output target exactly, as shown in Fig. 2(c). The solution appears to be reasonable also in terms of estimated input variables, as shown in Fig. 2(d).

4. Systematizing the formulation of PLS model inversion problems by optimization

In this Section, we outline our theoretical analysis of IbO of PLS models. We use a hierarchical approach, starting with the simplest case and gradually adding constraints to make the optimization problem and its solutions progressively more complex. We start by stating the optimization problem in the space of LVs in Section 4.1: we first analyze an unconstrained problem, then add linear constraints, and finally consider a problem with nonlinear constraints. In Section 4.2, we repeat the analysis formulating the problem in the space of input variables. We highlight the consistency with the algebraic inversion methods described in the Section 2.2, and we clearly state which solutions algorithm should be used for each step in our hierarchical structure of IbO. We also provide some recommendation on which constraints it is convenient/necessary to include and on how to do it. Note that in the following we will assume that output variables are independent, coherently with DI.

4.1. *Optimization in the space of latent variables*

One of the most prominent advantages of using a PLS model derived from daily production data to formulate the objective function of an optimization problem is that the optimization itself can be set in the space of LVs. This offers several advantages, including the implicit incorporation of process constraints and production policies within the problem, which are automatically respected (Ferrer, 2021; Jaeckle and MacGregor, 1998), and the fact that optimization variables (i.e., the LVs) are few in number and independent (Flores-Cerrillo and MacGregor, 2004). Therefore, we consider this case by first setting $\mathbf{z} = \mathbf{t}_{\text{des}}$ in (19) and solving the optimization problem to obtain $\hat{\mathbf{z}} = \hat{\mathbf{t}}_{\text{des}}$. The input vector is then obtained by (18), as in DI, which implies that the Q statistic of $\hat{\mathbf{x}}_{\text{des}}$ is null.

4.1.1. *Consistency with the DI solution*

In its simplest formulation, IbO relies on an unconstrained optimization problem that minimizes the quadratic difference between the desired output vector, $\mathbf{y}_{\text{des}}$, and the prediction of the PLS model by adjusting the latent variables:

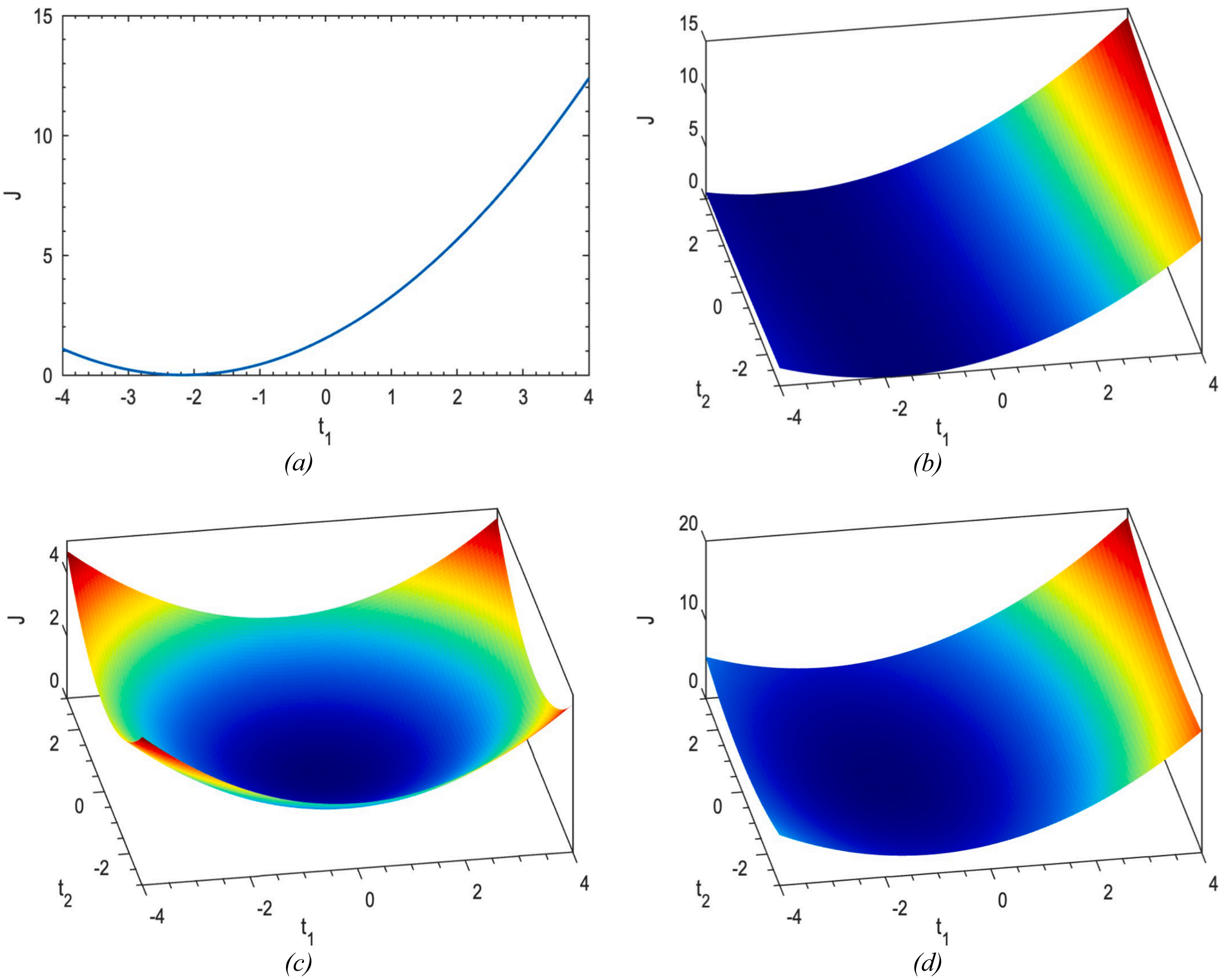

Fig. 3. Quadratic objective functions of IbO of PLS models for the example dataset. (a) Model with 1 LV ($A = V_Y$). (b) Model with 2 LVs ($A > V_Y$): the objective function is not strictly convex in this case and admits an infinite number of global minima. (c) Convex penalty term defined as the T^2 of the solution for a model with 2 LVs. (d) Penalized objective function for a model with 2 LVs obtained by addition of the objective function in (b) and the penalty term in (c), which regularizes the objective function making it strictly convex again.

$$\widehat{\mathbf{t}}_{\mathrm{des}} = \underset{\mathbf{t}_{\mathrm{des}}}{\operatorname{argmin}}\left[\left(\mathbf{y}_{\mathrm{des}} - \widetilde{\mathbf{Q}}\cdot\mathbf{t}_{\mathrm{des}}\right)^{\top}\cdot\left(\mathbf{y}_{\mathrm{des}} - \widetilde{\mathbf{Q}}\cdot\mathbf{t}_{\mathrm{des}}\right)\right], \tag{32}$$

which is an unconstrained QP problem. The objective function can be expressed as in (25) with:

$$\mathbf{H} = 2\widetilde{\mathbf{Q}}^{\top}\cdot\widetilde{\mathbf{Q}}, \tag{33}$$

$$\mathbf{f} = -2\widetilde{\mathbf{Q}}^{\top}\cdot\mathbf{y}_{\mathrm{des}}. \tag{34}$$

The problem in (32) admits an analytical solution:

$$\widehat{\mathbf{t}}_{\mathrm{des}} = \left(\widetilde{\mathbf{Q}}^{\top}\cdot\widetilde{\mathbf{Q}}\right)^{-1}\cdot\widetilde{\mathbf{Q}}^{\top}\cdot\mathbf{y}_{\mathrm{des}}. \tag{35}$$

We note that such elementary formulation of IbO is consistent with DI, as we can see from (12), a connection already realized by Flores-Cerrillo and MacGregor (2004).

However, we shall point out that the consistency holds true only if $A \le V_Y$. In this case, matrix $\mathbf{H} \in \mathbb{R}^A \times \mathbb{R}^A$ is a positive-definite symmetric matrix, therefore $J(\mathbf{t}_{\mathrm{des}})$ is strictly convex and admits a unique global minimum, as can be seen in Fig. 3(a). If $A > V_Y$, matrix $\mathbf{H}$ is only positive-semidefinite, therefore the problem is convex and admits an infinite number of equivalent global minima. Fig. 3(b) makes intuitively clear that the locus of minima is an $(A - V_Y)$-dimensional subspace of the space of LVs, which corresponds to the null space found in DI (compare Fig. 3(b) with Fig. 2(a), for example).

If $A > V_Y$, the analytical solution (35) does not apply as matrix $\widetilde{\mathbf{Q}}^{\top}\cdot\widetilde{\mathbf{Q}}$ is non-invertible. In DI, this case is handled by using the right generalized inverse to compute a particular solution to the inversion problem (i.e., $\widehat{\mathbf{t}}_{\mathrm{des,\,p}}$). An equivalent approach exists for IbO, as QP problems involving positive-semidefinite matrices can be handled by matrix factorization methods (Nocedal and Wright, 2006). However, an alternative, more intuitive way relies on incorporating a penalty term in the objective function of problem (32).While any penalty term is in principle admissible, a popular choice (García-Muñoz et al., 2006) is to state a soft constraint on the T^2 statistics of $\mathbf{t}_{\mathrm{des}}$. A generalized form of the problem is therefore:

$$\widehat{\mathbf{t}}_{\mathrm{des}} = \underset{\mathbf{t}_{\mathrm{des}}}{\operatorname{argmin}}\left[\left(\mathbf{y}_{\mathrm{des}} - \widetilde{\mathbf{Q}}\cdot\mathbf{t}_{\mathrm{des}}\right)^{\top}\cdot\mathbf{\Gamma}_1\cdot\left(\mathbf{y}_{\mathrm{des}} - \widetilde{\mathbf{Q}}\cdot\mathbf{t}_{\mathrm{des}}\right) + \gamma_2\mathbf{t}_{\mathrm{des}}^{\top}\cdot\mathbf{\Lambda}^{-1}\cdot\mathbf{t}_{\mathrm{des}}\right]. \tag{36}$$

The first addendum in the objective function aims at pushing the solution as close as possible to the target output. The diagonal weight matrix $\mathbf{\Gamma}_1$ assigns different weights to the output variables in the multivariate case. A reasonable choice (García-Muñoz et al., 2006) is to set the diagonal of $\mathbf{\Gamma}_1$ as the determination coefficients (in calibration) of the output variables, to account for the different degrees of confidence of the model in predicting each output; alternatively, setting $\mathbf{\Gamma}_1 = \mathbf{I}_{V_Y}$, with

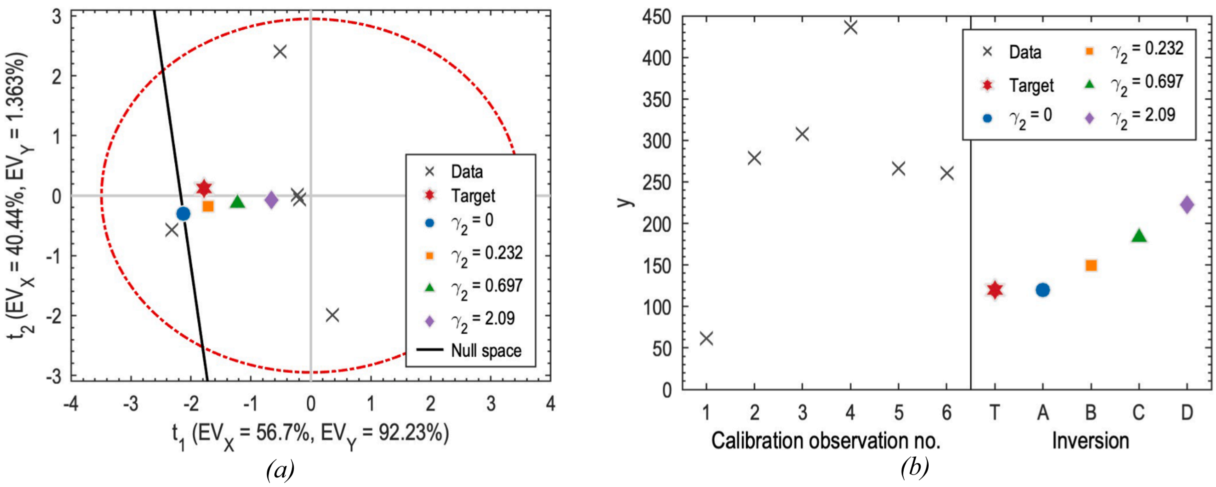

Fig. 4. Effect of the weight γ_2 given to the soft constraint on T^2 in the IbO problem in (36) shown as solutions in (a) the space of LVs and (b) the space of output variables.

$\mathbf{I}_{V_Y} \in \mathbb{R}^{V_Y} \times \mathbb{R}^{V_Y}$ the identity matrix, gives equal weights to all outputs, as in (32). The second addendum constitutes a soft constraint on the T^2 statistic of $\mathbf{t}_{\text{des}}$, i.e., a penalty term added to the objective function; in this case, the penalty term pushes the solution towards the origin of the space of LVs. Factor γ_2 is a weight for the soft constraint. A reasonable choice (Tomba et al., 2012) is $\gamma_2 = 1/T^2_{\text{lim}}$, where T^2_{lim} is confidence limit of T^2 at significance level α (see Appendix A for details); note that the numerator of the γ_2 expression can be increased or decreased to control the weight of the soft constraint. We note that the soft constraint is always strictly convex as $\mathbf{\Lambda}^{-1}$ is a diagonal matrix containing only positive elements. Fig. 3(c) shows the penalty term obtained by setting $\gamma_2 = 2/T^2_{\text{lim}}$ and using the χ^2 approach to estimate T^2_{lim} at $\alpha = 0.05$ significance level. Fig. 3(d) visualizes the overall objective function in (36) (setting $\mathbf{\Gamma}_1 = \mathbf{I}_{V_Y}$), which illustrates the role of the soft constraint in restoring the strict convexity of $J(\mathbf{t}_{\text{des}})$ even if $A > V_Y$.

We remark that (36) is still an unconstrainted QP problem, therefore the penalty term enables formulating analytical solutions. The objective functions can be manipulated to prove that:

$$\mathbf{H} = 2\left(\widetilde{\mathbf{Q}}^{\top}\cdot\mathbf{\Gamma}_1\cdot\widetilde{\mathbf{Q}} + \gamma_2\mathbf{\Lambda}^{-1}\right), \tag{37}$$

$$\mathbf{f} = -2\widetilde{\mathbf{Q}}^{\top}\cdot\mathbf{\Gamma}_1\cdot\mathbf{y}_{\text{des}}, \tag{38}$$

therefore, the analytical solution is:

$$\hat{\mathbf{t}}_{\text{des}} = \left(\widetilde{\mathbf{Q}}^{\top}\cdot\mathbf{\Gamma}_1\cdot\widetilde{\mathbf{Q}} + \gamma_2\mathbf{\Lambda}^{-1}\right)^{-1}\cdot\widetilde{\mathbf{Q}}^{\top}\cdot\mathbf{\Gamma}_1\cdot\mathbf{y}_{\text{des}}. \tag{39}$$

In light of (39), it is apparent that the soft constraint can be interpreted as a regularization term for the matrix inversion involved in the analytical solution of the IbO problem. This makes $\mathbf{H}$ diagonally dominant, therefore "fixing" the rank deficiency in the case $A > V_Y$. We can also recognize the similarity of (39) with the familiar form of ridge regression (Hoerl and Kennard, 1970), which is known for its ability to solve ill-conditioning problems by continuous shrinkage (Hastie et al., 2009).

However, note that the regularization term is introduced as a soft constraint, therefore it is weighted directly in the objective function, effectively "pushing" the estimated $\hat{\mathbf{y}}_{\text{des}} = \widetilde{\mathbf{Q}}\cdot\hat{\mathbf{t}}_{\text{des}}$ away from the target and towards the average value of the outputs in the calibration dataset. This effect is shown in Fig. 4 in the spaces of LVs and output variables: four solutions of (36) are reported, setting $\gamma_2 \in \left\{0, \frac{1}{T^2_{\text{lim}}}, \frac{3}{T^2_{\text{lim}}}, \frac{9}{T^2_{\text{lim}}}\right\}$ and $\mathbf{\Gamma}_1 = \mathbf{I}_{V_Y}$. Note that the case $\gamma_2 = 0$ yields the same solution as DI, as shown in Fig. 2. Additional details on the effect of the soft constraint can be found in García-Muñoz et al. (2006).

Table 3
Meaningful linear inequality and equality constraints for IbO of PLS models in the space of LVs stated as $\mathbf{A}\cdot\mathbf{t}_{\text{des}} \leq \mathbf{b}$ and $\mathbf{A}_{\text{eq}}\cdot\mathbf{t}_{\text{des}} \leq \mathbf{b}_{\text{eq}}$, respectively. If some of the variables are not to be constrained, remove the relevant rows from $\mathbf{A}$ (or $\mathbf{A}_{\text{eq}}$) and $\mathbf{b}$ (or $\mathbf{b}_{\text{eq}}$). To constraint linear combinations of the variables, pre-multiply matrix $\mathbf{A}$ (or $\mathbf{A}_{\text{eq}}$) by the matrix of linear combinations coefficients, $\mathbf{L}$, and replace the relevant bound (or value) by replacing $\mathbf{b}$ (or $\mathbf{b}_{\text{eq}}$).

Constraint	A or $\mathbf{A}_{\text{eq}}$	b or $\mathbf{b}_{\text{eq}}$
Inequality constraints		
Upper bounds on outputs	$\widetilde{\mathbf{Q}}$	$\mathbf{y}_{\text{UB}}$
Lower bounds on outputs	$-\widetilde{\mathbf{Q}}$	$-\mathbf{y}_{\text{LB}}$
Upper bounds on inputs	$\mathbf{P}$	$\mathbf{x}_{\text{UB}}$
Lower bounds on inputs	$-\mathbf{P}$	$-\mathbf{x}_{\text{LB}}$
Upper bounds on LVs	$\mathbf{I}_A$	$\mathbf{t}_{\text{UB}}$
Lower bounds on LVs	$-\mathbf{I}_A$	$-\mathbf{t}_{\text{LB}}$
Upper bounds on UCLof the null space	$\widetilde{\mathbf{Q}}$	$\text{UCL}(\mathbf{y}_{\text{des}})$
Lower bounds on LCLof the null space	$-\widetilde{\mathbf{Q}}$	$-\text{LCL}(\mathbf{y}_{\text{des}})$
Equality constraints		
Value of output	$\widetilde{\mathbf{Q}}$	$\mathbf{y}_{\text{eq}}$
Value of inputs	$\mathbf{P}$	$\mathbf{x}_{\text{eq}}$
Value of LVs	$\mathbf{I}_A$	$\mathbf{t}_{\text{eq}}$
Null space	$\widetilde{\mathbf{Q}}$	$\mathbf{y}_{\text{des}}$

4.1.2. Including linear constraints

DI is a simple algebraic method for PLS model inversion. While exploiting the correlation structure extracted from data by algebraic inversion offers confidence on physical constraints being respected by the solution of PLS model inversion (Ferrer, 2021), it might be desirable to set those constraints explicitly. This can be done by re-formulating the IbO problem as a constrained optimization.

The simplest constraints that one can add to the problem in (36) are linear equality and inequality hard constraints:

$$\mathbf{A}\cdot\mathbf{t}_{\text{des}} \leq \mathbf{b}, \tag{40}$$

$$\mathbf{A}_{\text{eq}}\cdot\mathbf{t}_{\text{des}} = \mathbf{b}_{\text{eq}}, \tag{41}$$

Note that including hard constraints turns IbO into a constrained QP problem, thus implying that a numerical solution method is required with consequent increase in the computational demand, which scales with the problem dimensionality (i.e., the number of LVs). Furthermore, note that we have neglected the bounds for optimization variable $\mathbf{t}_{\text{des}}$ in the constraints (40) and (41), as compared to $\mathbf{z}$ in (19), due to the fact

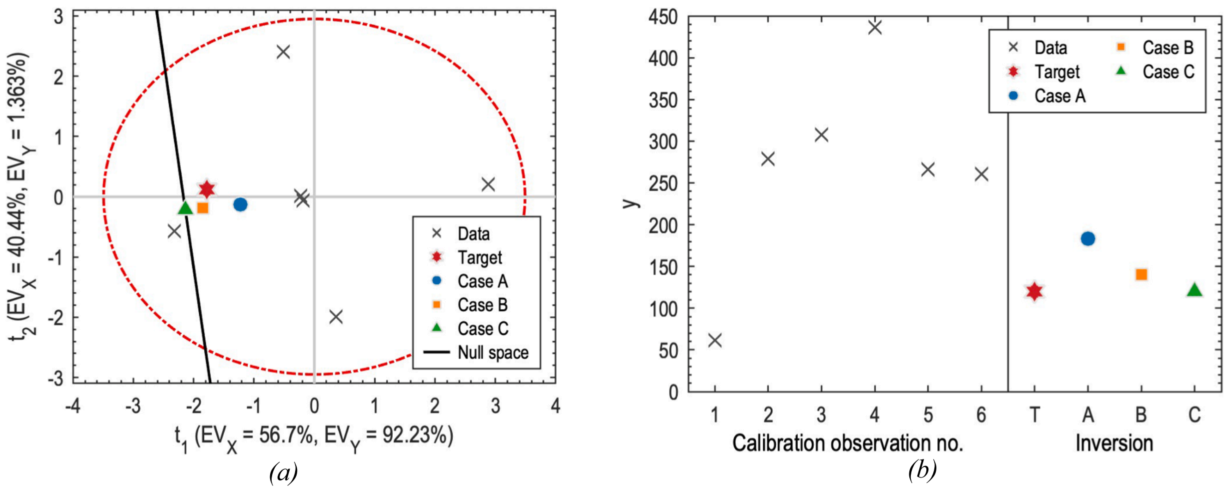

Fig. 5. Effect of the hard constraints in the IbO problem in shown as solutions in (a) the space of LVs and (b) the space of output variables. Case A: unconstrained solution. Case B: the output is upper bounded at 140. Case C: the solution is constrained to the null space.

that such bounds can be incorporated using the inequality constraints (40). In Table 3, we give an overview of some meaningful constraints, and briefly discuss them in the following.

We consider linear inequality constraints first. In (40), $\mathbf{A}$ represents the constraint matrix: it must have A columns and can have as many rows as constraints to be stated; $\mathbf{b}$ represents the constraint vector, which contains the values of the constraints. Inequality constraints can be used to bound the output variables: upper bounds can be stated by setting $\mathbf{A} = \widetilde{\mathbf{Q}}$ and $\mathbf{b} = \mathbf{y}_{\mathrm{UB}}$, while lower bounds can be stated by setting $\mathbf{A} = -\widetilde{\mathbf{Q}}$ and $\mathbf{b} = -\mathbf{y}_{\mathrm{LB}}$. Upper and lower bounds can be stated simultaneously by stacking the respective constraint matrices and vectors. Note that not all variables need to be constrained: if the v-th variable is not to be bounded, the corresponding rows from $\mathbf{A}$ and $\mathbf{b}$ are removed. One may also bound linear combinations of output variables by setting, for example, $\mathbf{A} = \mathbf{L}\cdot\widetilde{\mathbf{Q}}$ and $\mathbf{b} = \mathbf{l}_{Y_{\mathrm{UB}}}$. The rows of $\mathbf{L}$ contain the coefficients to formulate the linear combination of output variables to be bound, while $\mathbf{l}_{Y_{\mathrm{UB}}}$ contains the corresponding upper bounds; a similar formulation exists for lower bounds. Similarly, bounds can be set on input variables, LVs, and their linear combinations.

Equality constraints (41) can be stated setting matrix $\mathbf{A}_{\mathrm{eq}}$ in the same way as for the inequality constraints discussed above, while vector $\mathbf{b}_{\mathrm{eq}}$ must be set to the value variables must be constrained to. A particularly relevant equality constraint is stated by setting $\mathbf{A}_{\mathrm{eq}} = \widetilde{\mathbf{Q}}$ and $\mathbf{b}_{\mathrm{eq}} = \mathbf{y}_{\mathrm{des}}$. Recalling (15), this constraint "snaps" the solution of IbO to the null space (if it exists), thus allowing the optimizer to manipulate the solution based on other soft/hard constraints while not compromising the output, thus effectively offering a solution to the problem illustrated in Fig. 4. This approach is also discussed by García-Muñoz et al. (2006).

However, stating an equality constraint on the null space (i.e., on the desired output) might make the problem infeasible as the constraint requires the first addendum in the objective function (36) to be exactly zero, which might not be possible, especially if other hard constraints are specified. As the null space is affected by uncertainty, one might prefer to account for such uncertainty and bound the solution within the confidence interval of the null space by means of inequality constraints. The approach proposed by Facco et al. (2015) can be used to this end (see Appendix C for details): the upper bound is set as $\mathbf{A} = \widetilde{\mathbf{Q}}$ and $\mathbf{b} = \mathrm{UCL}(\mathbf{y}_{\mathrm{des}})$, while the lower bound is set as $\mathbf{A} = -\widetilde{\mathbf{Q}}$ and $\mathbf{b} = -\mathrm{LCL}(\mathbf{y}_{\mathrm{des}})$, where $\mathrm{UCL}(\mathbf{y}_{\mathrm{des}})$ and $\mathrm{LCL}(\mathbf{y}_{\mathrm{des}})$ are derived from (C.3) by using the $+$ and $-$ signs, respectively.

Fig. 5 illustrates three solutions of (36) subject to constraints (40) and (41) in the spaces of LVs and output variables, to illustrate the effect of hard constraints. In all cases, $\mathbf{\Gamma}_1 = \mathbf{I}_{V_Y}$ and $\gamma_2 = 3/T^2_{\mathrm{lim}}$. No hard constraint is stated on Case A (blue circle). In Case B (orange square), $\widehat{\mathbf{y}}_{\mathrm{des}} = \widetilde{\mathbf{Q}}\cdot\widehat{\mathbf{t}}_{\mathrm{des}}$ is upper-bounded to $\mathbf{y}_{\mathrm{UB}} = 140$. Finally, $\widehat{\mathbf{t}}_{\mathrm{des}}$ is constrained to the null space in Case C (green triangle).

Hard constraints are particularly relevant when some of the components of $\mathbf{y}_{\mathrm{des}}$ are unspecified, i.e., desired values are not specified for all output variables. In such a case, the diagonal elements of $\mathbf{\Gamma}_1$ corresponding to the unspecified outputs are set to 0, in such a way that such outputs will not have any weight on the objective function of the optimization problem (García-Muñoz et al., 2006; Tomba et al., 2012). The unspecified outputs can be left free or simply subject to equality or inequality constraints.

However, we must note that nulling one or more diagonal elements of $\mathbf{\Gamma}_1$ has implications on the optimization problem itself and on the possible constraints stated on the null space. We consider a case in which $\gamma_2 = 0$, therefore $\mathbf{H} = 2\widetilde{\mathbf{Q}}^{\top}\cdot\mathbf{\Gamma}_1\cdot\widetilde{\mathbf{Q}}$. If all the diagonal elements of $\mathbf{\Gamma}_1$ are non-null, then $\mathrm{rank}(\mathbf{H}) = \min\{V_Y, A\}$; $\mathbf{H}$ is invertible (i.e., an analytical solution to the unconstrained QP, in the form of (27), exists) as long as $V_Y \leq A$, while a null space of dimensionality $A - V_Y$ exists otherwise, and therefore (if $\mathbf{\Gamma}_1 = \mathbf{I}_{V_Y}$) the correspondence with DI holds entirely. However, if N_{unsp} diagonal elements of $\mathbf{\Gamma}_1$ are null, then $\mathrm{rank}(\mathbf{H}) = \min\{V_Y - N_{\mathrm{unsp}}, A\}$, which implies that $\mathbf{H}$ is invertible only if $V_Y - N_{\mathrm{unsp}} \leq A$, and this causes the dimensionality of the null space in IbO to increase to $A - V_Y + N_{\mathrm{free}}$, thus breaking the correspondence with DI.

If equality constraints on the null space are to be set, then the rows corresponding to the unspecified output variables must be removed from $\mathbf{A}_{\mathrm{eq}}$ and $\mathbf{b}_{\mathrm{eq}}$, in order to keep consistency between the objective function and the constraints. We also note that the null space uncertainty cannot be estimated due to the inconsistency with DI, as both the analytical methods discussed in Appendix C rely on DI. A quite tricky solution is to define a "reduced" output loading matrix in which the rows corresponding to the unspecified outputs have been nulled, using then such a matrix to estimate the null space uncertainty. However, in general we recommend not to set constraints on the null space confidence region if some output variables are unspecified.

4.1.3. Including nonlinear constraints

Data-driven models are valid only in the vicinity of the data used for calibration, i.e., the validity region covers only small portions of the spaces of input, output, and latent variables. The confidence limits of the model diagnostics can be used to restrict the region in which the model is trustworthy, also known as the knowledge space (Facco et al., 2015; Palací-López et al., 2019). It is common throughout the LVMI literature to incorporate this knowledge into the IbO problem formulation by

Table 4
Meaningful nonlinear inequality constraint functions for IbO of PLS models in the space of LVs stated as $C(\mathbf{t}_{\mathrm{des}}) \leq 0$.

Constraint	$C(\mathbf{t}_{\mathrm{des}})$
Confidence limit of T^2	$\mathbf{t}_{\mathrm{des}}^{\top} \cdot \mathbf{\Lambda}^{-1} \cdot \mathbf{t}_{\mathrm{des}} - T_{\mathrm{lim}}^2$
Upper bounds on UCLof the null space	$\widetilde{\mathbf{Q}} \cdot \mathbf{t}_{\mathrm{des}} - \mathrm{UCL}(\widehat{\mathbf{y}}_{\mathrm{des}}, \mathbf{t}_{\mathrm{des}})$
Lower bounds on LCLof the null space	$-\widetilde{\mathbf{Q}} \cdot \mathbf{t}_{\mathrm{des}} + \mathrm{LCL}(\widehat{\mathbf{y}}_{\mathrm{des}}, \mathbf{t}_{\mathrm{des}})$

stating a nonlinear hard constraint on the T^2 statistic of the solution, therefore formulating the optimization problem as in (36)(subject to constraints (40), (41), and additionally to:

$$C(\mathbf{t}_{\mathrm{des}}) = \mathbf{t}_{\mathrm{des}}^{\top} \cdot \mathbf{\Lambda}^{-1} \cdot \mathbf{t}_{\mathrm{des}} - T_{\mathrm{lim}}^2 \leq 0, \tag{42}$$

where $C(\mathbf{t}_{\mathrm{des}})$ represents a nonlinear constraint function. The effect of such a constraint is to bound the solution of the IbO problem within the confidence (hyper-)ellipse of the A-dimensional space of LVs (whose representation in the bidimensional score space of the illustrative case study is the dash-dotted line in Fig. 5(a)). Note that no hard constraint is set on Q because such statistic is always null when the optimization is formulated in the space of LVs.

While it appears reasonable to include by default the nonlinear constraint on T^2, we argue that it may represent an unnecessary complication under several points of view. Regardless of the objective function being quadratic, nonlinear constraints turn the optimization into an NLP problem, which require gradient-based search methods. This implies a remarkable increase in the computational burden to solve the problem and a decrease in the solution accuracy due to the iterative search method. However, we note that the constraint is convex (Nocedal and Wright, 2006), and therefore the overall NLP is still a convex problem and will eventually converge (within the given tolerance) to the global optimum. We also note that the nonlinear constraint is redundant with the soft constraint on T^2 included in the objective function. We discussed the importance of the soft constraint in Section 4.1.1 and believe that it naturally belongs to the formulation of the IbO problem. If properly weighted, the soft constraint will ensure the solution to fall within the model validity region, therefore rendering unnecessary the statement of an additional hard constraint (García-Muñoz et al., 2006). Last, but not least, the hard constraint would be active (i.e., bounding the solution) only if the target output to be achieved was projected outside of the model validity region (e.g., outside of the confidence ellipse). However, in such a case the validity of the quality target might be questioned in the first place, as it could not conform to the PLS model (Jaeckle and MacGregor, 1998). In summary, we deem the nonlinear constraint on T^2 not necessary in most cases of practical interest.

However, one particular nonlinear constraint could be worth considering in IbO of PLS models. In the previous Section, we proposed to bound the solution within the confidence region of the null space by imposing linear constraints (see Table 3). The method proposed by Facco et al. (2015) would be used by virtue of its linearity. If one wishes to consider also the observation leverage in the null space uncertainty estimation, the method proposed by Palací-López et al. (2019) has to be used. This method is nonlinear in the optimization variables $\mathbf{t}_{\mathrm{des}}$ (see Appendix C for details), therefore it can be used to formulate a nonlinear constraint function:

$$C(\mathbf{t}_{\mathrm{des}}) = \begin{pmatrix} -\widetilde{\mathbf{Q}} \\ \widetilde{\mathbf{Q}} \end{pmatrix} \cdot \mathbf{t}_{\mathrm{des}} - \begin{pmatrix} -\mathrm{LCL}(\widehat{\mathbf{y}}_{\mathrm{des}}, \mathbf{t}_{\mathrm{des}}) \\ \mathrm{UCL}(\widehat{\mathbf{y}}_{\mathrm{des}}, \mathbf{t}_{\mathrm{des}}) \end{pmatrix}, \tag{43}$$

where the first block of A rows of the constraint function refers to the lower confidence limit of the null space, while the second block bounds the upper confidence limit; $\mathrm{LCL}\left(\widehat{\mathbf{y}}_{\mathrm{des}_l}, \mathbf{t}_{\mathrm{des}}\right)$ and $\mathrm{UCL}\left(\widehat{\mathbf{y}}_{\mathrm{des}_l}, \mathbf{t}_{\mathrm{des}}\right)$ derive from (C.11) by considering the $-$ and $+$ signs, respectively, and considering the generic point $\mathbf{t}_{\mathrm{des}}$ as starting point of the method (i.e., by setting $\widehat{\mathbf{t}}_{\mathrm{des}_l} = \mathbf{t}_{\mathrm{des}}$ in (C.6) and thereafter, see Appendix C for details). Note that $\mathrm{LCL}(\widehat{\mathbf{y}}_{\mathrm{des}}, \mathbf{t}_{\mathrm{des}})$ and $\mathrm{UCL}(\widehat{\mathbf{y}}_{\mathrm{des}}, \mathbf{t}_{\mathrm{des}})$ are nonlinear functions of $\mathbf{t}_{\mathrm{des}}$, thus making (43) a nonlinear function. However, one should bear in mind the remark on unspecified output variables mentioned in Section 4.1.2, if constraints on the null space are to be stated. We summarize meaningful nonlinear constraint functions in Table 4.

In order to illustrate the effect of nonlinear constraints, we deliberately misspecify the target for PLS model inversion by setting $(x_1 \quad x_2) = (0 \quad 1)$ as the independent inputs, which, by (28), yields $\mathbf{y}_{\mathrm{des}} = -19.878$. This can happen when one wants to design a product that is very different from those that have been manufactured historically. It is immediately clear that such values are unacceptable given the range of calibration data reported in Table 1. We solve four cases of the PLS model inversion problem with such a target, and visualize the solutions in the space of LVs in Fig. 6(a), while Fig. 6(b) reports the corresponding model diagnostics. Note that in Fig. 6(a) we also visualize the null space and its upper confidence limit ($\alpha = 0.05$) estimated by the method by Palací-López et al. (2019). Fig. 6(b) makes clear that the target is misspecified, as the model diagnostics fall beyond the confidence limits. Concerning the four solutions, we set $\mathbf{\Gamma}_1 = \mathbf{I}_{V_Y}$ in all cases. Case A (blue circle) is a QP problem with $\gamma_2 = 0.3/T_{\mathrm{lim}}^2$ and no hard

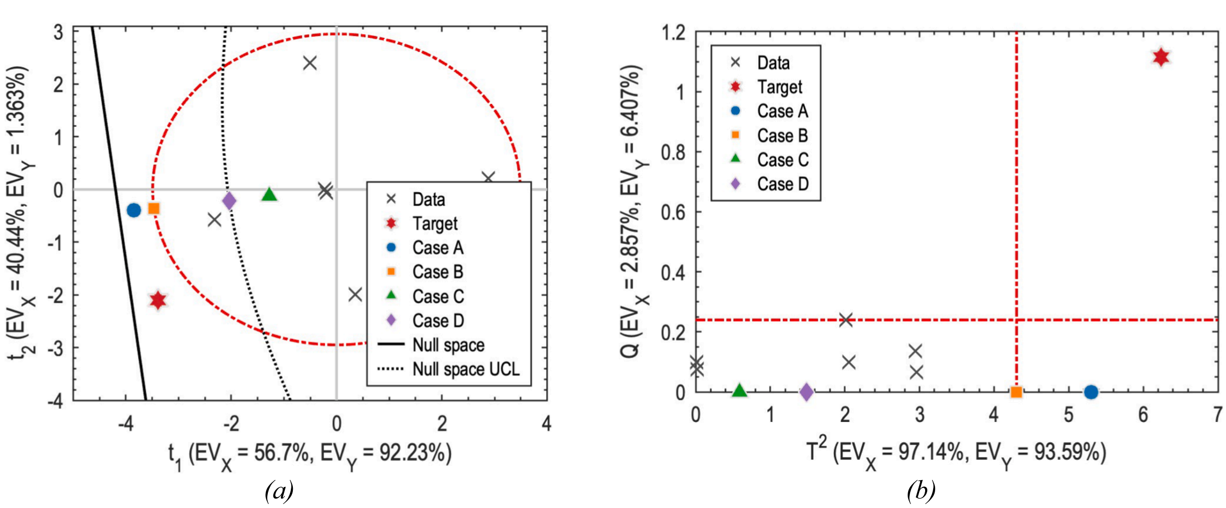

Fig. 6. Effect of the nonlinear hard constraints in the IbO problem (42) shown as (a) solutions in the space of LVs and (b) PLS model diagnostics. Case A: unconstrained solution with low γ_2. Case B: a nonlinear constraint on T^2 is added. Case C: unconstrained solution with high γ_2. Case D: a nonlinear constraint on the null space confidence region is added.

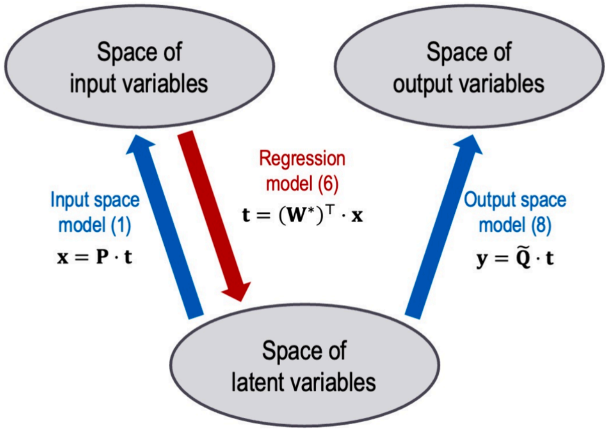

Fig. 7. Visualization of the relationships among the spaces of input variables, LVs, and output variables established by the PLS model.

constraint. In Case B (orange square), the problem in turned into an NLP by stating a hard constraint on T^2, which "snaps" the solution to the confidence ellipse. The solution can also be forced to fall within the confidence ellipse by increasing the γ_2: Case C (green triangle) is again QP problem with $\gamma_2 = 9/T^2_{\text{lim}}$ and no hard constraint. Finally, Case D (violet diamond) is an NLP problem with the same γ_2 used in Case C, but with an additional constraint on the null space confidence region.

4.2. Optimization in the space of input variables

Formulating the optimization problem in the space of LVs offers several advantages, as elucidated in the previous Section. Constraints can be stated also on input variables by exploiting (18). However, this strategy implicitly sets a requirement on the constraint values, which must satisfy (18), i.e., the constraints must conform to the correlation structure of the space of input variables captured by the PLS model. While this requirement seems reasonable, it might not be easy to satisfy in some cases, e.g., when the dimensionality of the space of input variables is very large (as may occur in several industrial cases) and/or the PLS model does not explain most of the variance of that space. This situation has been addressed by reformulating the PLS model inversion problem in such a way as to adjust the input variables directly (García-Muñoz et al., 2008; Tomba et al., 2012), therefore setting $\mathbf{z} = \mathbf{x}_{\text{des}}$ in (19) and solving the optimization problem to obtain $\widehat{\mathbf{z}} = \widehat{\mathbf{x}}_{\text{des}}$. The vector of latent variables can be computed by the PLS regression model, i.e., (3).

4.2.1. Inconsistency with the DI solution

IbO has originally been extended to use input variables as optimization variables by a two-step optimization strategy (García-Muñoz et al., 2008): first, the IbO problem is solved in the latent space to obtain $\widehat{\mathbf{t}}_{\text{des}}$; then, $\widehat{\mathbf{t}}_{\text{des}}$ is used as target in a second optimization problem formulated in the input space. The simplest, unconstrained formulation of the latter problem is:

$$\widehat{\mathbf{x}}_{\text{des}} = \underset{\mathbf{x}_{\text{des}}}{\operatorname{argmin}}\left[\left(\widehat{\mathbf{t}}_{\text{des}} - (\mathbf{W}^{*})^{\top}\cdot\mathbf{x}_{\text{des}}\right)^{\top}\cdot\left(\widehat{\mathbf{t}}_{\text{des}} - (\mathbf{W}^{*})^{\top}\cdot\mathbf{x}_{\text{des}}\right)\right]. \tag{44}$$

In general, the two-step optimization approach entails several drawbacks. Most notably, if any constraints on the output variables have been set in the first optimization, there is no guarantee that these constraints will be satisfied in the second step, except in the case where the very same constraints are set in the second problem as well. Therefore, formulating a single optimization problem directly in the space of input variables seems a preferable alternative (Tomba et al., 2012).

However, the formulation in (44) highlights a very important point of IbO in the space of input variables. The objective function can be expressed as in (25) with:

$$\mathbf{H} = 2\mathbf{W}^{*}\cdot(\mathbf{W}^{*})^{\top}, \tag{45}$$

$$\mathbf{f} = -2\mathbf{W}^{*}\cdot\widehat{\mathbf{t}}_{\text{des}}, \tag{46}$$

and, therefore, the analytical solution is:

$$\widehat{\mathbf{x}}_{\text{des}} = \left(\mathbf{W}^{*}\cdot(\mathbf{W}^{*})^{\top}\right)^{-1}\cdot\mathbf{W}^{*}\cdot\widehat{\mathbf{t}}_{\text{des}}. \tag{47}$$

Comparison of (47) and (18) reveals a crucial difference in the inversion routes taken by IbO formulated in the spaces of input variables and LVs, respectively: formulating the IbO problem in the space of LVs implies that the input data model (1) is used to project the LVs back onto the space of input variables by a simple matrix multiplication; on the other hand, when IbO is formulated in the space of input variables the regression model (3) is inverted to project the LVs onto the space of input variables.

We can visualize the relationships among the spaces of input variables, output variables and LVs established by the PLS model as in Fig. 7: the three spaces are connected by three "one-way bridges", which are the projections models. The spaces of LVs and output variables are connected by a bridge enabling one to move from the former to the latter, i.e., (2) or, in a regression setting, (8). On the other hand, the spaces of LVs and input variables are connected by two bridges, i.e., (1) and (3) or, equivalently, (6), enabling one to move in either direction. In PLS model inversion, the first step is always to move from the space of output variables to the space of LVs. As there is no direct path for such operation, one has to cross the only available bridge in the wrong direction, i.e., to invert (8). Once there, the natural way to return to the space of input variables is to cross a bridge in its natural direction, i.e., to exploit the input space model (1) as happens in DI and IbO formulated in the space of LVs. However, formulating IbO in the space of input variables implies that the second step is done by crossing the regression model bridge in the wrong direction, i.e., by inverting (6).

The different route taken by IbO in the space of input variables has several implications on PLS model inversion. The most apparent one is the loss of consistency with the DI solution; therefore, problem (44) will yield a (possibly only slightly) different solution with respect to DI even in the unconstrained case. The key difference is, however, that the optimization algorithm can now explore the whole space of input variables, not being constrained by the correlation structured modeled by PLS. This in turn implies that the Q statistic of the solution is not 0 anymore, which is a remarkable advantage and allows one to state constraints on the input variables with (in principle) arbitrary flexibility, while still obtaining a feasible solution. The price to pay for such additional flexibility is a (possibly) massive increase in the computational demand to solve the IbO problem, as the dimensionality of the optimization variables is now V_X, which is typically much larger than A. This point becomes particularly relevant in light of one severe limitation of IbO in the space of input variables discussed in Section 4.2.2: the possible ill-conditioning of the analytical solution procedure.

We note that the consistency of DI and IbO in the space of LVs can be restored by subjecting the problem in (44) to a special linear equality constraint:

$$\left(\mathbf{I}_{V_X} - \mathbf{P}\cdot(\mathbf{W}^{*})^{\top}\right)\cdot\mathbf{x}_{\text{des}} = \mathbf{0}_{V_X}, \tag{48}$$

where $\mathbf{0}_{V_X} \in \mathbb{R}^{V_X}$ is the null vector. The left-hand-side of (48) is the reconstruction residual of the input observation (see (11)), which is defined as the difference between $\mathbf{x}_{\text{des}}$ and its rank-A reconstruction obtained by first projecting $\mathbf{x}_{\text{des}}$ onto the space of LVs by (3), and then back onto the space of input variables by (1). Constraint (48) forces the solution to (44) to be a rank-A reconstruction of a (possibly) full-rank $\mathbf{x}_{\text{des}}$, which can be formulated as $\widehat{\mathbf{x}}_{\text{des}} = \mathbf{P}\cdot\widehat{\mathbf{t}}_{\text{des}}$, thus restoring the consistency with DI. Under a different interpretation, constraint (48) restricts the solution to lie on an A-dimensional subspace of the space of input variables (i.e., the space of LVs), allowing the optimizer to move the input variables only along the A directions defined by the constraint. However, note that, while the solution obtained in this way is again consistent with DI and IbO in the space of LVs, the computational cost to obtain it is still much larger due to the dimensionality of the optimization variables. Therefore, for practical cases we recommend using the IbO problem formulation described in Section 4.1 rather than using constraint (48).

4.2.2. Ill-conditioning and importance of soft constraints

The optimization problem of IbO can be formulated in the space of input variables as a single-step optimization problem (Tomba et al., 2012). In its simplest form:

$$\widehat{\mathbf{x}}_{\text{des}} = \underset{\mathbf{x}_{\text{des}}}{\operatorname{argmin}}\left[(\widehat{\mathbf{y}}_{\text{des}} - \mathbf{B}^{\top}\cdot\mathbf{x}_{\text{des}})^{\top}\cdot(\mathbf{y}_{\text{des}} - \mathbf{B}^{\top}\cdot\mathbf{x}_{\text{des}})\right]. \tag{49}$$

which is an unconstrained QP problem. The matrix and vector of the objective function can be formulated as:

$$\mathbf{H} = 2\mathbf{B}\cdot\mathbf{B}^{\top}, \tag{50}$$

$$\mathbf{f} = -2\mathbf{B}\cdot\mathbf{y}_{\text{des}}, \tag{51}$$

which yield the analytical solution:

$$\widehat{\mathbf{x}}_{\text{des}} = (\mathbf{B}\cdot\mathbf{B}^{\top})^{-1}\cdot\mathbf{B}\cdot\mathbf{y}_{\text{des}}. \tag{52}$$

However, this analytical solution can never be computed because $\mathbf{B}$ is a matrix with V_X rows and V_Y columns, thus $\mathbf{B}\cdot\mathbf{B}^{\top}$ is a matrix in $\mathbb{R}^{V_X}\times\mathbb{R}^{V_X}$ with rank V_Y. In virtually all product design applications of PLS, $V_X \gg V_Y$, therefore $\mathbf{B}\cdot\mathbf{B}^{\top}$ can never be inverted analytically, although matrix factorization (Nocedal and Wright, 2006) or regularized inversion (Arnese-Feffin et al., 2022) methods could be used. A null space would still have to be accounted for, in this case of very large dimensionality, i.e., $V_X - V_Y$, leading to a non-trivial complication.

In this case, it is convenient to use soft constraints in the objective function to regularize the inversion, similarly to what was done Section 4.1.1. In light of the discussion in Section 4.2.1, we can include soft constraints for both T^2 and Q, thus formulating the IbO problem as:

$$\begin{aligned}\widehat{\mathbf{x}}_{\text{des}} = \underset{\mathbf{x}_{\text{des}}}{\operatorname{argmin}}\Big[&(\widehat{\mathbf{y}}_{\text{des}} - \mathbf{B}^{\top}\cdot\mathbf{x}_{\text{des}})^{\top}\cdot\mathbf{\Gamma}_1\cdot(\mathbf{y}_{\text{des}} - \mathbf{B}^{\top}\cdot\mathbf{x}_{\text{des}}) \\ &+ \gamma_2\mathbf{x}_{\text{des}}^{\top}\cdot\mathbf{W}^{*}\cdot\mathbf{\Lambda}^{-1}\cdot(\mathbf{W}^{*})^{\top}\cdot\mathbf{x}_{\text{des}} + \gamma_3\mathbf{x}_{\text{new}}^{\top}\cdot(\mathbf{I}_{V_X} - \mathbf{P}\cdot(\mathbf{W}^{*})^{\top})^{\top}\cdot(\mathbf{I}_{V_X} \\ &- \mathbf{P}\cdot(\mathbf{W}^{*})^{\top})\cdot\mathbf{x}_{\text{new}}\Big].\end{aligned} \tag{53}$$

which yields an unconstrained QP problem. In (53), $\mathbf{\Gamma}_1$ is the weight matrix for the targets on output variables, while γ_2 and γ_3 are weights for the soft constraints on T^2 and Q, respectively. A good choice for γ_3 (Tomba et al., 2012) is $\gamma_3 = 1/Q_{\text{lim}}$, where Q_{lim} is the confidence limit of Q at significance level α (see Appendix A for details). The matrix and vector of the objective function are:

$$\begin{aligned}\mathbf{H} = 2\big(&\mathbf{B}\cdot\mathbf{\Gamma}_1\cdot\mathbf{B}^{\top} + \gamma_2\mathbf{W}^{*}\cdot\mathbf{\Lambda}^{-1}\cdot(\mathbf{W}^{*})^{\top} + \gamma_3(\mathbf{I}_{V_X} - \mathbf{P}\cdot(\mathbf{W}^{*})^{\top})^{\top}\cdot(\mathbf{I}_{V_X} \\ &- \mathbf{P}\cdot(\mathbf{W}^{*})^{\top})\big),\end{aligned} \tag{54}$$

$$\mathbf{f} = -2\mathbf{B}\cdot\mathbf{\Gamma}_1\cdot\mathbf{y}_{\text{des}}, \tag{55}$$

which can be used to obtain an analytical solution for the problem.

We remark that soft constraints are essential if IbO is formulated in the space of input variables to regularize the inversion of matrix $\mathbf{H}$, thus operating a similar effect as the one illustrated in Fig. 3, although in a space of much larger dimensionality. The solution can therefore be computed analytically, which entails significant advantages from the computational point of view. The effect of γ_3 is comparable to the effect of γ_2 discussed in Section 4.1.1: the greater γ_3, the smaller the Q statistics of the solution. Note that in the limit of $\gamma_3 \rightarrow +\infty$, $\widehat{\mathbf{x}}_{\text{des}}$ would be forced to conform to the correlation structure of the input space.

Table 5
Meaningful linear inequality and equality constraints for IbO of PLS models in the space of input variables stated as $\mathbf{A}\cdot\mathbf{x}_{\text{des}} \leq \mathbf{b}$ and $\mathbf{A}_{\text{eq}}\cdot\mathbf{x}_{\text{des}} \leq \mathbf{b}_{\text{eq}}$, respectively. If some of the variables are not to be constrained, remove the relevant rows from $\mathbf{A}$ (or $\mathbf{A}_{\text{eq}}$) and $\mathbf{b}$ (or $\mathbf{b}_{\text{eq}}$). To constraint linear combinations of the variables, premultiply matrix $\mathbf{A}$ (or $\mathbf{A}_{\text{eq}}$) by the matrix of linear combinations coefficients, $\mathbf{L}$, and replace the relevant bound (or value) by replacing $\mathbf{b}$ (or $\mathbf{b}_{\text{eq}}$).

Constraint	A or A_{eq}	b or b_{eq}
Inequality constraints		
Upper bounds on outputs	$\mathbf{B}^{\top}$	$\mathbf{y}_{\text{UB}}$
Lower bounds on outputs	$-\mathbf{B}^{\top}$	$-\mathbf{y}_{\text{LB}}$
Upper bounds on inputs	$\mathbf{I}_{V_X}$	$\mathbf{x}_{\text{UB}}$
Lower bounds on inputs	$-\mathbf{I}_{V_X}$	$-\mathbf{x}_{\text{LB}}$
Upper bounds on LVs	$(\mathbf{W}^{*})^{\top}$	$\mathbf{t}_{\text{UB}}$
Lower bounds on LVs	$-(\mathbf{W}^{*})^{\top}$	$-\mathbf{t}_{\text{LB}}$
Upper bounds on UCLof the null space	$\mathbf{B}^{\top}$	$\text{UCL}(\mathbf{y}_{\text{des}})$
Lower bounds on LCLof the null space	$-\mathbf{B}^{\top}$	$-\text{LCL}(\mathbf{y}_{\text{des}})$
Equality constraints		
Value of output	$\mathbf{B}^{\top}$	$\mathbf{y}_{\text{eq}}$
Value of inputs	$\mathbf{I}_{V_X}$	$\mathbf{x}_{\text{eq}}$
Value of LVs	$(\mathbf{W}^{*})^{\top}$	$\mathbf{t}_{\text{eq}}$
Null space	$\mathbf{B}^{\top}$	$\mathbf{y}_{\text{des}}$

Table 6
Meaningful nonlinear inequality constraint functions for IbO of PLS models in the space of input variables stated as $C(\mathbf{x}_{\text{des}}) \leq 0$.

Constraint	$C(\mathbf{x}_{\text{des}})$
Confidence limit of T^2	$\mathbf{x}_{\text{des}}^{\text{T}}\cdot\mathbf{W}^{*}\cdot\mathbf{\Lambda}^{-1}\cdot(\mathbf{W}^{*})^{\top}\cdot\mathbf{x}_{\text{des}} - T^2_{\text{lim}}$
Confidence limit of Q	$\mathbf{x}_{\text{des}}^{\top}\cdot(\mathbf{I}_{V_X} - \mathbf{P}\cdot(\mathbf{W}^{*})^{\top})^{\top}\cdot(\mathbf{I}_{V_X} - \mathbf{P}\cdot(\mathbf{W}^{*})^{\top})\cdot\mathbf{x}_{\text{des}} - Q_{\text{lim}}$
Upper bounds on UCLof the null space	$\mathbf{B}^{\top}\cdot\mathbf{x}_{\text{des}} - \text{UCL}(\widehat{\mathbf{y}}_{\text{des}}, (\mathbf{W}^{*})^{\top}\cdot\mathbf{x}_{\text{des}})$
Lower bounds on LCLof the null space	$-\mathbf{B}^{\top}\cdot\mathbf{x}_{\text{des}} + \text{LCL}(\widehat{\mathbf{y}}_{\text{des}}, (\mathbf{W}^{*})^{\top}\cdot\mathbf{x}_{\text{des}})$

4.2.3. Including hard constraints

Constraints can be incorporated in IbO also when the problem is formulated in the space of input variables. Considering both linear and nonlinear constraints, the problem can be formulated in (53) and subject to:

$$\mathbf{A}\cdot\mathbf{x}_{\text{des}} \leq \mathbf{b}, \tag{56}$$

$$\mathbf{A}_{\text{eq}}\cdot\mathbf{x}_{\text{des}} = \mathbf{b}_{\text{eq}}, \tag{57}$$

$$C(\mathbf{x}_{\text{des}}) \leq 0, \tag{58}$$

If only linear constraints (56) and (57) are set, the problem is a constrained QP, which ca be solved with reasonable efficiency by numerical methods. Linear constraints can be stated similarly to IbO in the space of LVs, as outlined in Section 4.1.2. Meaningful linear constraints are summarized in Table 5.

On the other hand, the inclusion of nonlinear constraints (58) turns the problem into an NLP. The computational burden to solve the problem is remarkably high in this case, as the optimization variables can have a very high dimensionality (possibly hundreds, or even thousands of input variables in the case of batch processes). Therefore, we recommend not using nonlinear constraints unless it is crucial to do so; their soft/linear counterparts should be used instead whenever possible. If deemed essential, nonlinear constraints can be set on the T^2 and Q statistics, and on the confidence region of the null space. Meaningful nonlinear constraint functions are summarized in Table 6.

Finally, note that target values of some output variables may not be specified, similarly to IbO in the space of LVs, i.e., the corresponding diagonal element of $\mathbf{\Gamma}_1$ can be nulled. In this respect, the discussion at the end of Section 4.1.2 applies entirely also in the case of IbO formulated in the space of input variables.

In Fig. 8, we illustrate some characteristics of the IbO problem (53)

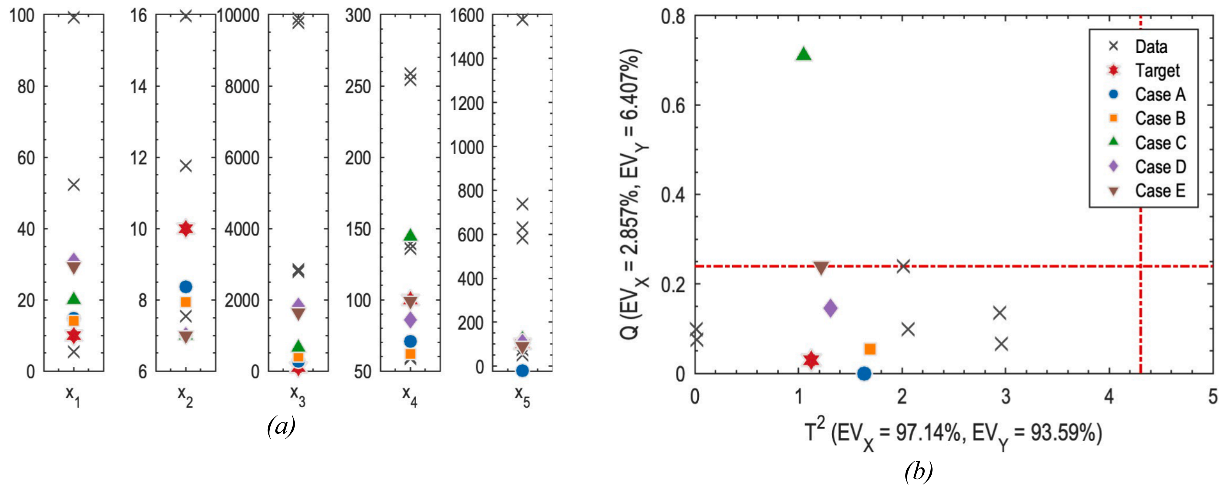

Fig. 8. Some characteristics of the IbO problem visualized as (a) solutions in the space of input variables, and (b) PLS model diagnostics. Case A; unconstrained and unweighted solutions with problem formulated in the space of LVs. Case B: unconstrained and unweighted solutions with problem formulated in the space of input variables. Case C: linear hard constraints on inputs. Case D: hard constraints on inputs may cause a large Q statistic, which can be remedied by stating soft constrains on Q. Case E: hard constraints on Q.

subject to (56), (57), and (58) in the input space by solving five different cases. Namely, we visualize the solutions in the space of input variables in Fig. 8(a), with their corresponding diagnostics in Fig. 8(b). We set $\boldsymbol{\Gamma}_1 = \mathbf{I}_{V_Y}$ in all cases and use the reasonably assigned target output introduced in Section 3. Cases A and B (blue circle and orange square, respectively) elucidate the effect of the different routes taken by IbO when formulated in the spaces of LVs and input variables, respectively, with $\gamma_2 = 0$ and $\gamma_3 = 0$. Despite of the two cases both achieving the target quality exactly, the designed input variables are slightly different (Fig. 8(a)). This is due to the different routes taken by the two approaches (Section 4.2.1), which implies that the solution of the IbO problem in the space of input variables has a non-null Q, as can be seen in Fig. 8(b). In Case C (green upwards triangle), we set $\gamma_2 = 1/T^2_{\text{lim}}$ and $\gamma_3 = 0$, and we state two hard constraints on the input variables: x_1 is lower bounded by $x_{1,\text{LB}} = 20$, and x_2 is upper bounded by $x_{2,\text{UB}} = 7$. Note that these constraints force the solution against the correlation structure captured by the PLS model, causing the Q statistic to be well beyond the confidence limit in Fig. 8(b). We fix this issue in Case D (violet diamond) by setting $\gamma_3 = 0.05/Q_{\text{lim}}$, which effectively takes the Q statistics below the control limit by adjusting the input variables, as we see in Fig. 8(a). Case D is still a computationally tractable QP problem; on the other hand, Case E (brown downwards triangle) is a computationally burdensome NLP problem in which we again set $\gamma_3 = 0$ and we state a nonlinear constraint on Q, effectively bounding the solution within the confidence limit of the statistic in Fig. 8(b). Note that, in Fig. 8(a), the solutions of Cases D and E do not differ significantly, thus reinforcing the suggestion to use soft constraints instead of hard constraints to keep the optimization problem simpler and computationally tractable.

5. General formulation of PLS model inversion problems

The objective functions used in the formulation of the IbO problem in the spaces of LVs and input variables, e.g., in (36) and (53), share remarkable similarities, yielding very similar matrices **H** and vectors **f**. Furthermore, the structure of linear constraints is identical, the only difference being in how the constraint matrices are calculated (e.g., compare Table 3 and Table 5). A similar observation can be done for nonlinear constraints, where the functions in Table 4 and Table 6 differ only in the matrices multiplying the optimization variables. Based on these observations, in this Section we propose a general formulation of IbO problems that can be adapted to both the spaces of LVs and input variables.

Table 7
Domain matrices for the general formulation of IbO of PLS models.

Domain matrix	$\mathbf{z} = \mathbf{t}_{\text{des}}$	$\mathbf{z} = \mathbf{x}_{\text{des}}$
$\mathbf{O}_{\text{O}}$	$\tilde{\mathbf{Q}}$	$\mathbf{B}^{\top}$
$\mathbf{O}_{\text{L}}$	$\mathbf{I}_A$	$(\mathbf{W}^{*})^{\top}$
$\mathbf{O}_{\text{I}}$	$\mathbf{P}$	$\mathbf{I}_{V_X}$

Our formulation relies on three domain matrices: $\mathbf{O}_{\text{O}}$, $\mathbf{O}_{\text{L}}$, and $\mathbf{O}_{\text{I}}$, which we can interpret as linear operators projecting the vector of generic optimization variables, $\mathbf{z}$, onto the spaces of output variables, LVs, and input variables, respectively, according to the equations:

$$\mathbf{y}_{\text{des}} = \mathbf{O}_{\text{O}} \cdot \mathbf{z}, \tag{59}$$

$$\mathbf{t}_{\text{des}} = \mathbf{O}_{\text{L}} \cdot \mathbf{z}, \tag{60}$$

$$\mathbf{x}_{\text{des}} = \mathbf{O}_{\text{I}} \cdot \mathbf{z}. \tag{61}$$

The form of the domain matrices depends on the domain of the IbO problem: if the optimization is to be carried out in the space of LVs, then $\mathbf{z} = \mathbf{t}_{\text{des}}$; on the other hand, $\mathbf{z} = \mathbf{x}_{\text{des}}$ if the optimization is set in the space of input variables. The domain matrices in the three cases are reported in Table 7.

We also formulate two scale matrices ($\boldsymbol{\Phi}$ and $\boldsymbol{\Psi}$), which depend on the domain matrices:

$$\boldsymbol{\Phi} = \mathbf{O}_{\text{L}}^{\top} \cdot \boldsymbol{\Lambda}^{-1} \cdot \mathbf{O}_{\text{L}}, \tag{62}$$

$$\boldsymbol{\Psi} = \mathbf{O}_{\text{I}}^{\top} \cdot \left(\mathbf{I}_{V_X} - \mathbf{P} \cdot (\mathbf{W}^{*})^{\top}\right)^{\top} \cdot \left(\mathbf{I}_{V_X} - \mathbf{P} \cdot (\mathbf{W}^{*})^{\top}\right) \cdot \mathbf{O}_{\text{I}}, \tag{63}$$

and can be used to compute the T^2 and Q statistics of $\mathbf{z}$ to set soft or hard constraints:

$$T^2 = \mathbf{z}^{\top} \cdot \boldsymbol{\Phi} \cdot \mathbf{z}, \tag{64}$$

Table 8
Meaningful linear inequality and equality constraints for the general formulation of IbO of PLS models stated as $\mathbf{A}\cdot\mathbf{z} \le \mathbf{b}$ and $\mathbf{A}_{\mathrm{eq}}\cdot\mathbf{z} \le \mathbf{b}_{\mathrm{eq}}$, respectively.

Constraint	A or $\mathbf{A}_{\mathrm{eq}}$	b or $\mathbf{b}_{\mathrm{eq}}$
Inequality constraints		
Upper bounds on outputs	$\mathbf{O}_{\mathrm{O}}$	$\mathbf{y}_{\mathrm{UB}}$
Lower bounds on outputs	$-\mathbf{O}_{\mathrm{O}}$	$-\mathbf{y}_{\mathrm{LB}}$
Upper bounds on inputs	$\mathbf{O}_{\mathrm{I}}$	$\mathbf{x}_{\mathrm{UB}}$
Lower bounds on inputs	$-\mathbf{O}_{\mathrm{I}}$	$-\mathbf{x}_{\mathrm{LB}}$
Upper bounds on LVs	$\mathbf{O}_{\mathrm{L}}$	$\mathbf{t}_{\mathrm{UB}}$
Lower bounds on LVs	$-\mathbf{O}_{\mathrm{L}}$	$-\mathbf{t}_{\mathrm{LB}}$
Upper bounds on UCLof the null space	$\mathbf{O}_{\mathrm{O}}$	$\mathrm{UCL}(\mathbf{y}_{\mathrm{des}})$
Lower bounds on LCLof the null space	$-\mathbf{O}_{\mathrm{O}}$	$-\mathrm{LCL}(\mathbf{y}_{\mathrm{des}})$
Equality constraints		
Value of output	$\mathbf{O}_{\mathrm{O}}$	$\mathbf{y}_{\mathrm{eq}}$
Value of inputs	$\mathbf{O}_{\mathrm{I}}$	$\mathbf{x}_{\mathrm{eq}}$
Value of LVs	$\mathbf{O}_{\mathrm{L}}$	$\mathbf{t}_{\mathrm{eq}}$
Null space	$\mathbf{O}_{\mathrm{O}}$	$\mathbf{y}_{\mathrm{des}}$

Table 9
Meaningful nonlinear inequality constraint functions for the general formulation of IbO of PLS models stated as $C(\mathbf{z}) \le 0$.

Constraint	$\mathrm{C}(\mathbf{z})$
Confidence limit of T^2	$\mathbf{z}^{\top}\cdot\mathbf{\Phi}\cdot\mathbf{z} - T^2_{\lim}$
Confidence limit of Q	$\mathbf{z}^{\top}\cdot\mathbf{\Psi}\cdot\mathbf{z} - Q_{\lim}$
Upper bounds on UCLof the null space	$\mathbf{O}_{\mathrm{O}}\cdot\mathbf{z} - \mathrm{UCL}(\widehat{\mathbf{y}}_{\mathrm{des}}, \mathbf{O}_{\mathrm{O}}\cdot\mathbf{z})$
Lower bounds on LCLof the null space	$-\mathbf{O}_{\mathrm{O}}\cdot\mathbf{z} + \mathrm{LCL}(\widehat{\mathbf{y}}_{\mathrm{des}}, \mathbf{O}_{\mathrm{O}}\cdot\mathbf{z})$

$$Q = \mathbf{z}^{\mathsf{T}}\cdot\mathbf{\Psi}\cdot\mathbf{z}. \tag{65}$$

Note that, if $\mathbf{z} = \mathbf{t}_{\mathrm{des}}$, then $\mathbf{x}_{\mathrm{des}} = \mathbf{P}\cdot\mathbf{t}_{\mathrm{des}}$ is a rank-A projection of $\mathbf{t}_{\mathrm{des}}$ onto the space of input variables. Therefore, the projection of $\mathbf{x}_{\mathrm{des}}$ onto the space of LVs is $(\mathbf{W}^*)^{\top}\cdot\mathbf{x}_{\mathrm{des}} = \mathbf{t}_{\mathrm{des}}$, which causes (65) to always yield 0, thus proving that (63) is a general form of the scale matrix for Q.

We can then leverage the domain and scale matrices to define a general optimization problem in the form of (19), where the objective function is:

$$J(\mathbf{z}) = (\mathbf{y}_{\mathrm{des}} - \mathbf{O}_{\mathrm{O}}\cdot\mathbf{z})^{\top}\cdot\mathbf{\Gamma}_1\cdot(\mathbf{y}_{\mathrm{des}} - \mathbf{O}_{\mathrm{O}}\cdot\mathbf{z}) + \gamma_2\mathbf{z}^{\top}\cdot\mathbf{\Phi}\cdot\mathbf{z} + \gamma_3\mathbf{z}^{\top}\cdot\mathbf{\Psi}\cdot\mathbf{z}, \tag{66}$$

which can be expressed as in (25) with matrices:

$$\mathbf{H} = 2\left(\mathbf{O}_{\mathrm{O}}^{\top}\cdot\mathbf{\Gamma}_1\cdot\mathbf{O}_{\mathrm{O}} + \gamma_2\mathbf{\Phi} + \gamma_3\mathbf{\Psi}\right), \tag{67}$$

$$\mathbf{f} = -2\mathbf{O}_{\mathrm{O}}^{\top}\cdot\mathbf{\Gamma}_1\cdot\mathbf{y}_{\mathrm{des}}. \tag{68}$$

Linear equality and inequality constraints on input variables, LVs, and output variables can be stated by using the domain matrices as shown in Table 8. Nonlinear constraints can be generalized in a similar way, as shown in Table 9.

We remark that the only decision required to the user of the proposed general formulation of IbO problems is the domain in which the optimization should be performed. If constraints on inputs, LVs, or outputs are to be stated, only the constraint values (i.e., bounds and equalities) are to be set by the user and assigned to the vectors $\mathbf{b}$ and $\mathbf{b}_{\mathrm{eq}}$, respectively, while the relevant constraint matrices $\mathbf{A}$ and $\mathbf{A}_{\mathrm{eq}}$ are adapted automatically based on the selected optimization domain. Constraints on "abstracted" entities, such as the model validity region, or the null space and its confidence region, can be stated by fully automated procedures, therefore requiring a simple logical indicator to decide whether to consider or neglect them.

We also remark that all the considerations on the computational costs of the solution procedures required by the various cases of IbO outlined in Sections 4.1 and 4.2 apply entirely to the proposed general formulation. Namely, the problem admits an analytical solution if no constraint is stated; a computationally efficient QP numerical solver can be used if only linear constraints are stated; a gradient-based NLP solver must be used if nonlinear constraints are considered. Furthermore, the computational demand increases with the dimensionality of the optimization variables, making IbO in the space of input variables naturally more demanding than its counterpart in the space of LVs. The cases are graphically illustrated in Fig. 9, with a clear indication of the class of problem and typical computational burden.

6. Conclusions

In this study, we thoroughly discussed latent-variable model inversion, a data-driven method to find the process conditions that are required to manufacture a product with assigned quality, by relying solely on historical data acquired during routine process operation. In particular, we considered inversion by optimization of partial least-squares (PLS) regression models. We carried out a systematic discussion of the available methods, elucidating the merits and drawbacks of each one based on several factors. The optimization problem can be formulated in the space of latent variables to force the solution to conform to the correlation structure of the data used for model calibration (i.e., to implicitly respect process constraints and/or production policies) or in the space of input variables for a greater flexibility and finer tuning of the solution. We analyzed the consistency of inversion by optimization with algebraic inversion methods in each one of these domains. We also extensively discussed the constraints that could possibly be stated on the optimization problem, highlighting the different effects of soft and hard constraints, and whether or not nonlinear constraints should be stated in place of simpler linear constraints. For each case, we clearly identified the solution algorithms required, discussing their computational burden and potential availability of an analytical solution. Finally, we proposed a general formulation of the PLS model inversion-by-optimization problem, which encompasses all the cases we have discussed throughout this study based on one single choice: the domain of the optimization problem. We supported our discussion with a numerical case study and provided the code to reproduce it. The code can also be used a general MATLAB

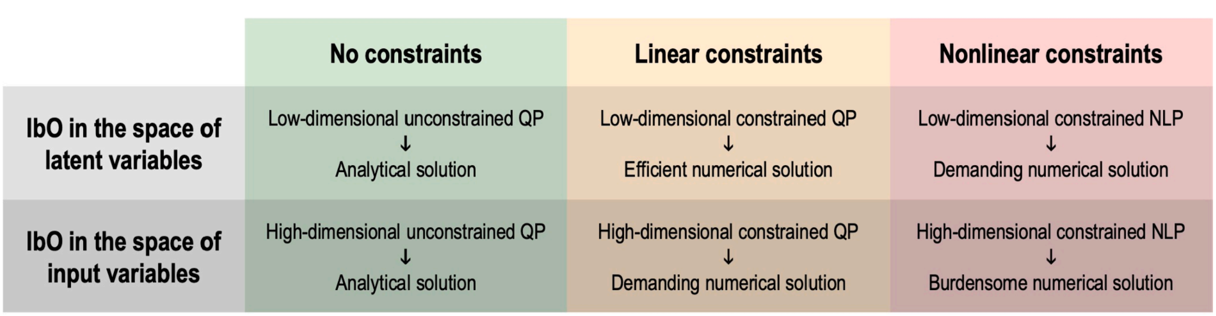

Fig. 9. Classification of IbO problems based on the optimization domain and type of constraints stated, with indication of the computational burden to solve the problem.

toolbox for PLS model inversion.

CRediT authorship contribution statement

Elia Arnese-Feffin: Writing – original draft, Visualization, Validation, Software, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Pierantonio Facco:** Writing – review & editing, Conceptualization. **Fabrizio Bezzo:** Writing – review & editing, Conceptualization. **Massimiliano Barolo:** Writing – review & editing, Supervision, Funding acquisition, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

The data used in this study are provided in Table 1. All the computations were carried out in MATLAB R2022a (The Mathworks, 2022) with in-house developed code. The code can be accessed at the following GitHub repository: https://github.com/EliaAF/PLSModelInversionPackage.

The code has been tested on MATLAB R2022a (The Mathworks, 2022) and provides general utilities for PLS model calibration, selection, diagnostics, and inversion; it may be used freely and is covered by the GNU general public license version 3.0.

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Appendix A. Estimators for confidence limits of PLS diagnostics

The PLS model diagnostics statistics, T^2 and Q, can be compared to appropriate confidence limits to determine their significance (Martin and Morris, 1996; Qin, 2003; Tracy et al., 1992). The confidence limit of the T^2 statistic can be estimated by the F distribution method (Jackson, 1959) or by the χ^2 distribution method (Nomikos and MacGregor, 1995a). The confidence limit of the Q statistic can be estimated by the Jackson-Mudholkar approach (Jackson and Mudholkar, 1979) or by the χ^2 distribution method (Nomikos and MacGregor, 1995a).

We consider the T^2 statistic first. The control limit of T^2 at significance level α based on the F distribution is defined as:

$$T^2_{\mathrm{lim}} = \frac{\mathrm{DOF}(N-1)(N+1)}{N(N-\mathrm{DOF})}F(\mathrm{DOF}, N-\mathrm{DOF})\,|_{1-\alpha}, \tag{A.1}$$

where DOF represents the degrees of freedom of the PLS model, while $F(\mathrm{DOF}, N-\mathrm{DOF})\,|_{1-\alpha}$ denotes the value of a F-variable with DOF and $N-$DOF degrees of freedom at the numerator and denominator, respectively, evaluated at probability $1-\alpha$. According to the so-called naïve approach, DOF $= A$; more sophisticated DOF estimators exist nonetheless (Krämer and Sugiyama, 2011; Van Der Voet, 1999). The control limit of T^2 at significance level α based on the χ^2 distribution with matching moments is defined as:

$$T^2_{\mathrm{lim}} = \frac{s^2_{T^2}}{2\overline{T^2}}\chi^2\left(2\left(\overline{T^2}/s_{T^2}\right)^2\right)\Big|_{1-\alpha}, \tag{A.2}$$

where $\overline{T^2}$ and s_{T^2} are the sample mean and standard deviation of T^2, respectively, computed using the values of the statistic derived from the calibration dataset, while $\chi^2\left(2\left(\overline{T^2}/s_{T^2}\right)^2\right)\Big|_{1-\alpha}$ is the value of a χ^2-variable with $2\left(\overline{T^2}/s_{T^2}\right)^2$ degrees of freedom evaluated at probability $1-\alpha$. Both the F-based and χ^2-based limits rely on the normality assumption of the values of $\mathbf{t}$ obtained from the calibration dataset; however, the χ^2 limit is recommended in general by virtue of its mild robustness to violations of the normality assumption (Qin, 2003).

According to the Jackson-Mudholkar approach, the control limit of Q at significance level α is defined as:

$$Q_{\mathrm{lim}} = \theta_1\left(1 + \frac{z|_{1-\alpha}h_0\sqrt{2\theta_2}}{\theta_1} + \frac{h_0(h_0-1)\theta_2}{\theta_1^2}\right)^{\frac{1}{h_0}}, \tag{A.3}$$

where:

$$\theta_i = \sum_{j=A+1}^{V_X}\left(\sigma_j^2\right)^i, \tag{A.4}$$

$$h_0 = 1 - \frac{2\theta_1\theta_3}{3\theta_2^2}. \tag{A.5}$$

In (A.3), $z|_{1-\alpha}$ is the value of a standard normal variable evaluated at probability $1-\alpha$, while the σ_j^2 in (A.4) is the variance of the $V_X - A$ LVs not considered in the PLS model. The control limit of Q at significance level α based on the χ^2 distribution with matching moments is defined as:

$$Q_{\mathrm{lim}} = \frac{s_Q^2}{2\overline{Q}}\chi^2\left(2\left(\overline{Q}/s_Q\right)^2\right)\Big|_{1-\alpha}, \tag{A.6}$$

where $\overline{Q}$ and s_Q are the sample mean and standard deviation of the Q, respecitvely, computed using the values of the statistic derived from the calibration dataset, while $\chi^2\left(2(\overline{Q}/s_Q)^2\right)\Big|_{1-\alpha}$ is the value of a χ^2-variable with $2(\overline{Q}/s_Q)^2$ degrees of freedom evaluated at probability $1-\alpha$. Similarly to the limits for T^2, both the Jackson-Mudholkar approach and the χ^2-based limits rely on the normality assumption of the values of Q obtained from the calibration dataset; the χ^2 limit is recommended due to its robustness (Qin, 2003).

Appendix B. PLS prediction uncertainty

As the $\widehat{\mathbf{y}}_{\text{new}}$ computed by the PLS model applied to a new input observation is an approximation of the true output observation $\mathbf{y}_{\text{new}}$, the value of which is generally unknown, considering the prediction uncertainty is of paramount importance to assess the reliability of the estimate. The confidence limit (CL) of the predicted value $\widehat{\mathbf{y}}_{\text{new}}$ at significance level α can be formulated as (Faber and Kowalski, 1997; Nomikos and MacGregor, 1995b; Zhang and García Muñoz, 2009):

$$\text{CL}(\widehat{\mathbf{y}}_{\text{new}}) = \widehat{\mathbf{y}}_{\text{new}} \pm \mathbf{s}_{\widehat{\mathbf{y}}_{\text{new}}} t(N-\text{DOF})\,|_{\frac{\alpha}{2}}, \tag{B.1}$$

where $t(N-\text{DOF})\,|_{\frac{\alpha}{2}}$ is the value of a t-distributed variable with $N-$DOF degrees of freedom evaluated at probability $\frac{\alpha}{2}$. The standard deviation of $\widehat{\mathbf{y}}_{\text{new}}$, $\mathbf{s}_{\widehat{\mathbf{y}}_{\text{new}}} \in \mathbb{R}^{V_Y}$, is estimated as:

$$\mathbf{s}_{\widehat{\mathbf{y}}_{\text{new}}} = \mathbf{RMSE}\sqrt{1+\frac{1}{N}+h_{\widehat{\mathbf{y}}_{\text{new}}}}, \tag{B.2}$$

where $h_{\widehat{\mathbf{y}}_{\text{new}}}$ is the leverage of the estimated $\widehat{\mathbf{y}}_{\text{new}}$ on the model:

$$h_{\widehat{\mathbf{y}}_{\text{new}}} = \mathbf{t}_{\text{new}}^{\top}\cdot\boldsymbol{\Lambda}^{-1}\cdot\mathbf{t}_{\text{new}}, \tag{B.3}$$

while $\mathbf{RMSE} \in \mathbb{R}^{V_Y}$ is the vector of root mean-squared errors in calibration of output variables:

$$\mathbf{RMSE} = \left(\frac{\sum_{n=1}^{N}(\mathbf{y}_n - \widehat{\mathbf{y}}_n)^2}{N-\text{DOF}}\right)^{0.5}. \tag{B.4}$$

Appendix C. Null space uncertainty in LVMI

We consider two simple analytical approaches to estimate the null space uncertainty: the method proposed by Facco et al. (2015), which is based on PLS prediction uncertainty, and its extension to include the effect of observation leverage proposed by Palací-López et al. (2019). We also point out their properties when used as hard constraints in IbO.

The approach by Facco et al. (2015) assumes that the target quality, $\mathbf{y}_{\text{des}}$, can be regarded as a prediction from the PLS model; its corresponding projection onto the space of LVs in the presence of a null space, $\widehat{\mathbf{t}}_{\text{des, p}}$, is obtained from (14). Therefore, one sets $\widehat{\mathbf{y}}_{\text{new}} = \mathbf{y}_{\text{des}}$ and first carries out the procedure outlined in Appendix B. The leverage of $\mathbf{y}_{\text{des}}$ is computed by (B.3):

$$h_{\mathbf{y}_{\text{des}}} = \widehat{\mathbf{t}}_{\text{des, p}}^{\top}\cdot\boldsymbol{\Lambda}^{-1}\cdot\widehat{\mathbf{t}}_{\text{des, p}}, \tag{C.1}$$

and used to estimate the standard deviation of $\mathbf{y}_{\text{des}}$ from (B.2):

$$\mathbf{s}_{\mathbf{y}_{\text{des}}} = \mathbf{RMSE}\sqrt{1+\frac{1}{N}+h_{\mathbf{y}_{\text{des}}}}, \tag{C.2}$$

which allows to compute the “confidence limit of $\mathbf{y}_{\text{des}}$” at significance level α by (B.1):

$$\text{CL}(\mathbf{y}_{\text{des}}) = \mathbf{y}_{\text{des}} \pm \mathbf{s}_{\mathbf{y}_{\text{des}}} t(N-\text{DOF})\,|_{\frac{\alpha}{2}}. \tag{C.3}$$

The confidence limit of $\mathbf{y}_{\text{des}}$ is then “inverted” by means of (14) as the estimate the confidence limit of $\widehat{\mathbf{t}}_{\text{des, p}}$:

$$\text{CL}\left(\widehat{\mathbf{t}}_{\text{des, p}}\right) = \widetilde{\mathbf{Q}}^{\top}\cdot\left(\widetilde{\mathbf{Q}}\cdot\widetilde{\mathbf{Q}}^{\top}\right)\cdot\text{CL}(\mathbf{y}_{\text{des}}), \tag{C.4}$$

which is then “propagated linearly” as in (17) to estimate the confidence limit of $\widehat{\mathbf{t}}_{\text{des, p}}$, thus of the null space:

$$\text{CL}\left(\widehat{\mathbf{t}}_{\text{des}}\right) = \text{CL}\left(\widehat{\mathbf{t}}_{\text{des, p}}\right) + \widehat{\mathbf{t}}_{\text{des, n}}. \tag{C.5}$$

One may immediately see that the method proposed by Facco et al. (2015) relies on the simple inversion of a constant “prediction uncertainty” estimated at $\mathbf{y}_{\text{des}}$, thus with constant observation leverage estimated by $\widehat{\mathbf{t}}_{\text{des, p}}$. We remark that the estimated confidence limit for the null space depends on the DI solution alone. Therefore, $\text{CL}(\mathbf{y}_{\text{des}})$ can be incorporated in IbO to state linear inequality constraints on the confidence region of the null space, being independent on the optimization variables in both cases $\mathbf{z} = \mathbf{t}_{\text{des}}$ and $\mathbf{z} = \mathbf{x}_{\text{des}}$.

On the other hand, the method proposed by Palací-López et al. (2019) adopts a more sophisticated approach, which also considers variable observation leverage along the null space. Consider a generic point $\widehat{\mathbf{t}}_{\mathrm{des}_l}$ along the subspace $\widehat{\mathbf{t}}_{\mathrm{des}}$, defined as in (17). The corresponding output can be computed as:

$$\widehat{\mathbf{y}}_{\mathrm{des}_l} = \widetilde{\mathbf{Q}}^{\top}\cdot\left(\widetilde{\mathbf{Q}}\cdot\widetilde{\mathbf{Q}}^{\top}\right)\cdot\widehat{\mathbf{t}}_{\mathrm{des}_l}, \tag{C.6}$$

which is then used to compute the residual associated with the considered point along the null space:

$$\mathbf{r}_{\mathrm{des}_l} = \mathbf{y}_{\mathrm{des}} - \widehat{\mathbf{y}}_{\mathrm{des}_l}. \tag{C.7}$$

The residual is projected back onto the space of LVs and used to propagate the inversion uncertainty onto the considered point of the null space, defining the "perturbated" scores as:

$$\widetilde{\mathbf{t}}_{\mathrm{des}_l} = \widehat{\mathbf{t}}_{\mathrm{des}_l} + \widetilde{\mathbf{Q}}^{\top}\cdot\left(\widetilde{\mathbf{Q}}\cdot\widetilde{\mathbf{Q}}^{\top}\right)\cdot\mathbf{r}_{\mathrm{des}_l}. \tag{C.8}$$

The perturbated scores account for the error associated with the null space on the reconstruction of $\mathbf{y}_{\mathrm{des}}$, thus can be used to obtain the leverage of $\widehat{\mathbf{y}}_{\mathrm{des}_l}$ as:

$$h_{\widehat{\mathbf{y}}_{\mathrm{des}_l}} = \widetilde{\mathbf{t}}_{\mathrm{des}_l}^{\top}\cdot\mathbf{\Lambda}^{-1}\cdot\widetilde{\mathbf{t}}_{\mathrm{des}_l}, \tag{C.9}$$

which allows one to estimate the standard deviation of $\widehat{\mathbf{y}}_{\mathrm{des}_l}$:

$$\mathbf{s}_{\widehat{\mathbf{y}}_{\mathrm{des}_l}} = \mathbf{RMSE}\sqrt{1+\frac{1}{N}+h_{\widehat{\mathbf{y}}_{\mathrm{des}_l}}}. \tag{C.10}$$

Finally, (B.1) is leveraged to compute the confidence limit of $\widehat{\mathbf{y}}_{\mathrm{des}_l}$ at a given significance level α:

$$\mathrm{CL}\left(\widehat{\mathbf{y}}_{\mathrm{des}_l},\widehat{\mathbf{t}}_{\mathrm{des}_l}\right) = \widehat{\mathbf{y}}_{\mathrm{des}_l} \pm \mathbf{s}_{\widehat{\mathbf{y}}_{\mathrm{des}_l}} t(N-\mathrm{DOF})\,|_{\frac{\alpha}{2}}, \tag{C.11}$$

and the confidence limit of the considered null space point, $\widehat{\mathbf{t}}_{\mathrm{des}_l}$, is obtained applying (14) to invert $\mathrm{CL}\left(\widehat{\mathbf{y}}_{\mathrm{des}_l},\widehat{\mathbf{t}}_{\mathrm{des}_l}\right)$, which yields:

$$\mathrm{CL}\left(\widehat{\mathbf{t}}_{\mathrm{des}_l}\right) = \widehat{\mathbf{t}}_{\mathrm{des}_l} \pm \widetilde{\mathbf{Q}}^{\top}\cdot\left(\widetilde{\mathbf{Q}}\cdot\widetilde{\mathbf{Q}}^{\top}\right)\cdot\mathbf{s}_{\widehat{\mathbf{y}}_{\mathrm{des}_l}} t(N-\mathrm{DOF})\,|_{\frac{\alpha}{2}}. \tag{C.12}$$

The procedure can be repeated for any generic points in the subspace $\widehat{\mathbf{t}}_{\mathrm{des}}$ to estimate the confidence limits of the whole subspace.

Note that we described the method with reference to a generic point along the null space, $\widehat{\mathbf{t}}_{\mathrm{des}_l}$. However, the method can be applied to any vector in the space of LVs, $\mathbf{t}_{\mathrm{des}}$. In this case, $\widetilde{\mathbf{t}}_{\mathrm{des}_l}$ is interpreted as the orthogonal projection of $\mathbf{t}_{\mathrm{des}}$ onto the null space (Palací-López et al., 2019). If $\mathbf{t}_{\mathrm{des}}$ is the vector of optimization variables in IbO, this makes the approach proposed by Palací-López et al. (2019) nonlinear in $\mathbf{t}_{\mathrm{des}}$ for it involves a quadratic function of the latent variables, as can be seen in (C.9), therefore it must be incorporated in the optimization problem as a nonlinear constraint. Note that the approach can be used also when IbO is formulated in the space of input variables by simply computing $\mathbf{t}_{\mathrm{des}} = \left(\mathbf{W}^{*}\right)^{\top}\cdot\mathbf{x}_{\mathrm{des}}$.

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