

# Objective Selection for Cancer Treatment: An Inverse Optimization Approach

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**Abstract.** In radiation therapy treatment-plan optimization, selecting a set of clinical objectives that are tractable and parsimonious yet effective is a challenging task. In clinical practice, this is typically done by trial and error based on the treatment planner’s subjective assessment, which often makes the planning process inefficient and inconsistent. We develop the objective selection problem that infers a sparse set of objectives for prostate cancer treatment planning based on historical treatment data. We formulate the problem as a non-convex bilevel mixed-integer program using inverse optimization and highlight its connection with feature selection to propose multiple solution approaches, including greedy heuristics, regularized problems, as well as application-specific methods that utilize anatomical information of the patients.

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*Keywords*— Objective selection, feature selection, inverse optimization, greedy algorithm, multi-objective optimization, radiation therapy treatment planning, regularization

## 1 Introduction

Cancer is the second-leading cause of death in the United States, with more than 1.7 million new cases and 600,000 deaths estimated in 2018 (American Cancer Society 2018). Approximately 40 percent of Americans will develop cancer in their lifetimes (American Cancer Society 2018). In this decade, cancer-associated expenditure will be between \$124.4 and \$157.7 billion (Mariotto et al. 2011).

Radiation therapy is one of the primary methods to treat cancer. Because many clinical parameters are involved in creating a clinically desirable treatment, such as the number, angles, and intensities of the

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beams, radiation therapy is typically designed using mathematical optimization (Shepard et al. 1999, Bortfeld 1999). One substantial challenge in radiation therapy is the conflict between multiple clinical goals, such as delivering a sufficient amount of radiation dose to the tumor, yet sparing nearby healthy organs. Moreover, each healthy organ responds to radiation differently; thus, various clinical objectives are required to address issues with different organs. Treatment planners typically employ multi-objective optimization techniques to find optimal treatment parameter settings that generate desirable trade-offs among the set of objectives (e.g., Romeijn et al. (2004), Craft et al. (2007), Shao and Ehrgott (2008)).

Though many commercial treatment planning systems offer dedicated tools to deal with the forward optimization of the planning process, planning objectives are typically chosen subjectively, based on the planner’s experience (Craft 2011). Treatment planners adjust the selection of the objectives and associated parameters by trial and error as they repeatedly solve the optimization problem and evaluate the resulting treatment plan (Zhang et al. 2011). Consequently, the entire planning process often becomes slow and leads to inconsistent, suboptimal treatment quality (Lee et al. 2013, Boutilier et al. 2015).

The quality of the treatment plan and the efficiency of the planning process are heavily affected by the choice of objective functions. The chosen objectives affect computational complexity as well as the realism of the optimization problem; for example, linear objective functions can make the problem computationally more efficient, but the resulting formulation may not adequately reflect clinical reality. In addition, it is beneficial if the objectives are widely applicable so the constructed model with the chosen objectives can be used repeatedly for many similar patients. Thus, it is crucial to find a sparse set of objectives that adequately reflect reality and efficiently generate high-quality treatment plans.

In this paper, we propose a novel, data-driven approach to select a sparse set of effective clinical objectives for radiation therapy treatment planning. Finding a good set of objectives that best represents previously exhibited clinical preferences can be viewed as a feature selection problem. Given an input set of historical treatment plans, we aim to learn objectives that can render the given treatments near optimal for the underlying multi-objective optimization problem. By doing so, we reproduce preferences that were implicit in the treatments, which can guide the generation of clinically desirable treatments for new patients efficiently. The task of inferring modeling optimization parameters from data has been widely studied in the inverse optimization literature. Hence, we employ an inverse optimization approach integrated with feature selection to develop the objective selection problem. Our framework not only selects a subset of objectives with a specified sparsity, but also simultaneously weights the selected subset of objectives. Specifically, our contributions in this work are as follows:

1. We propose a novel, data-driven approach to select the best subset of objectives in multi-objective optimization problems. We formulate the objective selection problem using inverse optimization and show that an extensive formulation can be formulated as a bilevel, non-convex mixed-integer program.
2. We establish a connection between objective selection and feature selection and adopt the solution techniques for feature selection to approximately solve the objective selection problem, including greedy algorithm and regularization approaches. We propose the application-specific, anatomy-based greedy algorithm that exploits the problem structure of cancer treatment planning.

## 2 Literature Review

Many different objectives have been proposed in IMRT planning, such as dose-volume objectives (Halabi et al. 2006, Wu et al. 2011), equivalent uniform dose (EUD) objectives (Wu et al. 2002, Choi and Deasy 2002), quadratic penalty objectives (Breedveld et al. 2006, Romeijn et al. 2006), and minimum, maximum,

and mean dose objectives and combinations of them (Thieke et al. 2002, Craft et al. 2012). Currently, there is no consensus on which objectives should be used for different cancers and patients; final specification is often a task for treatment planners within the trial-and-error process (Xing et al. 1999, Cotrutz et al. 2001).

There are many studies in the literature that relate to the computation of weights for a given set of objectives in radiation therapy. Xing et al. (1999) propose an algorithm that automates the iterative weight adjustment process guided by a scoring function that measures clinical acceptability. Zhang et al. (2006) use a “sensitivity-guided” approach to balance the importance of multiple objectives in the treatment planning process. Similarly, Zhang et al. (2011) include an automated parameter adjustment to iteratively alter the objective function within the treatment planning framework. Wilkens et al. (2007) prioritize objectives to construct a treatment plan progressively, where the order of the objectives indicates the relative importance instead of the weights. Lee et al. (2013) and Boutilier et al. (2015) employ inverse optimization and machine learning techniques to predict weights from the anatomical features of patients. However, these studies weight the entire pool of objectives; they do not focus on creating the optimization model by selecting objectives. The number of objectives and the complexity of the model is an important issue, especially with recent studies on automated- and knowledge-based treatment planning (Chanyavanich et al. 2011, McIntosh and Purdie 2016, Babier et al. 2018, Kearney et al. 2018, Mahmood et al. 2018).

Inverse optimization has received growing attention as a tool for using data to determine modeling parameters that lead to an efficient and effective optimization formulation. Inverse optimization generally seeks parameters of an objective function that best explain the system behavior or a decision-maker’s preferences for various types of optimization problems such as linear programs and network optimization problems (e.g., Burton and Toint (1992), Zhang and Liu (1996) and Ahuja and Orlin (2001)), convex optimization (Iyengar and Kang 2005, Keshavarz et al. 2011), and integer (Schaefer 2009) and mixed-integer programs (Lamperski and Schaefer 2015). Over the last decade, the scope of inverse optimization has expanded to accommodate noise, measurement errors, and uncertainty in data; the goal in such settings is to find the objective function parameters that make the input data as optimal as possible (Bertsimas et al. 2015, Aswani et al. 2018, Chan et al. 2019). In the presence of such imperfect data, the inverse problem is typically non-convex—Chan et al. (2014) and Chan et al. (2019) propose efficient exact algorithms when the underlying problem is linear; for general inverse convex programming, various approximations and heuristics have been proposed (Bertsimas et al. 2015, Aswani et al. 2018, Mohajerin Esfahani et al. 2018).

Inverse optimization has also been recently studied in the multi-objective optimization setting (Keshavarz et al. 2011, Chan and Lee 2018, Naghavi et al. 2019, Gebken and Peitz 2019). However, the existing inverse multi-objective optimization approaches focus only on finding optimal weighting factors for a pre-specified set of objectives. For example, Chan and Lee (2018) apply inverse optimization to radiation therapy treatment planning, yet their focus is to find weighting factors for a given set of objectives. Gebken and Peitz (2019) use a singular-value decomposition approach, but they focus only on finding objective weights for optimal solutions of unconstrained problems.

We observe that objective selection is a special case of feature selection in the sense that its goal is to find objectives that best fit the preferences exhibited in the given treatment data. Feature selection is a well-known problem in which one selects “a subset of variables from the input which can efficiently describe the input data while reducing effects from noise or irrelevant variables and still provide good prediction results” (Chandrashekar and Sahin 2014). Feature selection is NP-hard and computationally intractable in general (Amaldi and Kann 1998, Guyon and Elisseeff 2003), and numerous solution methods have been proposed including filter, regularization, and wrapper methods. Filter methods rely on ranking techniques and select features that have a rank above a pre-determined threshold (Chandrashekar and Sahin 2014).

In a regularized method, the extensive form of the feature selection problem is convexified and a penalty term is added to the objective function of the problem to encourage the selection of a sparse subset of features. Sparsity regularization requires an appropriate regularization parameter, which can be a difficult problem itself (Galatsanos and Katsaggelos 1992, Viloche Bazán and Francisco 2009). Wrapper methods use some black-box solver (see Martí (2015) for details) to evaluate the performance of a subset of features and employ a heuristic to select a good subset of features (Chandrashekar and Sahin 2014). Although some of the methods are known to produce an optimal subset of features theoretically (e.g., branch-and-bound), they often need to examine an exponential number of subsets. Thus, it is typically desirable to develop more computationally efficient methods with potentially some loss of optimality (Pudil et al. 1994).

As an alternative, sequential wrapper methods allow for the subset to dynamically change size, and the feature subset is evaluated at various iterations to determine when the subset is good enough. The *greedy algorithm*, known as forward selection in some data science contexts, is a sequential wrapper method prevalent in combinatorial optimization. In a greedy algorithm, features are selected iteratively based on which feature improves a given selection criterion. Although greedy algorithms can be sensitive to local optima, they are simple and the selection process interacts directly with the model produced by the selected features (Saeys et al. 2007).

Certain structural properties of the problem can impact the effectiveness of the greedy algorithm (Nemhauser et al. 1978). In particular, submodularity plays an important role in deriving performance guarantees (i.e., bounds) for the greedy algorithm in various machine learning problems (Krause et al. 2008, Shamaiah et al. 2010). In addition, the greedy algorithm has also been used for feature selection with non-submodular functions (e.g., Das and Kempe (2011)), as well as other optimization problems without an examination of submodularity (Gottlieb et al. 2003). Indeed, the greedy algorithm can efficiently obtain a good solution if the subproblems solved within the iterations have good structure, such as convexity. We show in Section 3 the objective selection problem contains a convex subproblem, which strengthens the case to use the greedy algorithm.

### 3 Methodology

In this section, we develop a mathematical framework to select objectives for radiation therapy treatment planning. Although our focus is on cancer treatment planning, we present the ensuing formulations in a general mathematical setting.

#### 3.1 Forward Multi-objective Optimization

Let  $\mathcal{K} = \{1, \dots, K\}$  be the index set for objectives  $f_1(\mathbf{x}), \dots, f_K(\mathbf{x})$ , where  $\mathbf{x} \in \mathbb{R}^n$ . Given a subset  $\mathcal{S} \subseteq \mathcal{K}$ , we define the forward multi-objective optimization (MO) problem as follows:

$$\begin{aligned} \text{MO}(\mathcal{S}) = \quad & \min_{\mathbf{x}} \quad \mathbf{f}(\mathbf{x}) = [f_k(\mathbf{x})]_{k \in \mathcal{S}} \\ & \text{subject to} \quad \mathbf{A}\mathbf{x} = \mathbf{b}, \\ & \mathbf{g}(\mathbf{x}) \leq \mathbf{0}, \end{aligned} \tag{MO}$$

where we use  $[f_k(\mathbf{x})]_{k \in \mathcal{S}}$  to denote a vector-valued function. The inequality constraints are defined by the vector function  $\mathbf{g} : \mathbb{R}^n \rightarrow \mathbb{R}^L$ , with  $\mathcal{L} = \{1, \dots, L\}$ , and the equality constraints are defined by  $\mathbf{A} \in \mathbb{R}^{m \times n}$  and  $\mathbf{b} \in \mathbb{R}^m$ . In the context of radiation therapy, the objectives  $f_k$  may correspond to penalties for excessive radiation exposure to different organs at risk,  $\mathbf{g}$ ,  $\mathbf{A}$ , and  $\mathbf{b}$  represent dose-delivery constraints for various

voxels in patient anatomy, and the decision variable  $\mathbf{x}$  represents a treatment plan expressed as the amount of radiation to be delivered from each “beamlet”. More details for radiation therapy-specific formulations are given in Section 4. We emphasize, however, that the methodology presented in this work applies to general multi-objective optimization problems and thus, we focus on the general MO framework above.

In general, there is no solution that can simultaneously minimize  $f_k$  for all  $k \in \mathcal{K}$ . Instead, the goal of MO is to find a set of solutions that are not dominated by other feasible solutions in any of the objectives. Formally, a solution to an MO problem is called *weakly Pareto optimal* if there does not exist  $\mathbf{y}$  that is feasible for  $\text{MO}(\mathcal{S})$  such that  $f_k(\mathbf{x}) > f_k(\mathbf{y})$  for all  $k \in \mathcal{S}$ . We let  $\Omega(\mathcal{S})$  be the set of weakly Pareto optimal solutions for  $\text{MO}(\mathcal{S})$ , also referred to as the Pareto surface.

**Assumption 1.** *The functions  $f_k$  and  $g_\ell$  are convex and differentiable for all  $k \in \mathcal{K}$  and  $\ell \in \mathcal{L}$ ,  $\mathbf{f}(\mathbf{x}) > \mathbf{0}$  for all  $\mathbf{x}$  feasible for  $\text{MO}(\mathcal{S})$  for all  $\mathcal{S} \subseteq \mathcal{K}$ , and Slater’s interior feasibility condition holds.*

Assumption 1 provides some basic structure to our objective selection framework, but it also permits the inclusion of nonlinear objectives and constraints.

### 3.2 Objective Selection Using Inverse Multi-objective Optimization

Given an input solution as data (e.g., a solution chosen by a decision maker), objective selection focuses on selecting a set of no more than  $\theta$  objectives (with weights) from a pool of candidate objectives that capture the preferences implicitly exhibited in the input. In other words, the objective selection problem can be seen as a form of inverse optimization to find objectives that render the given solution as close as possible to the Pareto surface associated with the objectives, in terms of some specified (optimality) distance function. Given a feasible input solution  $\hat{\mathbf{x}}$ , a set of objectives  $\mathcal{S}$ , and  $\mathbf{x} \in \Omega(\mathcal{S})$ , consider the following distance functions:

- $d^{[r]}(\mathbf{x}, \hat{\mathbf{x}}, \mathcal{S}) = \max_{k \in \mathcal{S}} \frac{f_k(\mathbf{x})}{f_k(\hat{\mathbf{x}})}$ ,
- $d^{[q]}(\mathbf{x}, \hat{\mathbf{x}}, \mathcal{S}) = \|\mathbf{f}(\mathbf{x}) - \mathbf{f}(\hat{\mathbf{x}})\|_q, q \in \{1, 2, \dots, \infty\}$ .

Although there are many other distance functions we can consider, the above functions are considered particularly relevant in the multi-objective optimization context in that achieving a (weakly) Pareto optimal solution  $\mathbf{x}$  that minimizes such distances from  $\hat{\mathbf{x}}$  is considered preserving the original trade-offs in the objective values (Eskelinen and Miettinen 2012, van Haveren et al. 2017). Though one might consider a more straightforward distance such as  $\|\hat{\mathbf{x}} - \mathbf{x}\|_q$ , recent studies show that this can cause the resulting objective values to be inconsistent with the input values  $\mathbf{f}(\hat{\mathbf{x}})$  and is more appropriate for single-objective optimization (Keshavarz et al. 2011, Chan and Lee 2018). Minimizing  $d^{[r]}$  above results in minimizing the (relative) duality gap of a weighted sum version of MO, i.e.,  $\frac{\sum_{k \in \mathcal{S}} \alpha_k f_k(\hat{\mathbf{x}})}{\sum_{k \in \mathcal{S}} \alpha_k f_k(\mathbf{x}^*)}$ , where  $\mathbf{x}^*$  is an optimal solution; moreover, using  $d^{[r]}$  leads to weight vectors that preserve relative tradeoff preferences (Chan and Lee 2018). We remark that  $d^{[r]}$  is not a metric strictly speaking; for instance, it does not obey the triangle inequality. However, it does lead to valuable insight about multi-objective trade-offs and provides structure to the objective selection problem that we exploit. Lin (2005) discusses uses of  $d^{[q]}$  for a specific case in which the input data correspond to a set of ideal solutions (optimal for a single-objective problem) for the same multi-objective problem. In Section 3.2.2, we relate  $d^{[r]}$  and  $d^{[q]}$  by connecting the relative gap to the norm of the difference in function values.

Our objective selection framework accepts multiple inputs. Given  $P$  inputs, the goal is to find a set of objectives such that the resulting Pareto surfaces are as close to the input solutions as possible. Let

$\mathcal{P} = \{1, \dots, P\}$  be the index set for the inputs and  $\widehat{\chi} = \{\widehat{\mathbf{x}}_{(p)}\}_{p \in \mathcal{P}}$ . Note that each input  $\widehat{\mathbf{x}}_{(p)}$  may originate from a different forward optimization problem, in which case objectives and constraint parameters from each optimization problem are also indexed by  $(p)$ . In the treatment planning context, each input is a previous clinical treatment plan for each patient.

We remark that the objectives across different input solutions share the same functional format so they can be considered the same ‘‘type’’. For example,  $f_{(1),1} : \mathbb{R}^{n(1)} \rightarrow \mathbb{R}$ , the first objective for input 1, and  $f_{(2),1} : \mathbb{R}^{n(2)} \rightarrow \mathbb{R}$ , the first objective for input 2, can both represent the  $L_2$  norm of the solution for the respective problems even though the dimensions of the domains differ in size. Thus, each objective index  $k \in \mathcal{K}$  represents the common type of the objectives consistent across the inputs. Each forward problem also leads to a different Pareto surface  $\Omega_{(p)}(\mathcal{S})$ .

We consider two distances between a set of input solutions and the respective Pareto surfaces:

- $\delta(\chi, \widehat{\chi}, \mathcal{S}) = \sum_{p \in \mathcal{P}} d_{(p)}(\mathbf{x}_{(p)}, \widehat{\mathbf{x}}_{(p)}, \mathcal{S})$
- $\gamma(\chi, \widehat{\chi}, \mathcal{S}) = \min_{\boldsymbol{\alpha} \in \mathcal{A}(\mathcal{S})} \left\{ \boldsymbol{\alpha}^\top \sum_{p \in \mathcal{P}} \mathbf{f}_{(p)}(\widehat{\mathbf{x}}_{(p)}) / \boldsymbol{\alpha}^\top \sum_{p \in \mathcal{P}} \mathbf{f}_{(p)}(\mathbf{x}_{(p)}) \right\},$

where  $\mathcal{A}(\mathcal{S}) = \{\boldsymbol{\alpha} \in \mathbb{R}_+^{\mathcal{K}} \setminus \{\mathbf{0}\} \mid \alpha_k = 0 \text{ for all } k \notin \mathcal{S}\}$  is the set of admissible weight vectors for a set of objectives  $\mathcal{S}$ . Different single input distance metrics may be used for  $\delta$ , for instance,  $d^{[r]}$ . Notice that  $\delta$  is a separable measure, unlike  $\gamma$ . We refer to  $\gamma$  as the *batch duality gap*. For most of this section, we focus on the separable case, but we also present results with the batch duality gap.

We write the objective selection problem (OS) with input set  $\mathcal{P}$  as follows:

$$\begin{aligned} \text{OS}(\widehat{\chi}) = \quad & \min_{\chi, \mathcal{S}} \delta(\chi, \widehat{\chi}, \mathcal{S}) \\ \text{subject to} \quad & \mathbf{x}_{(p)} \in \Omega_{(p)}(\mathcal{S}), \quad \forall p \in \mathcal{P}, \\ & 1 \leq |\mathcal{S}| \leq \theta, \\ & \mathcal{S} \subseteq \mathcal{K}. \end{aligned} \tag{OS}$$

For all input data points, the above problem finds a common set of objectives  $\mathcal{S}$ , i.e., the same types of objectives, although the underlying forward problem formulation is different across the inputs. If the input data points are all collected from the same forward optimization problem, we can rewrite the above formulation simply by replacing the first constraint with  $\mathcal{X} \subset \Omega(\mathcal{S})$ . We remark that the objective selection problem reduces to the multi-objective inverse problem of Chan et al. (2014) and Chan and Lee (2018) if  $\theta = |\mathcal{K}|$  and  $\mathcal{P}$  is a singleton.

### 3.2.1 Extensive Formulation

We first present a general extensive formulation for  $\text{OS}(\widehat{\chi})$ . Given that  $\mathbf{f}$  and  $\mathbf{g}$  are convex in the forward problem MO (Assumption 1), all weakly Pareto optimal solutions for  $\text{MO}(\mathcal{S})$  can be obtained by the following formulation with the weighted combination of the objectives:

$$\text{WMO}(\boldsymbol{\alpha}) = \min_{\mathbf{x}} \{\boldsymbol{\alpha}^\top \mathbf{f}(\mathbf{x}) \mid \mathbf{A}\mathbf{x} = \mathbf{b}, \mathbf{g}(\mathbf{x}) \leq \mathbf{0}\}. \tag{WMO}$$

Let  $\mathcal{O}(\boldsymbol{\alpha})$  denote the set of optimal solutions to  $\text{WMO}(\boldsymbol{\alpha})$ , and given input index  $p$ , let  $\mathcal{O}_{(p)}(\boldsymbol{\alpha})$  denote the optimal solutions of  $\text{WMO}(\boldsymbol{\alpha})$  with data  $\mathbf{f}_{(p)}, \mathbf{A}_{(p)}, \mathbf{b}_{(p)}$ , and  $\mathbf{g}_{(p)}$ .

**Lemma 1.** For any  $\mathcal{S} \subseteq \mathcal{K}$ , a solution  $\mathbf{x}$  is weakly Pareto optimal for  $\text{MO}(\mathcal{S})$  if and only if there exists a non-zero weight vector  $\boldsymbol{\alpha} \in \mathbb{R}_+^K$  with  $\alpha_k = 0$  for all  $k \notin \mathcal{S}$  such that  $\mathbf{x}$  is an optimal solution to  $\text{WMO}(\boldsymbol{\alpha})$ . That is,  $\mathbf{x} \in \Omega(\mathcal{S}) \iff \mathbf{x} \in \bigcup_{\boldsymbol{\alpha}} \{\mathcal{O}(\boldsymbol{\alpha}) \mid \boldsymbol{\alpha} \in \mathbb{R}_+^K \setminus \{\mathbf{0}\}, \alpha_k = 0 \text{ for all } k \notin \mathcal{S}\}$ .

Proof of Lemma 1 is omitted as it follows directly from Theorem 3.15 of Ehrgott (2005).

Let  $\mathcal{S}(\boldsymbol{\xi}) = \{k \in \mathcal{K} \mid \xi_k = 1\}$  where  $\boldsymbol{\xi} \in \mathbb{B}^K$  is a binary variable. From Lemma 1, an extensive formulation of OS for the set of  $P$  input data points,  $\widehat{\chi}$ , can be written as follows:

$$\begin{aligned} \min_{\boldsymbol{\alpha}, \boldsymbol{\xi}, \chi} \quad & \delta(\chi, \widehat{\chi}, \mathcal{S}(\boldsymbol{\xi})) & (1a) \\ \text{subject to} \quad & \sum_{k \in \mathcal{K}} \xi_k \leq \theta, & (1b) \\ & \boldsymbol{\alpha}_{(p)} \leq \boldsymbol{\xi}, \quad \forall p \in \mathcal{P}, & (1c) \\ & \boldsymbol{\alpha}_{(p)} \in \mathcal{A}(\mathcal{S}(\boldsymbol{\xi})), \quad \forall p \in \mathcal{P}, & (1d) \\ & \boldsymbol{\xi} \in \mathbb{B}^K, & (1e) \\ & \mathbf{x}_{(p)} \in \mathcal{O}_{(p)}(\boldsymbol{\alpha}_{(p)}), \quad \forall p \in \mathcal{P}. & (1f) \end{aligned}$$

The binary variable  $\boldsymbol{\xi}$  represents whether or not each candidate objective is chosen—if  $\xi_k = 0$ , objective  $k$  is not chosen as the corresponding weight  $\alpha_k$  is forced to be 0. We assume  $\alpha_k \leq 1$  for each objective  $k$ ; this is without loss of generality, as any weight vector for the forward problem MO can be scaled by a positive constant without affecting the set of optimal solutions. Note that the above formulation assumes each data point  $\widehat{\mathbf{x}}_{(p)}$  is associated with a different weight vector, i.e., collected from a decision maker with different preferences. If we assume that all data points represent the same preferences and thus should be assigned the same weight values, we modify the formulation by fixing  $\boldsymbol{\alpha}_{(p)} = \boldsymbol{\alpha}$ , for all  $p \in \mathcal{P}$ . Assuming each of the objectives  $f_{(p),k}$  for all  $k \in \mathcal{K}$  and constraint vectors  $\mathbf{g}_{(p)}$  are differentiable for all data points  $p \in \mathcal{P}$ , formulation (1) can be further rewritten as the following non-convex mixed-integer program:

$$\begin{aligned} \min_{\boldsymbol{\alpha}, \boldsymbol{\xi}, \chi, \boldsymbol{\sigma}, \boldsymbol{\pi}} \quad & \delta(\chi, \widehat{\chi}, \mathcal{S}(\boldsymbol{\xi})) & (2a) \\ \text{subject to} \quad & \sum_{k \in \mathcal{K}} \xi_k \leq \theta, & (2b) \\ & \boldsymbol{\alpha}_{(p)} \leq \boldsymbol{\xi}, & (2c) \\ & \boldsymbol{\alpha}_{(p)}^\top \mathbf{e} = 1, \quad \forall p \in \mathcal{P}, & (2d) \\ & \mathbf{A}_{(p)} \mathbf{x}_{(p)} = \mathbf{b}_{(p)}, \quad \forall p \in \mathcal{P}, & (2e) \\ & \mathbf{g}_{(p)}(\mathbf{x}_{(p)}) \leq \mathbf{0}, \quad \forall p \in \mathcal{P}, & (2f) \\ & \sum_{k \in \mathcal{K}} \alpha_{(p),k} \nabla f_{(p),k}(\mathbf{x}_{(p)}) + \sum_{\ell \in \mathcal{L}} \sigma_{(p),\ell} \nabla g_{(p),\ell}(\mathbf{x}_{(p)}) + \mathbf{A}^\top \boldsymbol{\pi}_{(p)} = \mathbf{0}, \quad \forall p \in \mathcal{P}, & (2g) \\ & \boldsymbol{\sigma}_{(p)} \circ \mathbf{g}_{(p)}(\mathbf{x}_{(p)}) = \mathbf{0}, \quad \forall p \in \mathcal{P}, & (2h) \\ & \boldsymbol{\sigma}_{(p)} \geq \mathbf{0}, \quad \forall p \in \mathcal{P}, & (2i) \\ & \boldsymbol{\alpha}_{(p)} \geq \mathbf{0}, \quad \forall p \in \mathcal{P}, & (2j) \\ & \boldsymbol{\xi} \in \mathbb{B}^K, & (2k) \end{aligned}$$

where constraints (2f)–(2j) represent the KKT conditions for data point  $p$ , replacing (1f), and  $(\circ)$  is the Hadamard product. Note that  $\boldsymbol{\alpha} = \{\boldsymbol{\alpha}_{(p)}\}_{p \in \mathcal{P}}$ , and similarly for  $\boldsymbol{\sigma}$  and  $\boldsymbol{\pi}$ .

**Proposition 1.**  $\mathcal{F}_1$ , the feasible region of (1), and  $\mathcal{F}_2$ , the feasible region of (2) are related as follows:

$$\{(\boldsymbol{\alpha}, \boldsymbol{\xi}, \chi) \mid (\boldsymbol{\alpha}, \boldsymbol{\xi}, \chi, \boldsymbol{\sigma}, \boldsymbol{\pi}) \in \mathcal{F}_2 \text{ for some } (\boldsymbol{\sigma}, \boldsymbol{\pi})\} = \{(\boldsymbol{\alpha}, \boldsymbol{\xi}, \chi) \in \mathcal{F}_1 \mid \boldsymbol{\alpha}_{(p)}^\top \mathbf{e} = 1, \text{ for all } p \in \mathcal{P}\}.$$

Thus, the optimal objective values of (1) and (2) are equal.

Note that (2) is a mixed-integer non-convex problem, which is intractable in general. We show that formulation (2) is tractable if the underlying forward problem is linear, i.e., all of the candidate objectives and the constraints are linear. Suppose  $\mathbf{f}_{(p)}$  and  $\mathbf{g}_{(p)}$  are both affine functions for each  $p \in \mathcal{P}$  so that the weighted forward MO for input  $p$  can be written as follows:

$$\min_{\mathbf{x}} \{\boldsymbol{\alpha}_{(p)}^\top \mathbf{C}_{(p)} \mathbf{x} \mid \mathbf{A}_{(p)} \mathbf{x} = \mathbf{b}, \mathbf{G}_{(p)} \mathbf{x} \leq \mathbf{h}_{(p)}\}. \quad (3)$$

Then the corresponding OS problem with input set  $\mathcal{P}$  can be written as a mixed-integer program:

$$\min_{\mathbf{x}, \boldsymbol{\alpha}, \boldsymbol{\pi}, \boldsymbol{\sigma}, \mathbf{s}, \boldsymbol{\xi}} \sum_{p \in \mathcal{P}} d_{(p)}(\mathbf{x}_{(p)}, \widehat{\mathbf{x}}_{(p)}, \mathcal{S}) \quad (4a)$$

$$\text{subject to } \sum_{k \in \mathcal{K}} \boldsymbol{\xi}_k \leq \boldsymbol{\theta}, \quad (4b)$$

$$\boldsymbol{\alpha}_{(p)} \leq \boldsymbol{\xi}, \quad \forall p \in \mathcal{P}, \quad (4c)$$

$$\boldsymbol{\alpha}_{(p)}^\top \mathbf{e} = 1, \quad \forall p \in \mathcal{P}, \quad (4d)$$

$$\mathbf{A}_{(p)} \mathbf{x}_{(p)} = \mathbf{b}_{(p)}, \quad \forall p \in \mathcal{P}, \quad (4e)$$

$$\mathbf{G}_{(p)} \mathbf{x}_{(p)} \leq \mathbf{h}_{(p)}, \quad \forall p \in \mathcal{P}, \quad (4f)$$

$$\boldsymbol{\alpha}_{(p)}^\top \mathbf{C}_{(p)} + \boldsymbol{\sigma}_{(p)}^\top \mathbf{G}_{(p)} + \boldsymbol{\pi}_{(p)}^\top \mathbf{A}_{(p)} = \mathbf{0}, \quad \forall p \in \mathcal{P}, \quad (4g)$$

$$\mathbf{h}_{(p)} - \mathbf{G}_{(p)} \mathbf{x}_{(p)} \leq M \mathbf{s}_{(p)}, \quad \forall p \in \mathcal{P}, \quad (4h)$$

$$\boldsymbol{\sigma}_{(p)} \leq M(1 - \mathbf{s}_{(p)}), \quad \forall p \in \mathcal{P}, \quad (4i)$$

$$\boldsymbol{\sigma}_{(p)} \geq \mathbf{0}, \quad \forall p \in \mathcal{P}, \quad (4j)$$

$$\boldsymbol{\alpha}_{(p)} \geq \mathbf{0}, \quad \forall p \in \mathcal{P}, \quad (4k)$$

$$\boldsymbol{\xi} \in \mathbb{B}^K, \quad (4l)$$

$$\mathbf{s}_{(p)} \in \mathbb{B}^L, \quad \forall p \in \mathcal{P}, \quad (4m)$$

where  $M$  is a suitably large constant. Observe that (4e)-(4k) again represent the KKT conditions in a slightly different way than in (2); we introduce auxiliary variables  $\mathbf{s}$  and big-M constraints to handle the complementary slackness. Again, if all  $P$  input solutions are assumed to represent the same preferences over the common set of objectives (i.e., common weights), we let  $\boldsymbol{\alpha}_{(p)} = \boldsymbol{\alpha}$ ,  $\forall p \in \mathcal{P}$ .

When  $\mathbf{f}_{(p)}$  and  $\mathbf{g}_{(p)}$  are nonlinear functions, the OS formulation is generally non-convex. To address the non-convexity, we observe that the general OS problem can be seen as a bilevel optimization problem, where the upper-level problem chooses the set of objectives first, followed by the lower-level problem that chooses the corresponding weight values. The challenge is that even the lower-level problem itself is not tractable due to the non-convexity in the KKT constraints (multiplication of  $\boldsymbol{\alpha}$  and  $\mathbf{f}(\mathbf{x})$  both of which are variables). In the sequel, we analyze the structure of the lower-level problem and show that it becomes tractable under some distance function  $d$ , enabling an efficient heuristic for the OS problem.

### 3.2.2 Restricted Inverse Problem

Consider  $\text{OS}(\widehat{\chi})$  as the following bilevel framework: the upper-level problem first picks a set of objectives; the lower-level problem follows and finds an optimal weight vector for each data point  $\widehat{\mathbf{x}}_{(p)}$  such that the associated distance function is minimized. We call the lower-level problem the restricted inverse problem (RP). Using reformulations, this bilevel problem can be expressed as a zero-sum problem. Given a pre-specified choice of objectives,  $\mathcal{S}$ , we present the following formulation to find a weight vector that minimizes  $d_{(p)}(\mathbf{x}_{(p)}, \widehat{\mathbf{x}}_{(p)}, \mathcal{S}) = \max_{k \in \mathcal{S}} \{f_{(p),k}(\mathbf{x}_{(p)})/f_{(p),k}(\widehat{\mathbf{x}}_{(p)})\}$  for each data point  $p$ :

$$\text{RP}(\widehat{\chi}, \mathcal{S}) = \min_{\mathcal{X}} \sum_{p \in \mathcal{P}} \max_{k \in \mathcal{K}} \{f_{(p),k}(\mathbf{x}_{(p)})/f_{(p),k}(\widehat{\mathbf{x}}_{(p)})\} \quad (5a)$$

$$\text{subject to } \mathbf{A}_{(p)} \mathbf{x}_{(p)} = \mathbf{b}_{(p)}, \quad \forall p \in \mathcal{P}, \quad (5b)$$

$$\mathbf{g}_{(p)}(\mathbf{x}_{(p)}) \leq \mathbf{0}, \quad \forall p \in \mathcal{P}. \quad (5c)$$

The objective function of the above problem can be rewritten as a convex function after including auxiliary variables and convex constraints.

**Proposition 2.** *Let  $\chi^* = \{\mathbf{x}_{(p)}^*\}_{p \in \mathcal{P}}$  be an optimal solution for  $\text{RP}(\widehat{\chi}, \mathcal{S})$ . Then, for all  $p \in \mathcal{P}$ :*

$$(i) \quad \mathbf{x}_{(p)}^* \in \Omega_{(p)}(\mathcal{S}).$$

$$(ii) \quad 1/\max_{k \in \mathcal{K}} \{f_{(p),k}(\mathbf{x}_{(p)}^*)/f_{(p),k}(\widehat{\mathbf{x}}_{(p)})\} \text{ is the minimum relative duality gap with respect to } \widehat{\mathbf{x}}_{(p)}.$$

*In addition, a convex reformulation of  $\text{RP}(\widehat{\chi}, \mathcal{S})$  exists where optimal weight vectors  $\alpha_{(p)}^*$ , such that  $\mathbf{x}_{(p)}^* \in \mathcal{O}_{(p)}(\alpha_{(p)}^*)$ , can be computed as Lagrange multipliers, for all  $p \in \mathcal{P}$ .*

Proposition 2 states that given a fixed subset of candidate objectives, one can solve the inverse problem with multiple inputs. Moreover, the weight vectors can be recovered using KKT conditions to compute the Lagrange multipliers. Thus,  $\text{RP}(\widehat{\chi}, \mathcal{S})$  can serve as a black-box solver in sequential wrapper algorithms common in feature selection (Theorem 1). Returning to the bilevel view of the objective selection problem, the lower-level problem can be reformulated as formulation (20), and the objective of the follower is to minimize  $\sum_{p \in \mathcal{P}} \epsilon_p$ , the sum of the reciprocals of the relative duality gaps; in other words, the follower maximizes the sum of the duality gaps. The goal of the leader, however, is to choose the subset that minimizes the sum of the duality gap. This illustrates that the objective selection problem in this case is a zero-sum bilevel problem (Theorem 1).

**Theorem 1.** *Given the distance functions  $d_{(p)}(\mathbf{x}, \widehat{\mathbf{x}}, \mathcal{S}) = \max_{k \in \mathcal{S}} \{f_{(p),k}(\mathbf{x})/f_{(p),k}(\widehat{\mathbf{x}})\}$ , for all  $p \in \mathcal{P}$ , we have*  

$$\text{OS}(\widehat{\chi}) = \min_{\mathcal{S} \subseteq \mathcal{K}, 1 \leq |\mathcal{S}| \leq \theta} \text{RP}(\widehat{\chi}, \mathcal{S}).$$

Given an appropriate restricted inverse problem for other distance functions, one can produce an analog of Theorem 1. However, in general, the corresponding restricted problem is non-convex (due to the KKT conditions that ensure Pareto optimality), which may be difficult to solve. Thus, the existence of a convex formulation for  $d^{[r]}$  is a special case.

An additional special case for which the restricted problem is tractable is when all of the objectives and constraints are affine, which leads to the mixed-integer linear program (4). However, many objectives in radiation therapy treatment planning are nonlinear. When  $\mathcal{P}$  is a singleton, another tractable restricted problem results from the distance function  $d^{[q,1]}(\mathbf{x}, \widehat{\chi}_{\mathcal{K}}, \mathcal{S}) = \left( \sum_{k \in \mathcal{S}} |f_k(\mathbf{x}) - f_k(\widehat{\mathbf{x}}_k)|^q \right)^{1/q}$ , a variant of  $d^{[q]}$ .

The distance function  $d^{[q,1]}$  relies on multiple “ideal” solutions that are optimized for a single objective:  $\widehat{\chi}_{\mathcal{K}} = \{\widehat{\mathbf{x}}_k\}_{k \in \mathcal{K}}$ , where  $\widehat{\mathbf{x}}_k \in \arg \min_{\mathbf{x}} \{f_k(\mathbf{x}) \mid \mathbf{A}\mathbf{x} = \mathbf{b}, \mathbf{g}(\mathbf{x}) \leq \mathbf{0}\}$ , for all  $k \in \mathcal{K}$  (Lin 2005); see the e-companion for details. In the radiation therapy context, however, this implies that the input data consists of  $|\mathcal{K}|$  treatment plans for the patient each arising from a distinct single-objective optimization problem, which is more restrictive. Hence, for increased clinical relevance and flexibility in the inputs, we focus on using  $d^{[r]}$ .

If the data points are assumed to come from forward problems with the same preferences, we consider the batch duality gap distance. The objective selection problem is:

$$\begin{aligned} \text{OS-W}(\widehat{\chi}) = \quad & \min_{\chi, \mathcal{S}} \quad \gamma(\chi, \widehat{\chi}, \mathcal{S}) \\ \text{subject to} \quad & \chi \in \widetilde{\Omega}(\mathcal{S}), \\ & 1 \leq |\mathcal{S}| \leq \theta, \\ & \mathcal{S} \subseteq \mathcal{K}, \end{aligned} \tag{OS-W}$$

where  $\widetilde{\Omega}(\mathcal{S}) = \bigcup_{\alpha \in \mathcal{A}(\mathcal{S})} \arg \min_{\chi} \{\alpha^\top \sum_{p \in \mathcal{P}} \mathbf{f}_{(p)}(\mathbf{x}_{(p)}) \mid \mathbf{A}_{(p)}\mathbf{x}_{(p)} = \mathbf{b}_{(p)}, \mathbf{g}_{(p)}(\mathbf{x}_{(p)}) \leq \mathbf{0}, \forall p \in \mathcal{P}\}$ . Here,  $W$  indicates that we select the same objectives and weights for all patients in the batch. We modify the RP formulation to find the common weight values for all data points (RP-W) for the given set of objectives.

$$\text{RP-W}(\widehat{\chi}, \mathcal{S}) = \min_{\mathbf{x}, \alpha} \left( \alpha^\top \sum_{p \in \mathcal{P}} \mathbf{f}_{(p)}(\mathbf{x}_{(p)}) \right) / \left( \alpha^\top \sum_{p \in \mathcal{P}} \mathbf{f}_{(p)}(\widehat{\mathbf{x}}_{(p)}) \right) \tag{6a}$$

$$\text{subject to} \quad \mathbf{A}_{(p)}\mathbf{x}_{(p)} = \mathbf{b}_{(p)}, \forall p \in \mathcal{P}, \tag{6b}$$

$$\mathbf{g}_{(p)}(\mathbf{x}_{(p)}) \leq \mathbf{0}, \forall p \in \mathcal{P}, \tag{6c}$$

$$\alpha \in \mathcal{A}(\mathcal{S}). \tag{6d}$$

**Theorem 2.** *There exists a convex reformulation of RP-W( $\widehat{\chi}, \mathcal{S}$ ) whose Lagrange multipliers are optimal weights that minimize the batch duality gap. Also,  $\text{OS-W}(\widehat{\chi}) = \min_{\mathcal{S} \subseteq \mathcal{K}, 1 \leq |\mathcal{S}| \leq \theta} \text{RP-W}(\widehat{\chi}, \mathcal{S})$ .*

Next we establish a relationship between the distance metrics  $d^{[r]}$  and  $d^{[q]}$ . For the single-input case, RP-S and RP-W are equivalent; thus, we simply denote this restricted problem by RP and refrain from labeling data with the subscript ( $p$ ). Given a subset  $\mathcal{T} \subseteq \mathcal{K}$ , let  $\|\cdot\|_{q, \mathcal{T}} : \mathbb{R}^{|\mathcal{T}|} \rightarrow \mathbb{R}$  be the  $q$ -norm in  $\mathbb{R}^{|\mathcal{T}|}$ . Also, let  $\mathbf{f}_{\mathcal{T}} = [f_k]_{k \in \mathcal{T}}$ .

**Proposition 3.** *Consider a single-input restricted inverse problem RP ( $\widehat{\mathbf{x}}, \mathcal{S}$ ) and an optimal solution ( $\mathbf{x}^*, \alpha^*$ ). Let  $\mathcal{S}^*$  be the support of  $\alpha^*$ , e.g.,  $\mathcal{S}^* = \{k \in \mathcal{S} \mid \alpha_k^* > 0\}$ . Then the relative gap of WMO( $\alpha^*$ ) at  $\widehat{\mathbf{x}}$  is*

$$\frac{\|\mathbf{f}_{\mathcal{S}^*}(\widehat{\mathbf{x}})\|_{q, \mathcal{S}^*}^q}{\|\mathbf{f}_{\mathcal{S}^*}(\widehat{\mathbf{x}})\|_{q, \mathcal{S}^*}^q - \|\mathbf{f}_{\mathcal{S}^*}(\widehat{\mathbf{x}}) - \mathbf{f}_{\mathcal{S}^*}(\mathbf{x}^*)\|_{q, \mathcal{S}^*}^q}.$$

Proposition 3 highlights a relationship between the proposed distance metrics as follows. Let  $\mathcal{S}$  and  $\mathcal{T}$  (with  $|\mathcal{S}| = |\mathcal{T}|$ ) be the support of two weight vectors obtained from optimal solutions of restricted problems, and assume that all of the candidate objectives  $f_k$  have been normalized such that  $f_k(\widehat{\mathbf{x}}) = 1$ , for all  $k \in \mathcal{S} \cup \mathcal{T}$ , thus  $\|\mathbf{f}_{\mathcal{S}}(\widehat{\mathbf{x}})\|_{q, \mathcal{S}} = \|\mathbf{f}_{\mathcal{T}}(\widehat{\mathbf{x}})\|_{q, \mathcal{T}}$ . Then if the minimum relative gap over  $\mathcal{S}$  at  $\widehat{\mathbf{x}}$  is  $r_{\mathcal{S}}$  (similarly for  $\mathcal{T}$ ) and  $r_{\mathcal{S}} > r_{\mathcal{T}}$ , we have  $\|\mathbf{f}_{\mathcal{S}}(\widehat{\mathbf{x}}) - \mathbf{f}_{\mathcal{S}}(\mathbf{x}^*)\|_{q, \mathcal{S}} > \|\mathbf{f}_{\mathcal{T}}(\widehat{\mathbf{x}}) - \mathbf{f}_{\mathcal{T}}(\mathbf{x}^*)\|_{q, \mathcal{T}}$ ; that is, in this case, a larger relative gap corresponds to a larger norm of the difference of function values.

Recall from Section 2 that one can view the objective selection problem as a feature selection problem because the goal is to find a sparse set of objectives (no more than  $\theta$  of them) of an optimization problem that fits the given input  $\widehat{\mathbf{x}}$  or set of inputs  $\widehat{\chi}$ . Theorems 1 and 2 reinforce this connection and demonstrate that the difficult objective selection problem exhibits structure that makes certain feature selection algorithms suitable. In particular, greedy approaches, widely used in feature selection problems, require solving a limited number of convex programs to find good sets of objectives and weights and thus may be a reasonable choice for the objective selection problems in treatment planning and other applications.

### 3.2.3 Regularization

Because the objection selection problem is closely related to feature selection, another natural solution approach is to use regularization. Let  $\boldsymbol{\lambda} \in \mathbb{R}_+^{|\mathcal{K}|}$ , then a regularized objective selection problem is

$$\text{RE}(\widehat{\mathbf{x}}) = \max_{\mathbf{x}, \boldsymbol{\alpha}} -\boldsymbol{\alpha}^\top \boldsymbol{\lambda} + (\boldsymbol{\alpha}^\top \mathbf{f}(\mathbf{x})) / (\boldsymbol{\alpha}^\top \mathbf{f}(\widehat{\mathbf{x}})) \quad (7a)$$

$$\text{subject to } \mathbf{x} \in \mathcal{O}(\boldsymbol{\alpha}), \quad (7b)$$

$$\boldsymbol{\alpha}^\top \mathbf{f}(\widehat{\mathbf{x}}) = 1, \quad (7c)$$

$$\boldsymbol{\alpha} \in \mathbb{R}_+^{|\mathcal{K}|}. \quad (7d)$$

This regularized model maximizes the reciprocal of the relative gap minus the regularization term. If the regularization parameter is  $\boldsymbol{\lambda} = \mathbf{0}$ , then (7) solves the inverse problem (not the objective selection problem) over all candidate objectives because minimizing the relative gap is equivalent to maximizing its reciprocal, assuming both are well defined.

Consider the following model (8) for a single input:

$$\text{REGP}(\widehat{\mathbf{x}}) = \min_{\mathbf{x}, \epsilon} \epsilon \quad (8a)$$

$$\text{subject to } f_k(\mathbf{x}) \leq \epsilon f_k(\widehat{\mathbf{x}}) + \lambda_k, \forall k \in \mathcal{K}, \quad (8b)$$

$$\mathbf{Ax} = \mathbf{b}, \quad (8c)$$

$$\mathbf{g}(\mathbf{x}) \leq \mathbf{0}. \quad (8d)$$

Define the optimal objective values of  $\text{RE}(\widehat{\mathbf{x}})$  and  $\text{REGP}(\widehat{\mathbf{x}})$  by  $z^{\text{RE}}$  and  $z^{\text{REGP}}$ , respectively. Theorem 3 reveals that  $\boldsymbol{\lambda}$  also serves as a regularization parameter in  $\text{REGP}(\widehat{\mathbf{x}})$  for the objective weights  $\boldsymbol{\alpha}$ .

**Theorem 3.** *If an optimal primal-dual pair for  $\text{REGP}(\widehat{\mathbf{x}})$  exists with zero absolute duality gap, then the dual multipliers of (8b) yield optimal weights to the regularized objective selection problem  $\text{RE}(\widehat{\mathbf{x}})$ .*

A common issue in regularization methods is determining regularization parameters such that the regularized problem mimics the original non-convex problem. In the context of objective selection, the regularization parameter  $\boldsymbol{\lambda}$  must be tuned to select an objective set of the appropriate sparsity. Finally, we remark that this regularization approach can extend to accept multiple inputs if one adapts the problem  $\text{RP-W}(\widehat{\mathbf{x}}_{(p)}, \mathcal{K})$  in a similar way by adding  $\boldsymbol{\lambda}$  to constraints (21a).

In our application of the objective selection approach to radiation therapy treatment planning, we adapt the feature selection perspectives and employ greedy algorithms to solve the computationally challenging problem. The specific algorithms that we propose further capitalize on application-specific knowledge as well as unique problem structure that enables anatomy-based heuristics. Thus, we first discuss structural details

of the radiation therapy treatment planning problems in the next section, and provide detailed illustrations of our solution approaches in Section 5.

## 4 Objective Selection in Radiation Therapy Treatment Planning

### 4.1 Radiation Therapy Context

We apply objective selection to intensity-modulated radiation therapy (IMRT) treatment planning and focus on prostate cancer. Prostate cancer is one of the most common cancer types in American men, accounting for nearly 20% of new cancer diagnoses in men in 2018 (American Cancer Society 2018). Furthermore, prostate cancer will be among the highest in cost increase of medical care from 2010 to 2020 (Mariotto et al. 2011). Although prostate cancer has a relatively high survival rate, complications due to radiation (e.g, radiation exposure to healthy organs) are still one of the biggest concerns about prostate cancer treatment (American Cancer Society 2018). The reasons above suggest it is critical to design high-quality treatment plans efficiently and consistently. Because there exist multiple clinical criteria, which are generally not achievable simultaneously, clinical trade-offs and associated preferences, reflected in the treatment planning objectives (and their weights), are critical features that describe the administered treatment.

### 4.2 Model Formulation

We specify the models presented in Section 3 with details specific to IMRT treatment planning for prostate cancer. General goals in treatment planning are to spare organs at risk (OARs) while delivering sufficient radiation dose to the tumor. In prostate cancer, generally four OARs are considered: the bladder, rectum, left femoral head, and right femoral head (Chanyavanich et al. 2011).

Let  $\mathcal{B}$  be the set of beamlets, where each beamlet  $b \in \mathcal{B}$  is associated with a decision variable  $w_b$  that determines the beamlet’s radiation intensity. The patient’s body is discretized into a set  $\mathcal{V}$  of volume elements called voxels. The amount of dose delivered to voxel  $v \in \mathcal{V}$  by beamlet  $b \in \mathcal{B}$  is denoted by  $D_{v,b}$  and the entire matrix by  $\mathbf{D} \in \mathbb{R}^{|\mathcal{V}| \times |\mathcal{B}|}$ . The anatomical regions of interest (ROIs) for prostate cancer treatment include the four OARs, the clinical target volume (CTV), the planning target volume (PTV), and the set of remaining voxels near the tumor, often referred to as normal tissue (NORMAL). The subsets of voxels that comprise each of the structures are denoted  $\mathcal{V}_{\text{CTV}}, \mathcal{V}_{\text{PTV}}, \mathcal{V}_{\text{Blad}}, \mathcal{V}_{\text{Rect}}, \mathcal{V}_{\text{LFem}}, \mathcal{V}_{\text{RFem}},$  and  $\mathcal{V}_{\text{Normal}},$  respectively.

The objective selection problem considers multiple forms of candidate objectives. To permit a wide range of objectives to be considered, we use both maximum dose and threshold penalty objectives (both linear and quadratic) for these four organs at risk. In addition, we propose objectives for the target volumes as well. For both the clinical target volume (CTV) and planning target volume (PTV), we include a quadratic target dose error objective and a heterogeneity objective that measures the variance in dose to the structure. We summarize the candidate objectives below and note that all of them map from  $\mathbb{R}^{|\mathcal{B}|}$  to  $\mathbb{R}$ .

1. Piecewise linear dose threshold functions (L1): Consider an OAR  $\rho \in \{\text{Blad}, \text{Rect}, \text{LFem}, \text{RFem}\}$  with threshold value  $\tau$  Gy. We define this objective function as  $f_{\tau,\rho}^{L1}(\mathbf{w}) = \frac{1}{|\mathcal{V}_\rho|} \sum_{v \in \mathcal{V}_\rho} \max\{\sum_{b \in \mathcal{B}} D_{v,b} w_b - \tau, 0\}$ .

We consider threshold values  $\tau \in \{0, 20, 40, 60\}$  Gy for the bladder and rectum and  $\tau \in \{0, 20\}$  Gy for the femoral heads.

2. Piecewise quadratic dose threshold functions (L2): For each  $\rho \in \{\text{Blad}, \text{Rect}, \text{LFem}, \text{RFem}\}$  with threshold value  $\tau$  Gy, we define the L2 objective function  $f_{\tau,\rho}^{L2}(\mathbf{w}) = \frac{1}{|\mathcal{V}_\rho|} \sum_{v \in \mathcal{V}_\rho} \max\{\sum_{b \in \mathcal{B}} D_{v,b} w_b - \tau, 0\}^2$ .

Structure \ Function Type	L1	Max	L2	DE	HD
Bladder	1-4	5	6-9		
CTV				10	11
Left Femoral Head	12-13	14	15-16		
PTV				17	18
Right Femoral Head	19-20	21	22-23		
Rectum	24-27	28	29-32		

Table 1: A summary of functions used in objective selection. L1 and L2 function labels increase with the threshold magnitude.

We consider threshold values  $\tau \in \{0, 20, 40, 60\}$  Gy for the bladder and rectum and  $\tau \in \{0, 20\}$  Gy for the femoral heads.

3. Maximum dose functions (Max): For each  $\rho \in \{\text{Blad}, \text{Rect}, \text{LFem}, \text{RFem}\}$ , the maximum dose objective function is  $f_{\rho}^{\text{Max}}(\mathbf{w}) = \max_{v \in \mathcal{V}_{\rho}} \sum_{b \in \mathcal{B}} D_{v,b} w_b$ .
4. Dose error functions (DE): Consider a target volume  $\rho \in \{\text{CTV}, \text{PTV}\}$  with target dose  $\phi_{\rho}$ . Define the target dose function by  $f_{\rho}^{\text{DE}}(\mathbf{w}) = \frac{1}{|\mathcal{V}_{\rho}|} \sum_{v \in \mathcal{V}_{\rho}} \left( \phi_{\rho} - \sum_{b \in \mathcal{B}} D_{v,b} w_b \right)^2$ . We consider a target dose of 80Gy for the CTV and 77 Gy for the PTV.
5. Heterogeneous dose functions (HD): For each target volume  $\rho \in \{\text{CTV}, \text{PTV}\}$ , define the function

$$f_{\rho}^{\text{HD}}(\mathbf{w}) = \frac{1}{|\mathcal{V}_{\rho}|} \sum_{v \in \mathcal{V}_{\rho}} \left( \sum_{b \in \mathcal{B}} D_{v,b} w_b - \sum_{v' \in \mathcal{V}_{\rho}} \sum_{b \in \mathcal{B}} D_{v',b} w_b \right)^2.$$

The L1 and L2 functions penalize radiation doses to OARs that exceed thresholds (i.e.,  $L_1$ -norm and squared  $L_2$ -norm, respectively). We note that we do not include equivalent uniform dose functions (Niemierko 1997) or other dose-volume objectives; they do not result in a convex optimization problem in general. However, such functions have been estimated by weighted combinations of mean and maximum dose functions in the literature (Nimerierko 1999, Thieke et al. 2002), which can be represented through the 0-threshold versions of L1 and L2 objectives and the maximum dose objectives. The DE objectives can be appropriate if a specific dose is thought to be preferable for a target volume, and HD objectives can promote homogeneity in the radiation delivered to a target volume (without a specific target dose). We note that all of the objectives are nonnegative; to make them strictly positive, we add a small constant term (.01) to each of them. Table 1 summarizes the labels for the functions in the candidate objective pool.

The radiation dose required for the CTV and PTV for prostate cancer treatment is generally hard-constrained within upper and lower bounds, denoted by  $u_{\rho}$  and  $l_{\rho}$ , where  $\rho \in \{\text{CTV}, \text{PTV}\}$ . As the bladder, rectum, and normal tissue are close to the CTV and PTV yet radiation dose to these structures are supposed to not exceed dose delivered to the CTV and PTV, dose upper bounds are also introduced to them, also denoted by  $u_{\rho}$ ,  $\rho \in \{\text{Blad}, \text{Rect}, \text{Normal}\}$ . Additional constraints are generally introduced to discourage heterogeneous intensity maps; we require the intensity of each beamlet to be within some fixed ratio (lower and higher) of the average beamlet intensity. Denote these ratios by  $\eta_L$  and  $\eta_U$ . Based on the above notation, the forward optimization model is included in the e-companion.

## 5 Solution Approaches

As mentioned, there is a close connection between feature selection and objective selection problems. This motivates the use of sequential forward selection approaches to approximately solve the objective selection problem. We consider the problem of selecting  $\theta = 6$  objectives, due to the six specific structures (bladder, rectum, left femoral head, right femoral head, CTV, and PTV). We propose three forward selection approaches to select objectives: one approach is a classical greedy algorithm that optimizes the distance function of the objective selection problem; the second approach iteratively searches through each ROI for the best objective in a greedy fashion; the third approach is a variant of the greedy algorithm that finds a solution even more efficiently by exploiting the unique structure of the problem that reflects patients’ anatomical characteristics. In addition to the forward selection approaches, we implement the regularization method. We also propose extensions of these approaches to select objectives for a group of patients.

### 5.1 Greedy Algorithms and Regularization

In the generic greedy algorithm, given a single data input (e.g., one patient), for each currently unselected objective, we solve the restricted problem  $\text{RP}(\hat{\mathbf{x}}, \mathcal{S})$  by setting  $\mathcal{S}$  to the union of the unselected objective and the current selected objective set. The objective that decreases the relative gap the most is added to the selected set, and the process repeats in the next iteration. We refer the reader to Nemhauser et al. (1978) for more details about the greedy algorithm. We denote this method *G-Solo* when it is applied to a single patient.

In the ROI-restricted greedy algorithm, given a prespecified ordering of the structures, at iteration  $k$ , we greedily select an objective from the  $k$ -th ROI. For instance, if the  $k$ -th ROI is the left femoral head, we solve the restricted problem considering a left femoral head objective (see Table 1) along with the currently selected objectives of the previous  $k - 1$  ROIs. The left femoral head objective that decreases the relative gap the most is added to the selected set, and we repeat the procedure for the next ROI. This method ensures that exactly one objective per structure is selected. We denote the ROI-restricted greedy algorithm by *GR-Solo*.

For the regularization approach, we solve (8) for the specified patient. We set  $\boldsymbol{\lambda}$  equal to six times the vector of ones in  $\mathbb{R}^{|\mathcal{K}|}$  so that the regularization term is  $6\|\boldsymbol{\alpha}\|_1$ , where  $\boldsymbol{\alpha}$  is the weight vector. We note that further optimization and parameter tuning may find a regularization penalty that works robustly. For a single patient, we refer to this approach as *R-Solo*.

### 5.2 Anatomy-Based Approach

Our specific application in radiation therapy offers some structure that can allow us to search for objectives in a different way beyond the relative gap. Each objective function  $f_k$  is characterized by its ROI’s matrix,  $\mathbf{D}_{\rho_k}$ , the type of objective (L1, L2, Max, DE, HD), and the threshold  $\tau_k$  (we interpret  $\tau_k = 0$  for objectives without thresholds). In particular, the  $\mathbf{D}_{\rho}$  matrices quantify the influence of each beamlet on each voxel and thus provide geometric information on the structures. Hence, we can define a metric that indicates the similarity of two objectives from the same patient in order to select dissimilar objectives, thus reducing redundancy, that describe past planning decisions. We let  $\hat{\gamma}(i, j)$  be the distance between the Gramian matrices  $\mathbf{D}_{\rho_i}$  and  $\mathbf{D}_{\rho_j}$  defined by Lim et al. (2019); additional details can be found in Section B. Then, we define the dissimilarity between  $f_i$  and  $f_j$  by  $\gamma(i, j) = 5\hat{\gamma}(i, j) + 5\mathbb{1}_{\text{type}(i) \neq \text{type}(j)} + |\tau_i - \tau_j|$ , where  $\mathbb{1}_{\text{type}(i) \neq \text{type}(j)}$  captures if objectives  $i$  and  $j$  are not of the same type (e.g., both L1). Thus,  $\gamma$  indicates the anatomical and function type similarity between two objectives from the same patient. Define the function  $T : \mathcal{K}^2 \rightarrow \mathbb{R}$  by

Method	Single Patient	Multiple Patients: Set (S), Weight (W)
Anatomy-based Greedy Alg.	A-Solo	G-Batch-S
Greedy Alg. by ROI	G-Solo	
Regularization	GR-Solo	R-Batch-W
	R-Solo	

Table 2: A summary of solution approaches for objective selection

$T(\mathcal{S}) = \sum_{i,j \in \mathcal{S}} \gamma(i,j)$ ; we call  $T$  the total edge function because it is the sum of edge weights of a weighted complete graph where each node corresponds to each objective  $i \in \mathcal{S}$  and  $\gamma(i,j)$  represents the edge weight. We refer to the set of edge weights  $\{\gamma(i,j)\}_{i,j \in \mathcal{K}}$  as an *E-vector*.

In the anatomy-based greedy algorithm for a single patient, which we call *A-Solo*, the first objective function is selected by minimizing the duality gap (i.e., solving problem (5) repeatedly with each candidate objective and choosing the objective that gives the minimum duality gap). Each subsequent objective is then selected by maximizing the increase in the total edge function  $T$  (see Algorithm 1 in Section B). As there is no optimization problem involved to add subsequent objectives and evaluating the total edge function is relatively easy and can be done *a priori*, this anatomy-based approach is faster than the generic greedy algorithm, G-Solo.

### 5.3 Batch-Input Objective Selection

Given a group of patients, we consider two different variants of the objective selection problem: (i) finding common objective sets for all patients in the same cluster and (ii) common objectives *and* weights for all patients in the same cluster.

- (i) Finding common objectives: Objectives are greedily selected based on the sum of individual duality gaps, which is obtained by solving patients' individual restricted inverse problems (5).
- (ii) Finding common objectives and weights: The regularization approach is generalized to accept apply to multiple patients. Objectives for the batch are computed as  $\tilde{\mathbf{f}}(\chi) = \sum_{p \in \mathcal{P}} \mathbf{f}(\mathbf{x}_p)$ , where  $\mathcal{P}$  is the batch of patients. We solve the regularization problem (8) using  $\tilde{\mathbf{f}}$  and input solution  $\chi$ , again using the regularization penalty of  $6\|\boldsymbol{\alpha}\|_1$ .

We refer to the first approach (i) as *G-Batch-S* because it uses the greedy algorithm on the group of patients to select common objectives (not weights). In the same way, we label (ii) as *R-Batch-W* because it uses the regularization approach to find common objectives and weights for the group of patients. A summary of solution approaches developed for objective selection is displayed in Table 2. Overall, the presented solution approaches can be used to develop a treatment planning procedure that reduces the time-intensive burden of manual objective selection.

## 6 Conclusion

In this paper, we introduce the objective selection problem that finds a set of convex objectives that capture the preferences in input data and produces weakly Pareto optimal solutions with respect to these preferences. We formulate the problem as a non-convex bilevel mixed-integer program using inverse optimization, and propose iterative and regularized approaches to approximately solve it by connecting objective selection

with feature selection. Moreover, we demonstrate that we can extend our objective selection framework to multiple patients. The proposed solution approaches for the objective selection problem can lead to efficient and streamlined treatment planning that avoids time-consuming and often unguided trial and error. Future work includes exploration into other distance metrics for the restricted inverse problem as well as further analysis of the anatomy-based greedy algorithm.

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## A Forward Model for IMRT Planning

We present the forward optimization model below. If OAR  $\rho$  has threshold objectives, we denote the set of thresholds by  $\mathcal{T}_\rho$ . Let  $\mathcal{S}_1 = \{\text{Blad, Rect, LFem, RFem}\}$  and  $\mathcal{S}_2 = \{\text{CTV, PTV}\}$ .

$$\min_{\mathbf{w}} \quad \sum_{\rho \in \mathcal{S}_1} \alpha_\rho^{\text{Max}} f_\rho^{\text{Max}}(\mathbf{w}) + \sum_{\tau \in \mathcal{T}_\rho} \alpha_{\tau, \rho}^{\text{L1}} f_{\tau, \rho}^{\text{L1}}(\mathbf{w}) + \alpha_{\tau, \rho}^{\text{L2}} f_{\tau, \rho}^{\text{L2}}(\mathbf{w}) + \sum_{\rho \in \mathcal{S}_2} \alpha_\rho^{\text{DE}} f_\rho^{\text{DE}}(\mathbf{w}) + \alpha_\rho^{\text{HD}} f_\rho^{\text{HD}}(\mathbf{w}) \quad (9)$$

$$\text{subject to} \quad \sum_{b \in \mathcal{B}} D_{v, b} w_b \geq l_\rho, \quad \forall v \in \mathcal{V}_\rho, \rho \in \mathcal{S}_2, \quad (10)$$

$$\sum_{b \in \mathcal{B}} D_{v, b} w_b \leq u_\rho, \quad \forall v \in \mathcal{V}_\rho, \rho \in \{\text{CTV, PTV, Blad, Rect, Normal}\}, \quad (11)$$

$$w_b - \frac{\eta_L}{|\mathcal{B}|} \sum_{b' \in \mathcal{B}} w_{b'} \geq 0, \quad \forall b \in \mathcal{B}, \quad (12)$$

$$w_b - \frac{\eta_U}{|\mathcal{B}|} \sum_{b' \in \mathcal{B}} w_{b'} \leq 0, \quad \forall b \in \mathcal{B}, \quad (13)$$

$$\mathbf{w} \in \mathbb{R}_+^{|\mathcal{B}|}. \quad (14)$$

Here,  $\mathbf{w}$  represent the beamlet intensities. Lower and upper bounds on permissible doses to voxels in structure  $r$  are given by  $l_\rho$  and  $u_\rho$ , respectively. The matrix  $\mathbf{D}$  maps the beamlets to the voxels. In addition,  $\eta_L$  and  $\eta_U$  prevent the beamlets from being too heterogeneous. These parameters are patient dependent, although they are similar across patients.

## B Anatomy-Based Heuristic Details

As stated in Section 5, each of the candidate objective functions in the IMRT forward problem is computed using an OAR-specific submatrix  $\mathbf{D}_\rho$  and a penalty threshold  $\tau_k$  specific to function  $f_k$ . Each of the candidate objective functions in the IMRT forward problem is computed using an OAR-specific submatrix  $\mathbf{D}_\rho$  and a penalty threshold  $\tau_k$  specific to function  $f_k$ . Let  $\mathcal{G}_k = \mathbf{D}_\rho^\top \mathbf{D}_\rho + \rho \mathbf{I}_k, \rho > 0$  so that  $\mathcal{G}_k$  is a positive definite matrix.

Lim et al. (2019) state that each symmetric positive definite cone  $\mathbb{S}_{++}^m$  has a “natural Riemannian metric”,  $\delta_2 : \mathbb{S}_{++}^m \times \mathbb{S}_{++}^m \rightarrow \mathbb{R}^+$ , defined by

$$\delta_2(A, B) = \left[ \sum_{i=1}^m \log^2(\lambda_j(A^{-1}B)) \right]^{1/2},$$

where  $\lambda_j$  denotes the  $j^{\text{th}}$  smallest eigenvalue of the matrix. The authors extend this notion to define a distance between two positive definite matrices of different sizes.

**Definition 1.** (Lim et al. 2019)

Let  $m_1 \leq m_2$  and let  $A^1 \in \mathbb{S}_{++}^{m_1}$  and  $A^2 \in \mathbb{S}_{++}^{m_2}$ . Let  $A_{11}^2$  denote the the upper left  $m_1 \times m_1$  principal

submatrix of  $A^2$ . Then

$$\delta_2^+(A^1, A^2) = \left[ \sum_{i=1}^{m_1} \min\{0, \log \lambda_i((A^1)^{-1} A_{11}^2)\}^2 \right]^{1/2},$$

where  $\lambda_i(A)$  is the  $i^{\text{th}}$  smallest eigenvalue of a symmetric positive definite matrix  $A$ .

Lim et al. (2019) show that when  $m_k = m_\ell$ ,  $\delta_2^+(\mathcal{G}_k, \mathcal{G}_\ell) + \delta_2^+(\mathcal{G}_\ell, \mathcal{G}_k) = \delta_2(\mathcal{G}_k, \mathcal{G}_\ell)$ . Additional details on this metric are in Lim et al. (2019). Using  $\delta_+^2$ , we define the anatomy-based similarity metric between two functions as:

$$\gamma(f_k, f_\ell) = \begin{cases} 2\delta_2^+(\mathcal{G}_k, \mathcal{G}_\ell), & \text{if } m_k < m_\ell, \\ \delta_2^+(\mathcal{G}_k, \mathcal{G}_\ell) + \delta_2^+(\mathcal{G}_\ell, \mathcal{G}_k), & \text{if } m_k = m_\ell. \end{cases} \quad (15a)$$

Pseudocode for the anatomy-based greedy heuristic is given in Algorithm 1. Note that here, we maximize dissimilarity.

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### Algorithm 1

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1: procedure ANATOMY-BASED GREEDY HEURISTIC
2:   Given:  $\widehat{\mathbf{x}}, \mathcal{K}, \theta, \gamma, |\mathcal{S}| = 1$ 
3:    $\mathcal{R} \leftarrow \mathcal{K} \setminus \mathcal{S}$ 
4:   for  $k \in \{2, \dots, \theta\}$  do
5:     for  $t \in \mathcal{R}$  do
6:        $z_t \leftarrow T(\mathcal{S} \cup \{t\})$ 
7:     Choose  $t^* \in \arg \max_{t \in \mathcal{T}} \{z_t\}$ 
8:      $\mathcal{S} \leftarrow \mathcal{S} \cup \{t^*\}$ 
9:      $\mathcal{R} \leftarrow \mathcal{R} \setminus \{t^*\}$ 
10:     $k \leftarrow k + 1$ 
return  $\mathcal{S}$ 

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## C Using Norms as Distance Functions

We focus primarily on objective selection based on minimizing the relative gap. However, other distance functions may be used. For instance, recall  $d^{[q]}(\mathbf{x}, \widehat{\mathbf{x}}, \mathcal{S}) = \|\mathbf{f}(\mathbf{x}) - \mathbf{f}(\widehat{\mathbf{x}})\|_q$ . This distance function has been considered in forward multi-objective optimization as a “min-norm method” (Lin 2005). One important example is when  $\widehat{\mathbf{x}}$  is such that  $f_k(\widehat{\mathbf{x}}) \leq \min_{\mathbf{x}} \{f_k(\mathbf{x}) \mid \mathbf{A}\mathbf{x} = \mathbf{b}, \mathbf{g}(\mathbf{x}) \leq \mathbf{0}\}$ , for all  $k \in \mathcal{K}$ . If  $\widehat{\mathbf{x}}$  is also feasible, it is clearly Pareto optimal, but such a feasible solution typically does not exist. Instead, we may consider a set of input points  $\widehat{\chi}_{\mathcal{K}} = \{\widehat{\mathbf{x}}_k\}_{k \in \mathcal{K}}$ , where  $\widehat{\mathbf{x}}_k \in \arg \min_{\mathbf{x}} \{f_k(\mathbf{x}) \mid \mathbf{A}\mathbf{x} = \mathbf{b}, \mathbf{g}(\mathbf{x}) \leq \mathbf{0}\}$  for each  $k \in \mathcal{K}$ . Lin (2005) calls solutions  $\widehat{\mathbf{x}}_k$  “ideal”.

We define the distance function  $d^{[q, \mathbb{I}]}(\mathbf{x}, \widehat{\chi}_{\mathcal{K}}, \mathcal{S}) = \left( \sum_{k \in \mathcal{S}} |f_k(\mathbf{x}) - f_k(\widehat{\mathbf{x}}_k)|^q \right)^{1/q}$ . In the sequel, we show that a restricted problem akin to (5) can be formulated, thus leading to an analog of Theorem 1. For simplicity, we consider the single input case where  $\mathcal{P}$  is a singleton. Consider the following restricted inverse

problem:

$$\text{RPQ}(\widehat{\chi}_{\mathcal{K}}, \mathcal{S}) = \min_{\mathbf{x}, \mathbf{y}} \sum_{k \in \mathcal{S}} y_k^q \quad (16a)$$

$$\text{subject to } f_k(\mathbf{x}) - f_k(\widehat{\mathbf{x}}_k) \leq y_k, \forall k \in \mathcal{S}, \quad (16b)$$

$$\mathbf{A}\mathbf{x} = \mathbf{b}, \quad (16c)$$

$$\mathbf{g}(\mathbf{x}) \leq \mathbf{0}. \quad (16d)$$

Note that (16) is a convex program.

**Proposition 4.** *Let  $\mathcal{S} \subseteq \mathcal{K}$  and let  $(\mathbf{x}^*, \mathbf{y}^*)$  be an optimal solution to (16). The objective value of (16) is  $\text{RPQ}(\widehat{\chi}_{\mathcal{K}}, \mathcal{S}) = (d^{[q,1]}(\mathbf{x}^*, \widehat{\chi}_{\mathcal{K}}, \mathcal{S}))^q$ . In addition, if  $\boldsymbol{\alpha}^*$  are the Lagrange multipliers of constraints (16b), then  $\mathbf{x}^* \in \mathcal{O}(\boldsymbol{\alpha}^*)$ ; hence  $\mathbf{x}^*$  is Pareto optimal.*

*Proof:* For each  $k \in \mathcal{S}$ ,  $\widehat{\mathbf{x}}_k$  is ideal; thus, for any  $(\mathbf{x}, \mathbf{y})$  feasible for  $\text{RPQ}(\widehat{\chi}_{\mathcal{K}}, \mathcal{S})$ ,  $|f_k(\mathbf{x}) - f_k(\widehat{\mathbf{x}}_k)| = f_k(\mathbf{x}) - f_k(\widehat{\mathbf{x}}_k)$ . Hence, it is clear that for any optimal  $(\mathbf{x}^*, \mathbf{y}^*)$ ,  $\sum_{k \in \mathcal{S}} (y_k^*)^q = (d^{[q,1]}(\mathbf{x}^*, \widehat{\chi}_{\mathcal{K}}, \mathcal{S}))^q$ .

The Lagrangian of  $\text{RPQ}(\widehat{\chi}_{\mathcal{K}}, \mathcal{S})$  is  $\mathcal{L}(\mathbf{x}, \mathbf{y}, \boldsymbol{\alpha}, \boldsymbol{\pi}, \boldsymbol{\sigma}) = \sum_{k \in \mathcal{S}} y_k^q + \sum_{k \in \mathcal{S}} \alpha_k (f_k(\mathbf{x}) - f_k(\widehat{\mathbf{x}}_k) - y_k) + \boldsymbol{\pi}^\top (\mathbf{A}\mathbf{x} - \mathbf{b}) + \boldsymbol{\sigma}^\top \mathbf{g}(\mathbf{x})$ . Consider the Lagrangian dual:

$$\max_{\mathbf{x}, \mathbf{y}, \boldsymbol{\alpha}, \boldsymbol{\pi}, \boldsymbol{\sigma}} \left\{ \inf_{\mathbf{x}, \mathbf{y}} \mathcal{L}(\mathbf{x}, \mathbf{y}, \boldsymbol{\alpha}, \boldsymbol{\pi}, \boldsymbol{\sigma}) \mid \boldsymbol{\alpha} \geq \mathbf{0}, \boldsymbol{\sigma} \geq \mathbf{0} \right\},$$

stationarity conditions:

$$\mathbf{A}^\top \boldsymbol{\pi} + \sum_{\ell=1}^L \sigma_\ell \nabla g_\ell(\mathbf{x}) + \sum_{k \in \mathcal{S}} \alpha_k \nabla f_k(\mathbf{x}) = \mathbf{0}, \quad (17a)$$

$$qy_k^{q-1} - \alpha_k = 0, \forall k \in \mathcal{S}, \quad (17b)$$

and complementary slackness:

$$\alpha_k (f_k(\mathbf{x}) - f_k(\widehat{\mathbf{x}}_k) - y_k) = 0, \forall k \in \mathcal{S}, \quad (18)$$

$$\boldsymbol{\sigma} \circ \mathbf{g}(\mathbf{x}) = \mathbf{0}. \quad (19)$$

Notice that  $\boldsymbol{\alpha} \geq \mathbf{0}$ , and  $\boldsymbol{\sigma} \geq \mathbf{0}$ , (16c)-(16d), (17a), and (19) are the KKT conditions for  $\text{WMO}(\boldsymbol{\alpha})$ . Hence, if  $(\mathbf{x}^*, \mathbf{y}^*, \boldsymbol{\alpha}^*, \boldsymbol{\pi}^*, \boldsymbol{\sigma}^*)$  is an optimal primal-dual pair of  $\text{RPQ}(\widehat{\chi}_{\mathcal{K}}, \mathcal{S})$ , then  $\mathbf{x}^* \in \mathcal{O}(\boldsymbol{\alpha}^*)$  and  $\mathbf{x}^*$  is Pareto optimal. In addition, (17b) implies  $\alpha_k^* = qy_k^{q-1}$ , for all  $k \in \mathcal{S}$ .  $\square$

**Remark 1.** *A result of the proof of Proposition 4 is that the weights are uniquely determined by the values  $f_k(\mathbf{x}) - f_k(\widehat{\mathbf{x}}_k)$ .*

**Theorem 4.** *Given the distance function  $d^{[q,1]}(\mathbf{x}, \widehat{\chi}_{\mathcal{K}}, \mathcal{S})$ , we have  $\text{OS}(\widehat{\chi}) = \min_{\mathcal{S} \subseteq \mathcal{K}, 1 \leq |\mathcal{S}| \leq \theta} \text{RPQ}(\widehat{\chi}_{\mathcal{K}}, \mathcal{S})$ .*

## D Omitted Proofs

PROPOSITION 1.  $\mathcal{F}_1$ , the feasible region of (1), and  $\mathcal{F}_2$ , the feasible region of (2) are related as follows:

$$\{(\boldsymbol{\alpha}, \boldsymbol{\xi}, \chi) \mid (\boldsymbol{\alpha}, \boldsymbol{\xi}, \chi, \boldsymbol{\sigma}, \boldsymbol{\pi}) \in \mathcal{F}_2 \text{ for some } (\boldsymbol{\sigma}, \boldsymbol{\pi})\} = \{(\boldsymbol{\alpha}, \boldsymbol{\xi}, \chi) \in \mathcal{F}_1 \mid \boldsymbol{\alpha}_{(p)}^\top \mathbf{e} = 1, \text{ for all } p \in \mathcal{P}\}.$$

Thus, the optimal objective values of (1) and (2) are equal.

*Proof:* Observe that (2f)-(2j) are the KKT conditions of the individual forward problems parametrized by  $\alpha_{(p)}$ , which implies that for each  $p \in \mathcal{P}$ ,  $\mathbf{x}_{(p)} \in \mathcal{O}_{(p)}(\alpha_{(p)})$  and there exists  $(\sigma_{(p)}, \pi_{(p)})$  such that (2f)-(2j) are satisfied. Further, (1b), (1c), and (1e) are respectively equivalent to (2b), (2c), and (2k). Additionally, given  $\alpha_{(p)}^\top \mathbf{e} = 1$  and (1c),  $\alpha_{(p)} \in \mathcal{A}(\mathcal{S}(\xi))$ . This proves the equality of the stated subsets.

The objective functions of (1) and (2) do not directly involve weight vectors. The weight vector in (1) can be scaled such that  $\alpha_{(p)}^\top \mathbf{e} = 1$  without loss of generality in the following sense: for any  $(\tilde{\alpha}, \tilde{\xi}, \tilde{\chi}) \in \mathcal{F}_1$ ,  $(\tilde{\alpha}/(\tilde{\alpha}^\top \mathbf{e}), \tilde{\xi}, \tilde{\chi}) \in \mathcal{F}_1$ , and  $\frac{\tilde{\alpha}}{\tilde{\alpha}^\top \mathbf{e}}^\top \mathbf{e} = 1$ , thus,  $(\tilde{\alpha}/(\tilde{\alpha}^\top \mathbf{e}), \tilde{\xi}, \tilde{\chi}) \in \{(\alpha, \xi, \chi) \mid (\alpha, \xi, \chi, \sigma, \pi) \in \mathcal{F}_2 \text{ for some } (\sigma, \pi)\}$ .

Thus, the two optimal objective values are equal.  $\square$

**PROPOSITION 2.** *Let  $\chi^* = \{\mathbf{x}_{(p)}^*\}_{p \in \mathcal{P}}$  be an optimal solution for  $RP(\widehat{\chi}, \mathcal{S})$ . Then, for all  $p \in \mathcal{P}$ :*

(i)  $\mathbf{x}_{(p)}^* \in \Omega_{(p)}(\mathcal{S})$ .

(ii)  $1/\max_{k \in \mathcal{K}} \{f_{(p),k}(\mathbf{x}_{(p)}^*)/f_{(p),k}(\widehat{\mathbf{x}}_{(p)})\}$  is the minimum relative duality gap with respect to  $\widehat{\mathbf{x}}_{(p)}$ .

In addition, a convex reformulation of  $RP(\widehat{\chi}, \mathcal{S})$  exists where optimal weight vectors  $\alpha_{(p)}^*$ , such that  $\mathbf{x}_{(p)}^* \in \mathcal{O}_{(p)}(\alpha_{(p)}^*)$ , can be computed as Lagrange multipliers, for all  $p \in \mathcal{P}$ .

*Proof:* Observe that

$$\begin{aligned} & \min_{\chi} \left\{ \sum_{p \in \mathcal{P}} \max_{k \in \mathcal{K}} \{f_k(\mathbf{x}_{(p)})/f_k(\widehat{\mathbf{x}}_{(p)})\} \mid (5b) - (5c) \right\} \\ &= \sum_{p \in \mathcal{P}} \min_{\chi} \{ \max_{k \in \mathcal{K}} \{f_k(\mathbf{x}_{(p)})/f_k(\widehat{\mathbf{x}}_{(p)})\} \mid (5b) - (5c) \text{ with respect to } p \}, \end{aligned}$$

as  $RP(\widehat{\chi}, \mathcal{S})$  is separable for each input  $p$ . Hence, by (Chan and Lee 2018, Proposition 3.1),  $\epsilon_{(p)}^* = \min_{\mathbf{x}, \epsilon} \{\epsilon_{(p)} \mid (20b) - (20c) \text{ with respect to } p\} = \frac{1}{z_{(p)}^*}$  for each  $p \in \mathcal{P}$ . Consider the reformulation of  $RP(\widehat{\chi}, \mathcal{S})$ :

$$\begin{aligned} & \min_{\mathbf{x}, \epsilon} \sum_{p \in \mathcal{P}} \epsilon_{(p)} \\ & \text{subject to } \mathbf{f}_{(p)}(\mathbf{x}_{(p)}) - \epsilon_{(p)} \cdot \mathbf{f}_{(p)}(\widehat{\mathbf{x}}_{(p)}) \leq \mathbf{0}, \quad \forall p \in \mathcal{P}, \end{aligned} \tag{20a}$$

$$\mathbf{A}_{(p)} \mathbf{x}_{(p)} = \mathbf{b}_{(p)}, \quad \forall p \in \mathcal{P}, \tag{20b}$$

$$\mathbf{g}_{(p)}(\mathbf{x}_{(p)}) \leq \mathbf{0}, \quad \forall p \in \mathcal{P}. \tag{20c}$$

It is easy to see that at optimality,  $\epsilon_{(p)}^* = \max_{k \in \mathcal{K}} \{f_k(\mathbf{x}_{(p)}^*)/f_k(\widehat{\mathbf{x}}_{(p)})\}$ , which shows the two formulations are equivalent. By Corollary 3.1 of Chan and Lee (2018),  $\epsilon_{(p)}^* = \frac{1}{z_{(p)}^*}$ , where  $z_{(p)}^*$  is the minimum relative duality gap (over all admissible weight vectors) of the forward problem for each  $p \in \mathcal{P}$ . Also,  $\mathbf{x}_{(p)}^* \in \mathcal{O}_{(p)}(\alpha_{(p)}^*)$ , where  $\alpha_{(p)}^*$  are the Lagrange multipliers for (20a), by the same result. Hence, for all  $p \in \mathcal{P}$ ,  $\frac{1}{\max_{k \in \mathcal{K}} \{f_k(\mathbf{x}_{(p)}^*)/f_k(\widehat{\mathbf{x}}_{(p)})\}} = 1/\epsilon_{(p)}^* = z_{(p)}^*$ , and  $\mathbf{x}_{(p)}^* \in \mathcal{O}_{(p)}(\alpha_{(p)}^*)$  implies (by Lemma 1) that  $\mathbf{x}_{(p)}^* \in \Omega_{(p)}(\mathcal{S})$ .  $\square$

**THEOREM 1.** *Given the distance functions  $d_{(p)}(\mathbf{x}, \widehat{\mathbf{x}}, \mathcal{S}) = \max_{k \in \mathcal{S}} \{f_{(p),k}(\mathbf{x})/f_{(p),k}(\widehat{\mathbf{x}})\}$ , for all  $p \in \mathcal{P}$ , we have  $OS(\widehat{\chi}) = \min_{S \subseteq \mathcal{K}, 1 \leq |S| \leq \theta} RP(\widehat{\chi}, \mathcal{S})$ .*

*Proof:* From Proposition 2,  $RP(\widehat{\chi}, \mathcal{S}) = \sum_{p \in \mathcal{P}} d_{(p)}(\mathbf{x}_{(p)}^*, \widehat{\mathbf{x}}_{(p)}, \mathcal{S}) = \sum_{p \in \mathcal{P}} \frac{1}{z_{(p)}^*} = \delta(\widehat{\chi}, \mathcal{S})$ . Hence,  $IMO(\widehat{\chi}) = \min_{S \subseteq \mathcal{K}, 1 \leq |S| \leq \theta} \delta(\widehat{\chi}, \mathcal{S}) = \min_{S \subseteq \mathcal{K}, 1 \leq |S| \leq \theta} RP(\widehat{\chi}, \mathcal{S})$ .  $\square$

**THEOREM 2.** *There exists a convex reformulation of  $RP-W(\widehat{\chi}, \mathcal{S})$  whose Lagrange multipliers are optimal weights that minimize the batch duality gap. Moreover,  $IMO-W(\widehat{\chi}) = \min_{S \subseteq \mathcal{K}, 1 \leq |S| \leq \theta} RP-W(\widehat{\chi}, \mathcal{S})$ .*

*Proof:* For each  $k \in \mathcal{S}$ , define the function  $F_k$  by  $F_k(\chi) = \sum_{p \in \mathcal{P}} f_k(\mathbf{x}_{(p)})$ , and let  $\mathbf{F}(\chi) = [F_k(\chi)]_{k \in \mathcal{S}}$ . Then each  $F_k$  is convex as it is the sum of convex functions. Consider the following reformulation of RP-W( $\widehat{\chi}, \mathcal{S}$ ):

$$\begin{aligned} \min_{\mathbf{x}, \epsilon} \quad & \epsilon \\ \text{subject to} \quad & F_k(\chi) - \epsilon \cdot F_k(\widehat{\chi}) \leq \mathbf{0}, \quad \forall k \in \mathcal{S}, \end{aligned} \quad (21a)$$

$$\mathbf{A}_{(p)} \mathbf{x}_{(p)} = \mathbf{b}_{(p)}, \quad \forall p \in \mathcal{P}, \quad (21b)$$

$$\mathbf{g}_{(p)}(\mathbf{x}_{(p)}) \leq \mathbf{0}, \quad \forall p \in \mathcal{P}. \quad (21c)$$

Observe that (21) is a convex program. We now show that (21) is the convex programming reformulation in the claim.

Note that (21) of the same form as (20) with only one input; for example,  $F_k$  replaces  $f_{(1),k}$  and  $[\mathbf{A}_{(1)}^\top, \dots, \mathbf{A}_{(P)}^\top]^\top$  replaces  $\mathbf{A}_{(1)}$ . Let  $(\epsilon^*, \chi^*)$  be an optimal solution to (21), and let  $\boldsymbol{\alpha}^*$  be the Lagrange multipliers corresponding to constraints (21a). By the same argument as that of Proposition 2,  $\frac{1}{\epsilon^*}$  is the minimum duality gap at  $\widehat{\chi}$  (over all admissible weight vectors  $\boldsymbol{\alpha}$ ) of the forward problem

$$\begin{aligned} \min_{\chi} \quad & \sum_{k \in \mathcal{S}} \alpha_k F_k(\chi) \\ \text{s.t.} \quad & \mathbf{A}_{(p)} \mathbf{x}_{(p)} = \mathbf{b}_{(p)}, \quad \forall p \in \mathcal{P}, \\ & \mathbf{g}_{(p)}(\mathbf{x}_{(p)}) \leq \mathbf{0}, \quad \forall p \in \mathcal{P}. \end{aligned}$$

and  $\chi^* \in \arg \min_{\chi} \left\{ \boldsymbol{\alpha}^{*\top} \sum_{p \in \mathcal{P}} \mathbf{f}(\mathbf{x}_{(p)}) \mid \mathbf{A}_{(p)} \mathbf{x}_{(p)} = \mathbf{b}_{(p)}, \mathbf{g}_{(p)}(\mathbf{x}_{(p)}) \leq \mathbf{0}, \forall p \in \mathcal{P} \right\} \subseteq \widetilde{\Omega}(\mathcal{S})$ . Thus,

$$\begin{aligned} \frac{1}{\epsilon^*} &= \min_{\boldsymbol{\alpha}, \chi} \{ \boldsymbol{\alpha}^\top \mathbf{F}(\chi) / \boldsymbol{\alpha}^\top \mathbf{F}(\widehat{\chi}) \mid \mathbf{g}_{(p)}(\mathbf{x}_{(p)}) \leq \mathbf{0}, \mathbf{A}_{(p)} \mathbf{x}_{(p)} = \mathbf{b}_{(p)}, \forall p \in \mathcal{P} \}, \\ &= \min_{\chi} \min_{\boldsymbol{\alpha}} \{ \boldsymbol{\alpha}^\top \mathbf{F}(\chi) / \boldsymbol{\alpha}^\top \mathbf{F}(\widehat{\chi}) \mid \mathbf{g}_{(p)}(\mathbf{x}_{(p)}) \leq \mathbf{0}, \mathbf{A}_{(p)} \mathbf{x}_{(p)} = \mathbf{b}_{(p)}, \forall p \in \mathcal{P} \}, \\ &= \min_{\chi} \gamma(\chi, \widehat{\chi}, \mathcal{S}). \end{aligned}$$

Hence, (21) solves RP-W( $\widehat{\chi}, \mathcal{S}$ ) and the optimal weights  $\boldsymbol{\alpha}^*$  are the Lagrange multipliers corresponding to (21a). Moreover, from the last equality, we have

$$\begin{aligned} & \min_{\mathcal{S} \subseteq \mathcal{K}} \{ \text{RP-W}(\widehat{\chi}, \mathcal{S}) \mid \chi \in \widetilde{\Omega}(\mathcal{S}), 1 \leq \mathcal{S} \leq \theta \} \\ &= \min_{\chi, \mathcal{S}} \{ \gamma(\chi, \widehat{\chi}, \mathcal{S}) \mid \chi \in \widetilde{\Omega}(\mathcal{S}), 1 \leq \mathcal{S} \leq \theta \}. \end{aligned} \quad \square$$

**PROPOSITION 3.** *Consider a single-input restricted inverse problem RP ( $\widehat{\mathbf{x}}, \mathcal{S}$ ) and an optimal solution ( $\mathbf{x}^*, \boldsymbol{\alpha}^*$ ). Let  $\mathcal{S}^*$  be the support of  $\boldsymbol{\alpha}^*$ , e.g.,  $\mathcal{S}^* = \{k \in \mathcal{S} \mid \alpha_k^* > 0\}$ . Then the relative gap of WMO( $\boldsymbol{\alpha}^*$ ) at  $\widehat{\mathbf{x}}$  is*

$$\frac{\|\mathbf{f}_{\mathcal{S}^*}(\widehat{\mathbf{x}})\|_{q, \mathcal{S}^*}^q}{\|\mathbf{f}_{\mathcal{S}^*}(\widehat{\mathbf{x}})\|_{q, \mathcal{S}^*}^q - \|\mathbf{f}_{\mathcal{S}^*}(\widehat{\mathbf{x}}) - \mathbf{f}_{\mathcal{S}^*}(\mathbf{x}^*)\|_{q, \mathcal{S}^*}^q}.$$

*Proof:* From Lagrangian duality arguments similar to those in the proof of Proposition 2,  $\alpha_k^* > 0$  only if

$f_k(\mathbf{x}^*) = \epsilon^* f_k(\hat{\mathbf{x}})$ , where  $\epsilon^*$  is the reciprocal of the duality gap of  $\text{WMO}(\boldsymbol{\alpha}^*)$  at  $\hat{\mathbf{x}}$ . Observe that

$$\begin{aligned} \|\mathbf{f}_{\mathcal{S}^*}(\hat{\mathbf{x}}) - \mathbf{f}_{\mathcal{S}^*}(\mathbf{x}^*)\|_{q, \mathcal{S}^*}^q &= \sum_{k \in \mathcal{S}^*} |f_k(\hat{\mathbf{x}}) - f_k(\mathbf{x}^*)|^q \\ &= \sum_{k \in \mathcal{S}^*} (f_k(\hat{\mathbf{x}}) - f_k(\mathbf{x}^*))^q \\ &= (1 - \epsilon^*) \sum_{k \in \mathcal{S}^*} (f_k(\hat{\mathbf{x}}))^q \\ &= (1 - \epsilon^*) \|\mathbf{f}_{\mathcal{S}^*}(\hat{\mathbf{x}})\|_{q, \mathcal{S}^*}^q, \end{aligned}$$

where we have used the fact that  $\epsilon^* \leq 1$  (and hence,  $f_k(\mathbf{x}^*) \leq f_k(\hat{\mathbf{x}})$ , for all  $k \in \mathcal{S}^*$ ) in the second equality. It follows that  $\epsilon^* = 1 - \frac{\|\mathbf{f}_{\mathcal{S}^*}(\hat{\mathbf{x}}) - \mathbf{f}_{\mathcal{S}^*}(\mathbf{x}^*)\|_{q, \mathcal{S}^*}^q}{\|\mathbf{f}_{\mathcal{S}^*}(\hat{\mathbf{x}})\|_{q, \mathcal{S}^*}^q}$ , and the claim follows after taking the reciprocal of both sides.  $\square$

**THEOREM 3.** *If an optimal primal-dual pair for  $\text{REGP}(\hat{\mathbf{x}})$  exists with zero absolute duality gap, then the dual multipliers of (8b) yield optimal weights to the regularized objective selection problem  $RE(\hat{\mathbf{x}})$ .*

*Proof:* Define the Lagrangian for  $\text{REGP}(\hat{\mathbf{x}})$  by  $\mathcal{L}(\mathbf{x}, \epsilon, \boldsymbol{\alpha}, \boldsymbol{\pi}, \boldsymbol{\sigma}) = \epsilon + \boldsymbol{\alpha}^\top (\mathbf{f}(\mathbf{x}) - \epsilon \mathbf{f}(\hat{\mathbf{x}}) - \boldsymbol{\lambda}) + \boldsymbol{\pi}^\top (\mathbf{A}\mathbf{x} - \mathbf{b}) + \boldsymbol{\sigma}^\top \mathbf{g}(\mathbf{x})$ . Given Slater's condition, strong duality holds. Let  $(\mathbf{x}^*, \epsilon^*)$  be an optimal primal solution. The Lagrangian dual problem for  $\text{REGP}(\hat{\mathbf{x}})$  is

$$\epsilon^* = \max_{\boldsymbol{\alpha}, \boldsymbol{\pi}, \boldsymbol{\sigma}} \left\{ \inf_{\mathbf{x}, \epsilon} \mathcal{L}(\mathbf{x}, \epsilon, \boldsymbol{\alpha}, \boldsymbol{\pi}, \boldsymbol{\sigma}) \mid \boldsymbol{\alpha} \geq \mathbf{0}, \boldsymbol{\sigma} \geq \mathbf{0} \right\}. \quad (22)$$

The Lagrangian function is convex as a function of  $\mathbf{x}$  and  $\epsilon$ , so the inner minimization problem can be replaced with stationarity conditions:

$$\epsilon^* = \max_{\boldsymbol{\alpha}, \boldsymbol{\pi}, \boldsymbol{\sigma}, \mathbf{x}, \epsilon} \mathcal{L}(\mathbf{x}, \epsilon, \boldsymbol{\alpha}, \boldsymbol{\pi}, \boldsymbol{\sigma}) \quad (23a)$$

$$\text{s.t.} \quad \sum_{k \in \mathcal{K}} \alpha_k \nabla f_k(\mathbf{x}) + \mathbf{A}^\top \boldsymbol{\pi} + \sum_{l=1}^L \sigma_l \nabla g(\mathbf{x}) = \mathbf{0}, \quad (23b)$$

$$\boldsymbol{\alpha}^\top \mathbf{f}(\hat{\mathbf{x}}) = 1, \quad (23c)$$

$$\boldsymbol{\alpha} \geq \mathbf{0}, \boldsymbol{\sigma} \geq \mathbf{0}. \quad (23d)$$

Because an optimal primal-dual pair exists, the primal constraints, as well as some of the complementary slackness constraints, can be added to the dual problem:

$$\epsilon^* = \max_{\boldsymbol{\alpha}, \boldsymbol{\pi}, \boldsymbol{\sigma}, \mathbf{x}, \epsilon} \mathcal{L}(\mathbf{x}, \epsilon, \boldsymbol{\alpha}, \boldsymbol{\pi}, \boldsymbol{\sigma}) \quad (24a)$$

$$\text{s.t.} \quad \sum_{k \in \mathcal{K}} \alpha_k \nabla f_k(\mathbf{x}) + \mathbf{A}^\top \boldsymbol{\pi} + \sum_{l=1}^L \sigma_l \nabla g(\mathbf{x}) = \mathbf{0}, \quad (24b)$$

$$\boldsymbol{\alpha}^\top \mathbf{f}(\hat{\mathbf{x}}) = 1, \quad (24c)$$

$$\boldsymbol{\sigma} \circ \mathbf{g}(\mathbf{x}) = \mathbf{0}, \quad (24d)$$

$$\boldsymbol{\alpha} \geq \mathbf{0}, \boldsymbol{\sigma} \geq \mathbf{0}, \quad (24e)$$

$$\mathbf{A}\mathbf{x} = \mathbf{b}, \quad (24f)$$

$$\mathbf{g}(\mathbf{x}) \leq \mathbf{0}. \quad (24g)$$

By the complementary slackness and stationarity conditions, any feasible solution  $(\bar{\alpha}, \bar{\pi}, \bar{\sigma}, \bar{\mathbf{x}}, \bar{\epsilon})$  to (24) satisfies  $\mathcal{L}(\bar{\alpha}, \bar{\pi}, \bar{\sigma}, \bar{\mathbf{x}}, \bar{\epsilon}) = \bar{\alpha}^\top (\mathbf{f}(\bar{\mathbf{x}}) - \boldsymbol{\lambda})$ . In addition, the primal, dual, and optimality constraints collectively imply

$$\epsilon^* = \max_{\boldsymbol{\alpha}, \mathbf{x}} \boldsymbol{\alpha}^\top (\mathbf{f}(\mathbf{x}) - \boldsymbol{\lambda}) \quad (25a)$$

$$\text{s.t. } \mathbf{x} \in \mathcal{O}(\boldsymbol{\alpha}), \quad (25b)$$

$$\boldsymbol{\alpha}^\top \mathbf{f}(\hat{\mathbf{x}}) = 1, \quad (25c)$$

$$\boldsymbol{\alpha} \geq \mathbf{0}. \quad (25d)$$

The resulting optimization problem, (25), is  $\text{RE}(\hat{\mathbf{x}})$ ; thus,  $z^{\text{RE}} = z^{\text{REGP}}$ . Moreover, if  $(\mathbf{x}^*, \epsilon^*, \boldsymbol{\alpha}^*, \boldsymbol{\pi}^*, \boldsymbol{\sigma}^*)$  is an optimal primal-dual pair for  $\text{REGP}(\hat{\mathbf{x}})$ , then  $(\mathbf{x}^*, \boldsymbol{\alpha}^*)$  is an optimal solution to  $\text{RE}(\hat{\mathbf{x}})$ .  $\square$