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Lexicographic Reference Point Method for Automatic Treatment Planning in Radiation Therapy

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"Lexicographic Reference Point Method for Automatic Treatment Planning in Radiation Therapy"

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Abstract

Treatment plan generation in radiation therapy is a multicriteria optimization problem, in which multiple, often conflicting, criteria need to be optimized simultaneously. Several methods can be used to obtain Pareto optimal treatment plans, meaning that no criterion can be improved without deteriorating another criterion. The focus is on the 2-phase ϵ-constraint (2pϵc) method and the reference point method (RPM), which both automatically generate Pareto optimal intensity modulated radiation therapy (IMRT) plans. Although the plans of the 2pϵc method are of high quality, several optimizations need to be performed. For the RPM, only a single optimization is needed per plan. The aim of this thesis is configure the RPM so that the resulting treatment plans are of the same quality as the treatment plans generated by the 2pϵc method, and thereby reducing the computation time.

The 2pϵc method prioritizes the criteria and assigns goal values to them. Then, each criterion is iteratively optimized and constrained according to a rule (depending on whether the goal value was met or not). The number of optimizations needed scales linearly with the number of criteria. A specific configuration of the RPM, namely the lexicographic reference point method (LRPM), maintains the lexicographic ordering of the criteria.

Both the 2pϵc method and the LRPM have been tested on 30 prostate cancer patients and 2 head-and-neck cancer patients. For the 30 prostate cancer patients, all treatment plans generated by the LRPM were found of similar quality when compared to the plans generated by the 2pϵc method. On average, the computation time of the LRPM was 3 minutes, which is a speed-up factor of nearly 12. For the 2 head-and-neck cancer patients, the plans of the LRPM were considered as good as or better than the plans of the 2pϵc method with a speed-up factor for the computation time of 3-4.

Preface

This Master thesis was written in order to finish the Master of Science programme in Applied Mathematics at the Delft University of Technology. The graduation project was carried out at the Erasmus MC - Cancer Institute in Rotterdam.

Before the graduation project started, I just finished my internship, also carried out at the Erasmus MC - Cancer Institute in Rotterdam. During my internship, I gained interest in applying my mathematical knowledge in the medical environment. Near the end of my internship, my supervisor at the Erasmus MC - Cancer Institute, Sebastiaan Breedveld, proposed a graduation project. Although I planned to do another project originally, I took the opportunity to do the graduation project and remain in the pleasant working environment.

First of all, I want to thank the colleagues at the Erasmus MC - Cancer Institute. In particular, I would like to thank my supervisor, Sebastiaan Breedveld, for giving me this opportunity. Sebastiaan, thank you for explaining how mathematics is applied in the field of radiation therapy. I also want to thank Sebastiaan for letting me thoroughly analyze the theoretical aspects of the multicriteria methods and providing me with all the test data. Our discussions about multicriteria optimization helped me a lot to tackle the practical issues I faced when applying mathematics.

Secondly, I want to thank the other thesis committee members, Arnold Heemink, Marleen Keijzer and Dion Gijswijt. Marleen, your suggestions and feedback led to an improvement of both the structure and readability of this thesis. I like to thank Dion for his useful suggestions and comments on the first part of this thesis.

Finally, I want to thank my family for their mental support during this project.

Rens van Haveren
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Contents

Notation

A brief overview of the mathematical notations used throughout this thesis.

Notation	Explanation
m	$m \in \mathbb{N}$ represents the number of decision variables
n	$n \in \mathbb{N}$ represents the number of criteria
$\mathbb{R}^m$	decision space
$\mathbb{R}^n$	criterion space
f	criterion vector function $f : \mathbb{R}^m \to \mathbb{R}^n$
$X \subseteq \mathbb{R}^m$	feasible set in decision space
$Y = f(X) \subseteq \mathbb{R}^n$	feasible set in criterion space
X_{wP}	the set of all weakly Pareto optimal points
X_P	the set of all Pareto optimal points
X_{pP}	the set of all properly Pareto optimal points
Y_{wN}	the set of all weakly nondominated points
Y_N	the set of all nondominated points
Y_{pN}	the set of all properly nondominated points
$[N]$	index set $\{1, 2, \ldots, N\}$
$x < y$	$x, y \in \mathbb{R}^N$ with $x_i < y_i$ for all $i \in [N]$
$x \leqslant y$	$x, y \in \mathbb{R}^N$ with $x_i \leqslant y_i$ for all $i \in [N]$
$x = y$	$x, y \in \mathbb{R}^N$ with $x_i = y_i$ for all $i \in [N]$
$\mathbb{R}^N_{>0}$	the positive orthant of R^N, $\{x \in \mathbb{R}^N \mid x > 0\}$
$\mathbb{R}^N_{\geqslant 0}$	the nonnegative orthant of R^N, $\{x \in \mathbb{R}^N \mid x \geqslant 0\}$
$B(x, \eta)$	open ball around x with radius $\eta > 0$
$\text{int } E$	interior of a set E
$\text{bd } E$	boundary of a set E
$\overline{E}$	closure of a set E

CHAPTER 1

Introduction

In this thesis we will dig into the world of *multicriteria optimization*: an optimization problem in which multiple criteria (real-valued functions) need to be optimized simultaneously. In everyday life we are faced with these problems. For simple problems, the human brain automatically considers the available options and comes up with a decision based on common sense, intuition, previous experiences, chance or a combination of these. As an example, buying a soda can be considered as a multicriteria optimization problem since multiple *criteria*, such as the price and brand, can be decisive for the final purchase. Often, these criteria conflict which, in this case, means that the soda with the lowest price does not correspond with the top brand and vice versa. In multicriteria optimization we search for the "best" compromise between the criteria, however the choice made is often different for various groups of people. In other words, there is no consensus on what the "best" compromise is.

The problem of choosing the soda that fits you best does not seem that important, however in other cases making such a choice can literally be a case of life and death. This thesis focuses on a real-life application of multicriteria optimization, namely in the field of radiation therapy. Radiation therapy is commonly applied as part of a cancer treatment with the aim to control or destroy malignant cells (the tumour) while sparing the surrounding healthy tissue as much as possible. There are a lot of possible treatment plans that have a high probability of controlling or destroying the malignant cells as desired, but the main difficulty is to select a treatment plan that minimizes damage to the surrounding healthy tissue in such a way that the quality of life after the treatment is optimal. Selecting a treatment plan is too complex for the human brain, hence we need mathematical modeling and programming to tackle these problems.

Currently, treatment plans are automatically generated at the Erasmus MC - Cancer Institute with an in-house developed approach, called the *2-phase ϵ-constraint method* (see Breedveld et al. (2007, 2009)). This method has proven to produce treatment plans of high clinical quality, but requires a lot of computation time. Another method, the *reference point method* needs significantly less computation time to produce a treatment plan. However, it is not known whether the *reference point method* can be configured so that it generates high quality treatment plans. The research question of this thesis is:

> *Can the reference point method be configured so that it generates treatment plans that are of similar clinical quality when compared to the treatment plans generated by the 2-phase ϵ-constraint method, and how much reduction in computation time can be realized?*

In order to understand why the *2-phase ϵ-constraint method* and the *reference point method* are of particular interest, we start with an analysis on multicriteria optimization and multicriteria methods. From this analysis, we are able to understand the principles of both methods which will help us to configure the *reference point method*.

The remainder of this introductory chapter is organized as follows: in Section 1.1 and Section 1.2 we get more familiar with the concept of a multicriteria optimization problem. Section 1.1 provides an example of a multicriteria optimization problem and Section 1.2 describes the problems faced in the field of radiation therapy. We conclude this chapter with the outline of the thesis (Section 1.3).

1.1 Multicriteria optimization

In this section, we informally introduce the concept of a multicriteria optimization problem. In these problems, multiple quantities have to be optimized simultaneously. More often than not, the optimum of one quantity does not correspond to the optimum of any of the other quantities. Compromises between the different quantities have to be made to obtain a solution, however the opinion on what a "good compromise" is may differ. A multicriteria optimization problem is best explained with an example.

EXAMPLE 1.1. Suppose that we want to buy a house. For many people, buying a house is the biggest financial transaction they make during, so making the right decision is important. Suppose that we have found 5 suitable houses and that the final decision will be made according to their prices and the travel time to work. We prefer a low-priced house with a short travel time to our work. The data of the 5 houses is gathered in Table 1.1 and is also visualized in Figure 1.1.

TABLE 1.1: Overview of the criteria and available houses in Example 1.1.

Criterion	House A	House B	House C	House D	House E
Price (10000 Euros)	13	13	17	19	16
Travel time to work (Minutes)	55	75	65	15	30

Ideally, there would be a house that is not only the cheapest of the alternatives but also has the least travel time to our work. Unfortunately, this is not the case as can be seen in Table 1.1 or Figure 1.1. House A and B are the cheapest but House D has the least travel time to work.

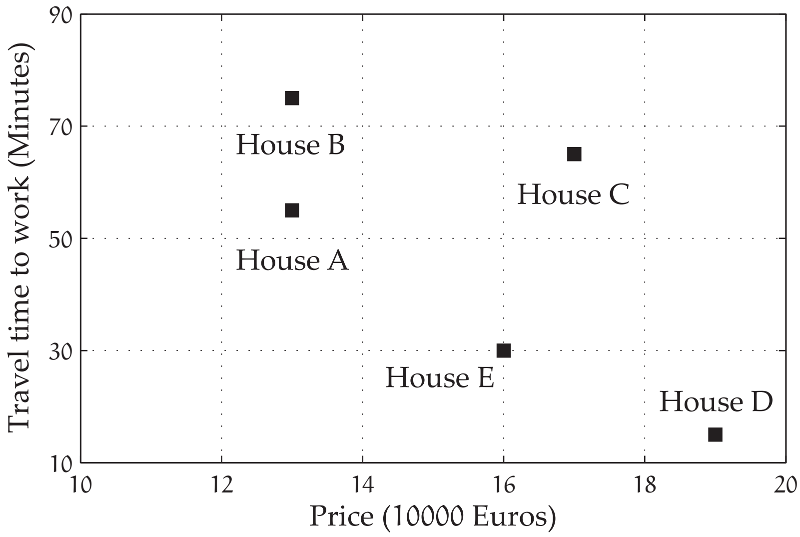

FIGURE 1.1: Visualization of the criterion values in Table 1.1 in a two-dimensional coordinate system.

There are several observations that should be made here. First, we note that any sensible human being should choose between Houses A, D or E. House B is not a good alternative since House A has less travel time to work for the same price. House C would even be a worse choice than House B since both House A and E are cheaper with less travel time to work. Secondly, we note that if we only had one criterion the choice would be easy. If we would only be interested in the cheapest house then we would buy either House A or B, and be indifferent about the actual choice between these 2 houses. If our only interest would be minimizing the travel time to work, House D would be the optimal choice.

Which of the choices between House A, D or E is best cannot be said. Some people would buy House A while others buy House D or E depending on their priorities. Is reducing the traveling time by 40 minutes worth an increase of 6000 euros in the price of a house? For some it will (making House D a better alternative than House A), for others it will not (making House A a better alternative than House D). House E is the best alternative for people who prefer compromising a bit on both the price and travel time.

In Example 1.1, we have 5 houses to choose from, namely House A-E. We gather all possibilities in the set X, in this case

$$X = \{\text{House A},\ \text{House B},\ \text{House C},\ \text{House D},\ \text{House E}\}.$$

Also, we have two quantities which influence the final decision. In this case, the quantities are:

1. The price of the house,

2. The travel time to work.

Notice that the quantities include a unit, the first quantity (price) is expressed in the unit 10000 Euros and the second quantity (travel time) is expressed in the unit minutes. So generally, it is possible that the quantities involved in a multicriteria optimization problem have different units. Additionally, it must be specified (per quantity) whether high values or low values are preferred. In Example 1.1, we prefer low prices and little travel time, so we want to minimize both quantities.

The data per quantity of the 5 available houses are gathered in the set Y. In this case (see Table 1.1),

$$Y = \{(13, 55),\ (13, 75),\ (17, 65),\ (19, 15),\ (16, 30)\},$$

where the first coordinate represents the price (in 10000 Euros) and the second coordinate represents the travel time to work (in minutes). Since we prefer lower values for both quantities, our preferences go to the pairs $(13, 55)$, $(19, 15)$ and $(16, 30)$ (see Figure 1.1) representing House A, D and E.

Mathematically, the Houses A,D and E can be seen as optimal choices. In Chapter 3, several mathematical definitions for optimal choices in a multicriteria optimization problem are formally introduced.

1.2 Radiation therapy

For more than half of all patients diagnosed with cancer, radiation therapy is selected as part of the treatment*. Radiation therapy may be used in combination with *surgery* and/or *chemotherapy*. Radiation therapy can also be used alone as cancer treatment.

Radiation therapy uses ionizing radiation to control or destroy malignant cells (the tumour). The ionizing radiation deposits energy to the cancer cells damaging their DNA (molecules inside the cells that carry genetic information). Cancer cells whose DNA are sufficiently damaged, are beyond repair and stop dividing. However, the surrounding healthy tissue is damaged as well in radiation therapy, which should be minimized as much as possible while still irradiating the tumour sufficiently. The amount of radiation that may safely be delivered to healthy tissue (the DNA is still damaged, but is repaired over time so that the tissue keeps functioning as it should) is known for different parts of the body. This information is taken into account to obtain a high quality treatment plan.

Radiation therapy can be divided into:

1. *external beam radiation therapy*,

2. *brachytherapy*,

*http://www.cancer.gov/cancertopics/factsheet/Therapy/radiation

3. *radioisotope therapy*.

The differences concern the position of the radiation source. In external beam radiation therapy the radiation is directed at the tumour from outside the body. In brachytherapy, the radiation sources are placed inside or close to the tumour. Radioisotope therapy delivers radioisotopes though infusion or oral ingestion. The focus of this thesis is on external beam radiation therapy with X-ray beams (photons), which is the most commonly used form of radiation therapy.

In external beam radiation therapy, the patient is irradiated from certain external directions forming beams. For every beam direction, a predetermined dose is delivered to the patient. The directions and the doses are configured in such a way that the radiation beams overlap the tumour volume, which receives a sufficient dose.

When external beam radiation therapy is selected as part of the treatment for a cancer patient, a treatment plan has to be developed by a *radiation oncologist*. This treatment plan needs to ensure that the tumour receives a sufficient dose while the dose delivered to surrounding tissue remains at acceptable levels. To achieve this, we need information about the geometrical shapes of the tumour and the surrounding healthy tissue (mostly organs). To obtain this spatial information, a CT-scan is made in which the tumour and surrounding organs are delineated. Mostly, there are around 10 to 20 organs (or other structures) surrounding the tumour. An example of a CT-slice can be seen in Figure 1.2, where a tumour is located in the prostate. Healthy tissues surrounded by the prostate include the rectum, anus, bladder and hips.

After a treatment plan is made and approved, the patient will undergo several radiation sessions which may last 2 to 10 weeks. In each radiation session, a fraction of the total dose is delivered. This is done to allow the healthy tissue to recover in between the sessions.

The mathematical details involved in radiation treatment planning are introduced in Chapter 5.

1.3 Outline of the thesis

This thesis consists of two parts. In the first part we discuss the fundamentals of multicriteria optimization. In the second part, the focus is on the application of multicriteria optimization in the field of radiation therapy.

Part I introduces the theoretical foundations of multicriteria optimization. We discuss existence and connectedness for several notions of optimality. Also, some of the many available methods used in multicriteria optimization are introduced.

Chapter 2 gives an overview of the preliminaries needed for the subsequent chapters. Some basic results concerning continuity, connectedness, compactness and convexity are gathered for Euclidean spaces. These notions do not only play an important role in the conventional single criteria optimization, but also in multicriteria optimization. The results presented in this chapter and many more can be found in Armstrong (1983), Boyd and Vandenberghe (2004), Hiriart-

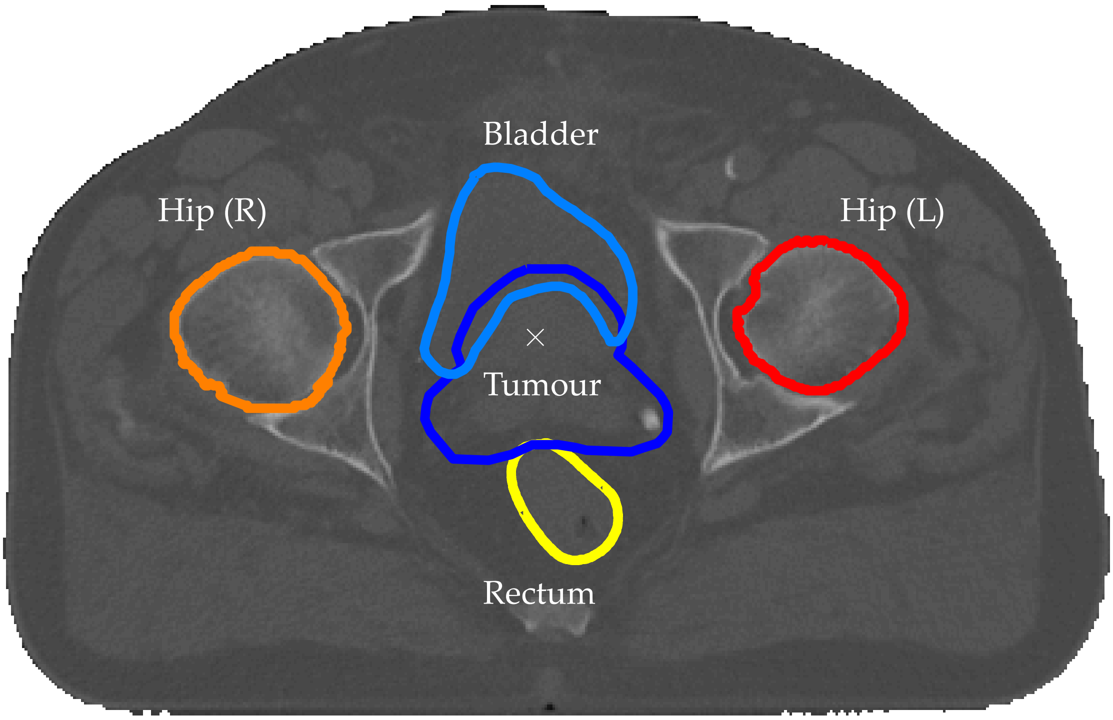

FIGURE 1.2: CT-slice of a prostate cancer patient. The prostate tumour is surrounded by several healthy organs including the rectum, bladder and hips.

Uruty and Lemaréchal (1993), Rockafellar (1970) and Rudin (1976). This chapter is finalized with a recap of Zorn's Lemma.

In Chapter 3 we present a general setting for multicriteria optimization problems. For these problems, several notions of optimality are defined. As we have seen in Example 1.1, a multicriteria optimization problem generally has multiple "optimal" solutions. Which one of these alternatives is preferred depends mostly on the decision maker (DM), as subjective motives are often decisive. The main focus of this chapter is on existence and connectedness results for the several notions of optimality. Books about these topics include Ehrgott (2005) and Sawaragi et al. (1985), of which the latter uses a more general setting of multicriteria optimization problems.

Chapter 4 presents several methods used to "solve" multicriteria optimization problems. There is a wide range of available methods, most can be found in Mietinnen (1999) as well as their theoretical properties. We will only discuss the *weighted sum method*, *ϵ-constraint method*, *2-phase ϵ-constraint method* and *reference point method*.

In Part II of this thesis, the focus is on applying the *reference point method* for automated treatment planning in radiation therapy. We consider the *2-phase ϵ-constraint method* as the golden standard. We will investigate whether the *reference point method* can be configured in such a way that it generates treatment plans that are of similar clinical quality as the treatment plans generated by the *2-phase ϵ-constraint method*.

In Chapter 5, the setting of the multicriteria optimization problems that we encounter in radiation therapy is described. These multicriteria optimization problems are known as *fluence map optimization*.

In Chapter 6 we attempt to configure the *reference point method* in such a way that it automatically generates high quality treatment plans.

In Chapter 7 we compare the treatment plans generated by the *2-phase ϵ-constraint method* and the *reference point method*. We will do so for different patient groups, namely for prostate cancer patients as well as for head-and-neck cancer patients.

Chapter 8 concludes the thesis. Here, we summarize Part I and discuss whether the *reference point method* has the potential to generate treatment plans of similar quality when compared to the *2-phase ϵ-constraint method*. Also, recommendations on further research are discussed.

Part I

Theory of multicriteria optimization

CHAPTER 2

Mathematical preliminaries

Before we are able to analyze *multicriteria optimization problems*, some mathematical background is needed. More specifically, the concepts of continuity, connectedness, compactness and convexity from real analysis are needed. These concepts are covered in more detail in Armstrong (1983), Boyd and Vandenberghe (2004), Hiriart-Uruty and Lemaréchal (1993), Rockafellar (1970) and Rudin (1976) and have a key role in regular single criteria optimization problems. Although the results we present in this chapter are available in more general settings, our focus is on finite dimensional Euclidean spaces since these are the only relevant spaces in the application of multicriteria optimization.

This chapter is concluded with Zorn's Lemma, which will help us in the next chapter to guarantee existence of "optimal" solutions for general multicriteria optimization problems. Zorn's Lemma is formulated as in Ehrgott (2005).

2.1 Real analysis

Throughout this section, let $M, N \in \mathbb{N}$ be fixed. We will define the notions of continuity, connectedness, compactness and convexity as well as some of their properties. Continuity, connectedness and compactness are defined for *Euclidean spaces*, that is, a pair $(\mathbb{R}^N, d_N)$ where $d_N : \mathbb{R}^N \times \mathbb{R}^N \to [0, \infty)$ is the *Euclidean metric*:

$$d_N(x, y) := \sqrt{\sum_{i \in [N]} (x_i - y_i)^2}. \tag{2.1.1}$$

Convexity is defined for subsets of $\mathbb{R}^N$ and for functions $f : E \to \mathbb{R}$ where $E \subseteq \mathbb{R}^N$. Also, we formulate regular single criteria convex optimization problems. These optimization problems have pleasant properties that we also want to exploit in multicriteria optimization.

2.1.1 Continuity

In this section, we state the definition of continuity for functions $f : E \to \mathbb{R}^N$, where $E \subseteq \mathbb{R}^M$, alongside some basic properties.

In order to define continuity, we define the *open ball* around $x \in E$ with radius $\eta > 0$:

$$B(x, \eta) := \{y \in E \mid d_M(x, y) < \eta\}. \tag{2.1.2}$$

We also need to define open and closed sets as well as the *closure* of a set. Recall that for a sequence $(x^k)_{k\in\mathbb{N}} \subseteq \mathbb{R}^n$, we denote $x^k \to x \in \mathbb{R}^n$ if for every $\eta > 0$ the open ball $B(x, \eta)$ contains infinitely many elements of $(x^k)_{k\in\mathbb{N}}$. If such a sequence exists for $x \in \mathbb{R}^N$, we say that x is a *limit point*.

Definition 2.1 (Open/closed set). *A set $F \subseteq \mathbb{R}^N$ is called*

- open *if for every $x \in F$ there is a $\eta > 0$ such that $B(x, \eta) \subseteq F$.*
- closed *if $\mathbb{R}^N \setminus F$ is open.*

For any set $F \subseteq \mathbb{R}^N$, its closure (denoted as $\overline{F}$) is given by:

$$\overline{F} := \{x \in \mathbb{R}^N \mid \textit{there is a } (x^k)_{k\in\mathbb{N}} \subseteq F \textit{ with } x^k \to x\}. \tag{2.1.3}$$

For any set $F \subseteq \mathbb{R}^N$ it holds that $F \subseteq \overline{F}$ and $F = \overline{F}$ if and only if F is closed. The latter is an alternative and often useful characterization of a closed set, namely a set is closed if and only if it contains all its limit points. Also, note the dependency on the metric in Definition 2.1.

With these concepts, we are able to define continuity.

Definition 2.2 (Continuity). *Let $E \subseteq \mathbb{R}^M$. A function $f : E \to \mathbb{R}^N$ is called continuous at $x \in E$ if for all $(x^k)_{k\in\mathbb{N}} \subseteq E$ with $x^k \to x$ it holds that $f(x^k) \to f(x)$.*

The function f is called continuous *if f is continuous at every $x \in E$.*

Note that this definition needs to be understood in the right context, in this case $x^k \to x$ means $d_M(x, x^k) \to 0$ and $f(x^k) \to f(x)$ means $d_N(f(x), f(x^k)) \to 0$.

Often, continuity is a convenient property. In our case, we need continuity as it preserves *connectedness* and *compactness* which is mentioned later in this chapter. Also, continuity and *convexity* are closely related.

There are more characterizations of continuity. Before mentioning some of these, it is convenient to introduce a notation for the *preimage* of a set under a function $f : E \to \mathbb{R}^N$. For $F \subseteq \mathbb{R}^N$ we denote the *preimage* of F under f as

$$f^{-1}(F) := \{x \in E \mid f(x) \in F\}. \tag{2.1.4}$$

Some useful characterizations of continuity are gathered in Proposition 2.1.

PROPOSITION 2.1. *The following statements are equivalent for a function* $f : E \to \mathbb{R}^N$.

1. f *is continuous,*
2. *for every open set* $O \subseteq \mathbb{R}^N$*, the preimage* $f^{-1}(O) \subseteq E$ *is open,*
3. *for every closed set* $G \subseteq \mathbb{R}^N$*, the preimage* $f^{-1}(G) \subseteq E$ *is closed.*

Proof. For a proof, see Rudin (1976). □

2.1.2 Connectedness

This section is devoted to (path) connected sets. This concept is needed for the next chapter where we want to prove that certain "solution sets" are connected. Therefore, we need some properties of (path) connected sets.

We start with defining (path) connectedness of a subset $E \subseteq \mathbb{R}^N$.

DEFINITION 2.3 (Path-connected)**.** *A set* $E \subseteq \mathbb{R}^N$ *is called* path connected *if for every* $x^1, x^2 \in E$ *there is a continuous mapping* $f : [0,1] \to E$ *with* $f(0) = x^1$ *and* $f(1) = x^2$.

DEFINITION 2.4 (Connected)**.** *A set* $E \subseteq \mathbb{R}^N$ *is* connected *if there are no two nonempty open sets* $O_1, O_2 \subseteq \mathbb{R}^N$ *such that*

$$E \subseteq O_1 \cup O_2, \qquad E \cap O_1 \neq \varnothing, \qquad E \cap O_2 \neq \varnothing, \qquad E \cap O_1 \cap O_2 = \varnothing.$$

The notion of (path) connectedness again depends on the metric, in this case the Euclidean metric (2.1.1). Path connected sets and connected sets are closely related, to see this we need the following lemma.

LEMMA 2.2. *Let* $E \subseteq \mathbb{R}$*, then* E *is connected if and only if it is an interval.*

Proof. See Armstrong (1983) for a proof. □

Note that for $\mathbb{R}^N$ with $N > 1$, a connected set does not need to be a multi-dimensional interval. Lemma 2.2 implies that the sets in Example 2.1 are connected.

EXAMPLE 2.1. The following sets are connected since they are intervals,

- the real line $\mathbb{R} = (-\infty, \infty)$,
- $\mathbb{R}_{>0} := (0, \infty)$,
- $\mathbb{R}_{\geqslant 0} := [0, \infty)$.

The next lemma states that path connectedness is a stronger condition than connectedness.

LEMMA 2.3. *If* $E \subseteq \mathbb{R}^N$ *is path connected then it is also connected.*

Proof. For a proof, see Armstrong (1983). $\square$

Next, we treat some basic results concerning connected sets.

LEMMA 2.4. *If* $E \subseteq \mathbb{R}^N$ *is connected and* $E \subseteq F \subseteq \overline{E}$*, then* F *is connected.*

Proof. See Armstrong (1983) for a proof. $\square$

Note that in particular, it holds that if $E \subseteq \mathbb{R}^N$ is connected then the closure $\overline{E}$ is also connected.

Another basic result concerning connected sets is that the Cartesian product of connected sets is connected.

LEMMA 2.5. *If* $E \subseteq \mathbb{R}^M$ *and* $F \subseteq \mathbb{R}^N$ *are connected then* $E \times F$ *is connected.*

Proof. A proof can be found in Armstrong (1983). $\square$

Note that this result extends to the case where we construct the Cartesian product of finitely many connected sets. With Lemma 2.5 we can extend Example 2.1.

EXAMPLE 2.2. Let $N \in \mathbb{N}$, then the following sets are connected:

- $\mathbb{R}^N$, since $\mathbb{R}^N = \mathbb{R} \times \mathbb{R} \times \ldots \times \mathbb{R}$,
- $\mathbb{R}^N_{>0}$, since $\mathbb{R}^N_{>0} := \mathbb{R}_{>0} \times \mathbb{R}_{>0} \times \ldots \times \mathbb{R}_{>0}$,
- $\mathbb{R}^N_{\geqslant 0}$, since $\mathbb{R}^N_{\geqslant 0} := \overline{\mathbb{R}^N_{>0}}$,
- $\mathbb{R}^N_{\geqslant 0} \setminus \{0\}$, since $\mathbb{R}^N_{>0} \subseteq \mathbb{R}^N_{\geqslant 0} \setminus \{0\} \subseteq \overline{\mathbb{R}^N_{>0}} (= \mathbb{R}^N_{\geqslant 0})$.

The particular sets in Example 2.2 play a key role in multicriteria optimization and their connectedness turns out to be of major importance in the next chapter.

Lemma 2.6 shows a useful property, namely that continuous images of a connected sets are again connected.

LEMMA 2.6. *Let* $M, N \in \mathbb{N}$ *and let* $E \subseteq \mathbb{R}^M$ *be connected. If the function* $f : E \to \mathbb{R}^N$ *is continuous then* $f(E)$ *is connected.*

Proof. Suppose $f(E)$ is not connected, then there are two nonempty open $O_1, O_2 \subseteq \mathbb{R}^N$ such that

$$f(E) \subseteq O_1 \cup O_2, \qquad f(E) \cap O_1 \neq \varnothing, \qquad f(E) \cap O_2 \neq \varnothing, \qquad f(E) \cap O_1 \cap O_2 = \varnothing.$$

Taking the preimage in the first condition we obtain

$$E \subseteq f^{-1}(f(E)) \subseteq f^{-1}(O_1 \cup O_2) = f^{-1}(O_1) \cup f^{-1}(O_2),$$

Since $f(E) \cap O_1 \neq \varnothing$ there is a $y \in f(E)$ and $y \in O_1$. Hence we can find a $x \in E$ with $f(x) = y$ so that $x \in E \cap f^{-1}(O_1)$, which is thus nonempty. Similarly $E \cap f^{-1}(O_2) \neq \varnothing$. Also,

$$E \cap f^{-1}(O_1) \cap f^{-1}(O_2) \subseteq f^{-1}(f(E)) \cap f^{-1}(O_1) \cap f^{-1}(O_2) = f^{-1}(f(E) \cap O_1 \cap O_2) = \varnothing.$$

Since f is continuous the sets $f^{-1}(O_1)$ and $f^{-1}(O_2)$ are open (Proposition 2.1), hence E is not connected. □

2.1.3 Compactness

In this section, some results concerning compactness in $(\mathbb{R}^N, d_N)$ are provided. Compactness turns out to be of great importance in multicriteria optimization, in particular in combination with continuity.

We start by defining an open cover,

DEFINITION 2.5 (Open cover). *A collection* $\{O_i\}_{i\in I}$ *of open subsets of* $\mathbb{R}^N$ *is called an* open cover *of a set* $E \subseteq \mathbb{R}^N$ *if*

$$E \subseteq \bigcup_{i\in I} O_i.$$

Here, I *is some index set.*

Now, we are able to define compactness,

DEFINITION 2.6 (Compactness). *A subset* $E \subseteq \mathbb{R}^N$ *is called* compact *if every open cover of* E *contains a finite subcover. More explicitly, for every open cover* $\{O_i\}_{i\in I}$ *of* E*, there is a finite subset* $J \subseteq I$ *such that*

$$E \subseteq \bigcup_{j\in J} O_j.$$

Note that every finite set is compact which follows directly from the finiteness of the set. One of the basic results concerning compact sets is that closed subsets of a compact set are compact.

LEMMA 2.7. *Suppose* E *is closed,* F *is compact and* $E \subseteq F \subseteq \mathbb{R}^N$*. Then* E *is compact.*

Proof. See Rudin (1976) for a proof. □

Similar to connectedness, a continuous function maps compact sets to compact sets.

LEMMA 2.8. *Let* $M, N \in \mathbb{N}$ *and* $E \subseteq \mathbb{R}^M$ *be compact. If* $f : E \to \mathbb{R}^N$ *is a continuous function then* $f(E)$ *is compact.*

Proof. Let $\{O_i\}_{i\in I}$ be an open cover of $f(E)$, that is

$$f(E) \subseteq \bigcup_{i\in I} O_i.$$

Since the preimages $f^{-1}(O_i)$ are open for all $i \in I$ (Proposition 2.1) it holds that

$$E \subseteq f^{-1}(f(E)) \subseteq f^{-1}\left(\bigcup_{i\in I} O_i\right) = \bigcup_{i\in I} f^{-1}(O_i),$$

so $\{f^{-1}(O_i)\}_{i\in I}$ is an open cover of E. The compactness of E implies that there is a finite subset $J \subseteq I$ such that

$$E \subseteq \bigcup_{j\in J} f^{-1}(O_j),$$

hence

$$f(E) \subseteq f\left(\bigcup_{j\in J} f^{-1}(O_j)\right) = \bigcup_{j\in J} f\left(f^{-1}(O_j)\right) \subseteq \bigcup_{j\in J} O_j.$$

We may conclude that $f(E)$ is compact. □

While the above results hold for general metric spaces, the next famous result is restricted to Euclidean spaces. This theorem, known as the *Heine-Borel Theorem*, characterizes compact sets in Euclidean spaces.

THEOREM 2.9 (Heine-Borel). *A set $E \subseteq \mathbb{R}^N$ is compact if and only if E is closed and bounded.*

Proof. A proof of this theorem can for instance be found in Rudin (1976). □

Recall that a set $E \subseteq \mathbb{R}^N$ is *bounded* if there is a $x \in \mathbb{R}^N$ and $r \in \mathbb{R}_{>0}$ such that for all $y \in E$ we have $d_N(x, y) < r$. As a consequence of Heine-Borel we have the following convenient result which states that a continuous function on a compact set attains its minimum and maximum.

THEOREM 2.10. *If $E \subseteq \mathbb{R}^M$ is a nonempty compact set and $f : E \to \mathbb{R}$ is continuous then f attains its minimum and maximum on E.*

Proof. See Rudin (1976). Note that this follows directly from the Heine-Borel Theorem, as $f(E)$ is compact (Lemma 2.8) it is closed and bounded. □

2.1.4 Convexity

Convexity is important in the field of optimization. Also in analysis the notion of convexity is useful, in particular its relation with connectedness and continuity.

Let us start by defining convexity for subsets of $\mathbb{R}^N$.

DEFINITION 2.7 (Convex set). *A set $E \subseteq \mathbb{R}^N$ is called* convex *if for all $x^1, x^2 \in E$ and $\alpha \in [0, 1]$ it holds that*

$$\alpha x^1 + (1 - \alpha)x^2 \in E.$$

As an immediate consequence, note that convex sets are always (path) connected.

COROLLARY 2.11. *If* $E \subseteq \mathbb{R}^N$ *is convex then it is (path) connected.*

Proof. For every $x^1, x^2 \in E$ we define $f : [0,1] \to E$ by $f(\alpha) = \alpha x^1 + (1-\alpha)x^2$ which is well defined due to the convexity of E. The map f is continuous and satisfies $f(0) = x^1$ and $f(1) = x^2$. Therefore, E is path connected hence also connected (Lemma 2.3). □

In words, a set is convex if the line segment between any two points remains in the set itself. Actually in $\mathbb{R}$, a set E is convex if and only if it is (path) connected if and only if it is an interval. Another basic results concerning convex sets is that the intersection of arbitrary many convex sets is again convex.

PROPOSITION 2.12. *For any family of convex sets* $\{E_i\}_{i \in I}$ *the set*

$$\bigcap_{i \in I} E_i$$

is convex.

Proof. Clear from the definition, see also Rockafellar (1970). □

The notion of convexity is not only defined for sets but also for functions. Convex sets and convex functions are closely related, see Rockafellar (1970).

DEFINITION 2.8 ((Strictly) convex function)**.** *Let* $E \subseteq \mathbb{R}^N$ *be convex and let* $f : E \to \mathbb{R}$ *be a function. Then* f *is called*

- convex *if for all* $x^1, x^2 \in E$ *and* $\alpha \in [0,1]$ *it holds that*

$$f(\alpha x^1 + (1-\alpha)x^2) \leqslant \alpha f(x^1) + (1-\alpha)f(x^2).$$

- strictly convex *if for all* $x^1, x^2 \in E$ *with* $x^1 \neq x^2$ *and* $\alpha \in (0,1)$ *it holds that*

$$f(\alpha x^1 + (1-\alpha)x^2) < \alpha f(x^1) + (1-\alpha)f(x^2).$$

Note that the convexity of the set E guarantees that for every $x^1, x^2 \in E$ and $\alpha \in [0,1]$ we have $\alpha x^1 + (1-\alpha)x^2 \in E$, so that applying the function f to this element is a well defined operation. Also note that every strictly convex function is convex.

Examples of convex functions that we will encounter are linear combinations of convex functions and the maximum of a convex function.

LEMMA 2.13. *Suppose* $E \subseteq \mathbb{R}^N$ *is convex and* $f_i : E \to \mathbb{R}$ *is (strictly) convex for* $i \in [N]$*. for any* $\lambda \in \mathbb{R}^N_{\geqslant 0} \setminus \{0\}$ *it holds that*

1. *the function* $\sum_{i \in [N]} \lambda_i f_i(x)$ *is (strictly) convex,*

2. *the function* $\max_{i\in[N]}\{\lambda_i f_i(x)\}$ *is convex.*

Proof. See Boyd and Vandenberghe (2004) for a proof. □

On an open domain, convexity turns out to be a stronger condition than continuity which is often a useful property.

THEOREM 2.14. *Let* $E \subseteq \mathbb{R}^N$ *be open and let* $f : E \to \mathbb{R}$ *be convex, then* f *is continuous.*

Proof. A proof of this fundamental result can be found in Rockafellar (1970). □

Note that this theorem is false for a closed domain since f may be discontinuous at the boundary points while maintaining convexity.

Another pleasant property of convex functions is that any *local minimum* is a *global minimum*. . Recall that if $E \subseteq \mathbb{R}^N$ is the domain of a function $f : E \to \mathbb{R}$, then a point $\hat{x} \in E$ is called

- a *local minimum* if there exists a $\eta > 0$ such that $f(\hat{x}) \leqslant f(x)$ for all $x \in E \cap B(\hat{x}, \eta)$,
- a *global minimum* if $f(\hat{x}) \leqslant f(x)$ for all $x \in E$.

LEMMA 2.15. *Let* $E \subseteq \mathbb{R}^N$ *be a closed and convex set and let* $f : E \to \mathbb{R}$ *be convex. Then*

1. *any local minimum of* f *is a global minimum,*
2. *the solution set* $\{\hat{x} \in E \mid f(\hat{x}) = \inf_{x\in E} f(x)\}$ *is closed and convex.*

Proof. A proof can be found in Hiriart-Uruty and Lemaréchal (1993). □

This property is exploited in single criteria minimization problems. When looking for the minimum of a convex function, it suffices to find a local minimum.

For strictly convex functions the solution set has the following useful property.

LEMMA 2.16. *Let* $E \subseteq \mathbb{R}^n$ *be convex and let* $f : E \to \mathbb{R}$ *be a strictly convex function, then the solution set* $\{\hat{x} \in E \mid f(\hat{x}) = \inf_{x\in E} f(x)\}$ *consists of at most one point.*

Proof. See Rockafellar (1970) or Boyd and Vandenberghe (2004) for a proof. □

This property is often used to guarantee uniqueness of a solution. We will also resort to this lemma in the next chapter.

Convex optimization

A lot of theory is known for the single criteria optimization problems, see Hiriart-Uruty and Lemaréchal (1993), Rockafellar (1970) and Boyd and Vandenberghe (2004). An important subclass is *nonlinear convex optimization*, which focuses on optimization problems of the form

$$\begin{aligned} &\min_{x\in X} && f_0(x) \\ &\text{subject to} && g_j(x) \leqslant 0 \quad j \in [q], \end{aligned} \tag{2.1.5}$$

where $q \in \mathbb{N}, X \subseteq \mathbb{R}^M$ and for which the nonlinear *objective function* $f_0 : \mathbb{R}^m \to \mathbb{R}$ is convex and the nonlinear convex functions $g_j : \mathbb{R}^m \to \mathbb{R}$ are convex for all $j \in [q]$. Some of the advantages of convex optimization problems (2.1.5) are mentioned in Lemma 2.15 and Lemma 2.16. As a consequence, algorithms searching for a local minimum can be used to find the actual global minimum.

In this thesis, the method used for solving the nonlinear convex optimization problems is based on the *primal-dual interior-point method*, see Breedveld (2013, chap. 11.8) and Wright (1997). We will not discuss this method into further detail.

2.2 Zorn's Lemma

In this section, Zorn's Lemma is formulated according to Ehrgott (2005). We first define some binary relations and the concept of a partially ordered set.

Let E be a set. A *binary relation on* E is a collection of ordered pairs of elements of E. We denote a *binary relation on* E as $\preceq \subseteq E \times E$. The binary relations needed for Zorn's Lemma are mentioned in Definition 2.9. We use the notation $x^1 \preceq x^2$ for $x^1, x^2 \in E$ if $(x^1, x^2) \in \preceq$.

DEFINITION 2.9 (Reflexivity, antisymmetry, transitivity and totality)**.** *A relation* $\preceq$ *on a set* E *is called*

- reflexive *if* $x^1 \preceq x^1$ *for all* $x^1 \in E$,
- antisymmetric *if* $x^1 \preceq x^2$ *and* $x^2 \preceq x^1$ *imply* $x^1 = x^2$ *for all* $x^1, x^2 \in E$,
- transitive *if* $x^1 \preceq x^2$ *and* $x^2 \preceq x^3$ *imply* $x^1 \preceq x^3$ *for all* $x^1, x^2, x^3 \in E$,
- total *if* $x^1 \preceq x^2$ *or* $x^2 \preceq x^1$ *for all* $x^1, x^2 \in E$.

With these relations we are able to define *partially ordered sets* and *totally ordered sets*.

DEFINITION 2.10 (Partially/totally ordered set)**.** *Let* $\preceq$ *be a binary relation on a set* E*. The pair* $(E, \preceq)$ *is called*

- *a* partially ordered set *if* $\preceq$ *is reflexive, antisymmetric and transitive.*
- *a* totally ordered set *if* $\preceq$ *is antisymmetric, transitive and total,*

A partially ordered set $(E, \preceq)$ *is called* inductively ordered *if every totally ordered subset of* $(E, \preceq)$ *(also called a chain in* E*) has a lower bound.*

If $A \subseteq E$, then a *lower bound* l *of* A of a totally ordered set $(E, \preceq)$ satisfies $l \in A$ and $l \preceq x$ for all $x \in A$. An example of partially ordered sets are given in Example 2.3.

EXAMPLE 2.3. For every $N \in \mathbb{N}$, the pair $(\mathbb{R}^N_{\geqslant 0}, \leqslant)$ is partially ordered. Here the relation $\leqslant$ is given by

$$x \leqslant x' \quad \text{if and only if} \quad x_i \leqslant x'_i, \text{ for all } i \in [N],$$

where $x = (x_1, \dots, x_N), x' = (x'_1, \dots, x'_N) \in \mathbb{R}^N_{\geqslant 0}$.

Zorn's Lemma can now be formulated.

THEOREM 2.17 (Zorn's Lemma)**.** *If a partially ordered set $(E, \preceq)$ is inductively ordered, then E contains a minimal element with respect to $\preceq$, that is, there is a $\hat{x} \in E$ such that $x \preceq \hat{x}$ implies $\hat{x} \preceq x$ for all $x \in E$.*

Often, Zorn's Lemma is formulated differently as is the definition of inductively ordered. Usually, in Definition 2.10 the word *lower* is replaced by *upper* and in Zorn's Lemma the word *minimal* is replaced with *maximal*. However, for every relation $\preceq$ we can define a relation $\preceq^*$ by

$$x^2 \preceq^* x^1 \quad \text{if and only if} \quad x^1 \preceq x^2,$$

where $x^1, x^2 \in E$. Zorn's Lemma is formulated as in Theorem 2.17 since this is the context in which Zorn's Lemma will be applied.

Example 2.3 states that the pairs $(\mathbb{R}^N_{\geqslant 0}, \leqslant)$ are partially ordered for every $N \in \mathbb{N}$. This observation will be important in the next chapter.

CHAPTER 3

Multicriteria analysis

Some fundamental concepts and properties of multicriteria analysis will be covered in this chapter. We first introduce a mathematical description of a *multicriteria optimization problem*. Where in a regular single criteria optimization problem only one objective function needs to be optimized, multiple objective functions (or criteria) need to be optimized simultaneously in a multicriteria optimization problem. These functions are often conflicting, which means that an improvement of one of the objectives leads to a deterioration of another.

Because of the often conflicting nature of the objective functions, there is no such concept as an "optimal" solution in contrast to solutions of single criteria optimization problems. Instead, compromises (or *trade-offs*) have to be made between the objective functions, so there are no unique "optimal" solutions to (non-trivial) multicriteria optimization problems. In this chapter, we will introduce several notions of optimality and show how they are related to each other.

After this basic framework of multicriteria optimization has been set, we will obtain analytical results concerning these notions of optimality. More specifically, we investigate the existence and connectedness of the optimality notions.

Before continuing, we note that the notation and terminology used in the literature varies quite a bit. To mention some, Chankong and Haimes (1983), Ehrgott (2005), Mietinnen (1999) and Sawaragi et al. (1985) each use different notations and terminology. To avoid confusion, it is important to clarify the notation and terminology used in this thesis. The notation is covered in the Notation section of this thesis (of which we repeat the most important ones), the terminology is discussed in this chapter and is according to Ehrgott (2005). The results derived in this chapter can be found in Ehrgott (2005) and Sawaragi et al. (1985), of which the latter presents the results in a more general context.

3.1 Multicriteria optimization framework

This section introduces the basic framework of multicriteria optimization. First, we introduce the general form of a multicriteria optimization problem along with the terminology involved.

Then, we define notions of optimality which are most common in practice. Examples will be given to get more familiar with the optimality notions. We will see that we may have a rather large set of points which are all considered "optimal". On the other hand, it may be that a multicriteria optimization problem does not contain any "optimal" point.

3.1.1 Formulation multicriteria optimization problem

The functions in a multicriteria optimization problem that need to be optimized are referred to as *criteria* (often called *objectives* as well in the literature). A *decision vector* is a real vector in which each entry represents a decision variable. We reserve $m \in \mathbb{N}$ and $1 < n \in \mathbb{N}$ as the *number of decision variables* and the *number of criteria* respectively. Furthermore, the corresponding Euclidean spaces $\mathbb{R}^m$ and $\mathbb{R}^n$ are called the *decision space* and the *criterion space* respectively.

An index set that will be used extensively in this thesis is $\{1, 2, \dots, N\}$ for some $N \in \mathbb{N}$, therefore we introduce the following notation

$$[N] := \{1, 2, \dots, N\}.$$

The n criteria are denoted as $f_i : \mathbb{R}^m \to \mathbb{R}$ for $i \in [n]$. These criteria are combined in the *criterion vector* function $f : \mathbb{R}^m \to \mathbb{R}^n$ given by $f(x) = (f_1(x), \dots, f_n(x))$, a function from the decision space to the criterion space. An important, and often strict subset of the decision space, is the *feasible set* which is the set of all possible points which satisfy the constraints of the multicriteria optimization problem. The feasible set thus consists of all candidate solutions to the optimization problem and is denoted by $X \subseteq \mathbb{R}^m$. The corresponding set $Y = f(X) \subseteq \mathbb{R}^n$ then represents the feasible set in the criterion space:

$$\begin{aligned} X &:= \{x \in \mathbb{R}^m \mid x \text{ is a feasible decision vector}\}, \\ Y &:= \{f(x) \in \mathbb{R}^n \mid x \in X\}. \end{aligned} \tag{3.1.1}$$

We refer to both $X \subseteq \mathbb{R}^m$ and $Y \subseteq \mathbb{R}^n$ as feasible sets, since it is clear that X corresponds to the feasible set in the decision space and Y to the feasible set in the criterion space.

Now we can define a multicriteria optimization problem. Assume that all the criteria need to be minimized simultaneously (this assumption can be made without loss of generality since maximization can be achieved by negating the associated criteria). For a criterion vector function $f : \mathbb{R}^m \to \mathbb{R}^n$ and a feasible set $X \subseteq \mathbb{R}^m$, the corresponding multicriteria minimization problem is denoted as:

$$\min_{x \in X} f(x). \tag{3.1.2}$$

It is unclear how to interpret the minimum in (3.1.2) since the minimum is taken over a subset of $\mathbb{R}^n$, where $n > 1$. The problem is that for certain outcomes we cannot determine which one is preferred (which is no issue in one dimension). For example, if $n = 2$, and the two outcomes $(1,2)$ and $(2,1)$ are feasible then it is unclear which is better. As in Example 1.1, subjectivity determines which outcome is preferred.

A multicriteria optimization problem (3.1.2) can thus have more than one solution. However, there are also outcomes for which we can decide which one is preferred (for example, if $n = 2$, then $(1,1)$ is preferred over $(2,2)$). This enables us to mathematically define optimality for multicriteria optimization problems of the form (3.1.2). In the next part we will discuss the most common notions of optimality. Examples will be given to clarify how the notions are related.

3.1.2 Notions of optimality

As mentioned before, an "optimal" point is often not unique. The optimality notions serve to reduce the feasible set (all candidate solutions) to a set of "optimal" points. For this set of points, we are unable to objectively decide which one is best.

Before defining the notions of optimality, it is convenient to define generalized (in)equalities for vectors. For two vectors $x = (x_1, x_2, \ldots, x_n), y = (y_1, y_2, \ldots, y_n) \in \mathbb{R}^n$ we denote,

- $x < y$ if and only if $x_i < y_i$ for all $i \in [n]$,
- $x \leqslant y$ if and only if $x_i \leqslant y_i$ for all $i \in [n]$,
- $x = y$ if and only $x_i = y_i$ for all $i \in [n]$.

In two dimensions, the inequalities are depicted in Figure 3.1.

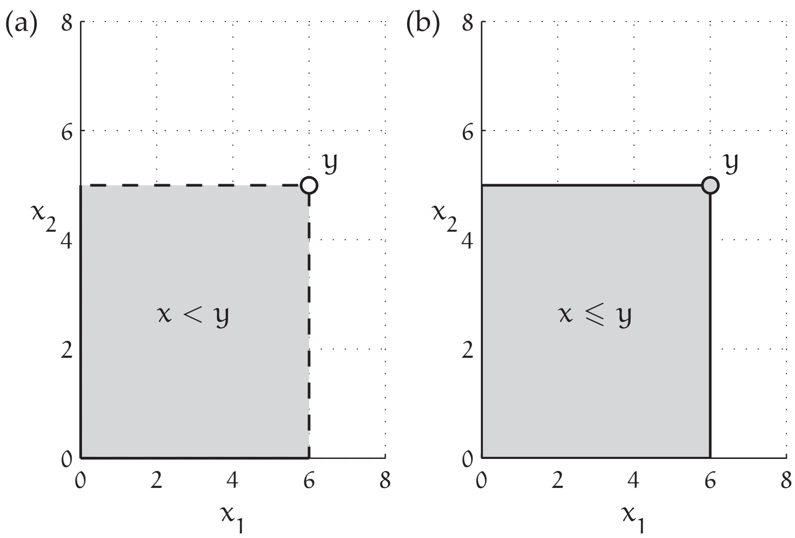

FIGURE 3.1: Vector inequalities in $\mathbb{R}^2$. In (a) the set of all $x \in \mathbb{R}^2$ with $x < y$ is shown and in (b) the set of all $x \in \mathbb{R}^2$ with $x \leqslant y$ is shown.

Now, we can define the optimality notion which is most relevant in practice, namely the notion of *Pareto optimal* and *nondominated* points.

DEFINITION 3.1 (Pareto optimal/nondominated point). *A feasible point* $\hat{x} \in X$ *is called* Pareto optimal *if there is no* $x \in X$ *such that* $f(x) \leqslant f(\hat{x})$ *and* $f_j(x) < f_j(\hat{x})$ *for at least one* $j \in [n]$*. The set of all Pareto optimal points is denoted as* X_P*:*

$$X_P := \{\hat{x} \in X \mid \hat{x} \text{ is Pareto optimal}\}.$$

A feasible point $\hat{y} \in Y$ *is called* nondominated *if there is a* $\hat{x} \in X_P$ *such that* $\hat{y} = f(\hat{x})$*. The set of all nondominated points is denoted as* Y_N*:*

$$Y_N := f(X_P) = \{f(\hat{x}) \in Y \mid \hat{x} \in X_P\}.$$

Nondominated points thus have the property that an improvement in one of the criteria must lead to a deterioration in at least one of the other criteria. If, for example, all the outcomes of a multicriteria optimization problem (3.1.2) are given by

$$\begin{aligned} f(x^1) &= (2,2), \\ f(x^2) &= (1,2), \\ f(x^3) &= (2,1), \end{aligned}$$

then x^1 is not Pareto optimal and $f(x^1)$ is a *dominated point* (that is, $f(x^1) \in Y \setminus Y_N$) since $(1,2) \leqslant (2,2)$ and $1 < 2$. Here, points x^2 and x^3 are Pareto optimal and $f(x^1)$ and $f(x^2)$ are nondominated*.

Next, we define *weakly Pareto optimal* and *weakly nondominated* points which are closely related to the notions in Definition 3.1 (as one may have suspected).

DEFINITION 3.2 (Weakly Pareto optimal/weakly nondominated point). *A feasible point* $\hat{x} \in X$ *is called* weakly Pareto optimal *if there is no* $x \in X$ *such that* $f(x) < f(\hat{x})$*. The set of all weakly Pareto optimal points is denoted as* X_{wP}*:*

$$X_{wP} := \{\hat{x} \in X \mid \hat{x} \text{ is weakly Pareto optimal}\}.$$

A feasible point $\hat{y} \in Y$ *is called* weakly nondominated *if there is a* $\hat{x} \in X_{wP}$ *such that* $\hat{y} = f(\hat{x})$*. The set of all weakly nondominated points is denoted as* Y_{wN}*:*

$$Y_{wN} := f(X_{wP}) = \{f(\hat{x}) \in Y \mid \hat{x} \in X_{wP}\}.$$

In words, a weakly nondominated point is characterized by the property that not every

*In the literature, for example in Chankong and Haimes (1983), Ehrgott (2005), Mietinnen (1999) and Sawaragi et al. (1985), the same term for optimal point in both the decision and criterion space is used. We decided to use the terminology in Ehrgott (2005), which distinguished optimal points in the decision and criterion space avoiding confusion between two different types of points.

criteria can be improved. For example, suppose all the outcomes are

$$f(z^1) = (2,2,2),$$
$$f(z^2) = (1,2,2),$$
$$f(z^3) = (1,1,1),$$

then z^1 is not weakly Pareto optimal and $f(z^1)$ is not weakly nondominated since $(1,1,1) < (2,2,2)$. While both z^2 and z^3 are weakly Pareto optimal and $f(z^2)$ and $f(z^3)$ are both weakly nondominated, the only Pareto optimal point is z^3 and $f(z^3)$ is the only nondominated point since $(1,1,1) \leqslant (1,2,2)$ and $1 < 2$.

The last notion of optimality we introduce is called *proper Pareto optimality*. This notion takes the *trade-offs* between the criteria into account. A trade-off is a measure for the ratio of change in criteria values for two different decision vectors.

DEFINITION 3.3 (Trade-off)**.** *Let $i, j \in [n]$ with $i \neq j$ and $x^1, x^2 \in X$ such that $f_j(x^1) \neq f_j(x^2)$, then the* trade-off *between f_i and f_j is given by*

$$\Lambda_{i,j}(x^1, x^2) := \frac{f_i(x^1) - f_i(x^2)}{f_j(x^2) - f_j(x^1)}.$$

Note that $\Lambda_{i,j}(x^1, x^2) = \Lambda_{i,j}(x^2, x^1)$ and $\Lambda_{i,j}(x^1, x^2)\Lambda_{j,i}(x^1, x^2) = 1$ for $x^1, x^2 \in X$ (in case the trade-offs are well defined). If, in addition, $x^1, x^2 \in X_P$ and $f(x^1) \neq f(x^2)$ then there is a pair $i, j \in [n]$ $(i \neq j)$ for which $\Lambda_{i,j}(x^1, x^2) > 0$. With the trade-offs, a *decision maker* (DM) can compare the ratios of change between the criteria for two feasible decision vectors.

Now, we can define proper Pareto optimality. In words, the properly Pareto optimal set consists of those Pareto optimal decision vectors for which the trade-offs are bounded.

DEFINITION 3.4 (Properly Pareto optimal, properly nondominated)**.** *A feasible point $\hat{x} \in X$ is called* properly Pareto optimal *if it is Pareto optimal ($\hat{x} \in X_P$) and there exists an $M \in \mathbb{R}_{>0}$ such that for all $i \in [n]$ and $x \in X$ with $f_i(x) < f_i(\hat{x})$ there is at least one $j \in [n]$ with $f_j(\hat{x}) < f_j(x)$ and*

$$\Lambda_{i,j}(\hat{x}, x) = \frac{f_i(\hat{x}) - f_i(x)}{f_j(x) - f_j(\hat{x})} \leqslant M.$$

The set of all properly Pareto optimal points is denoted as X_{pP}:

$$X_{pP} := \{\hat{x} \in X \mid \hat{x} \textit{ is properly Pareto optimal}\}.$$

A feasible point $\hat{y} \in Y$ is called properly nondominated *if there is an $\hat{x} \in X_{pP}$ such that $\hat{y} = f(\hat{x})$. The set of all properly nondominated points is denoted as Y_{pN}:*

$$Y_{pN} := f(X_{pP}) = \{f(\hat{x}) \in Y \mid \hat{x} \in X_{pP}\}.$$

Now that the notions of optimality are introduced, remark how they are related. First, note that if a feasible point in the criterion space cannot be improved in any coordinate without deteriorating in *at least one* of the others it certainly cannot be improved in *all* coordinates. So, from Definition 3.1 and Definition 3.2 we may conclude that all Pareto optimal (nondominated) points are also weakly Pareto optimal (weakly nondominated). Secondly, note that a properly Pareto optimal point (Definition 3.4) is necessarily Pareto optimal. The same holds for a properly nondominated point. Summarized, the following inclusions hold:

$$\begin{aligned} X_{pP} &\subseteq X_P \subseteq X_{wP}, \\ Y_{pN} &\subseteq Y_N \subseteq Y_{wN}. \end{aligned} \tag{3.1.3}$$

Next, we provide some examples to get more familiar with these notions of optimality.

First, we show that the inclusions (3.1.3) can be strict for Pareto optimal and weakly Pareto optimal points. In fact, it may occur that X_P and Y_N are empty (no Pareto optimal and nondominated points) while X_{wP} and Y_{wN} are rather large (a lot of weakly Pareto optimal and weakly nondominated points). Such a situation is sketched in Example 3.1.

EXAMPLE 3.1. Suppose that the feasible set is $X = \mathbb{R} \setminus \{0\}$. Consider the criteria $f_1, f_2 : \mathbb{R} \to \mathbb{R}$ given by:

$$\begin{aligned} f_1(x) &= \max(1, x+1), \\ f_2(x) &= \max(2, 2-x). \end{aligned} \tag{3.1.4}$$

The criteria are plotted in Figure 3.2.

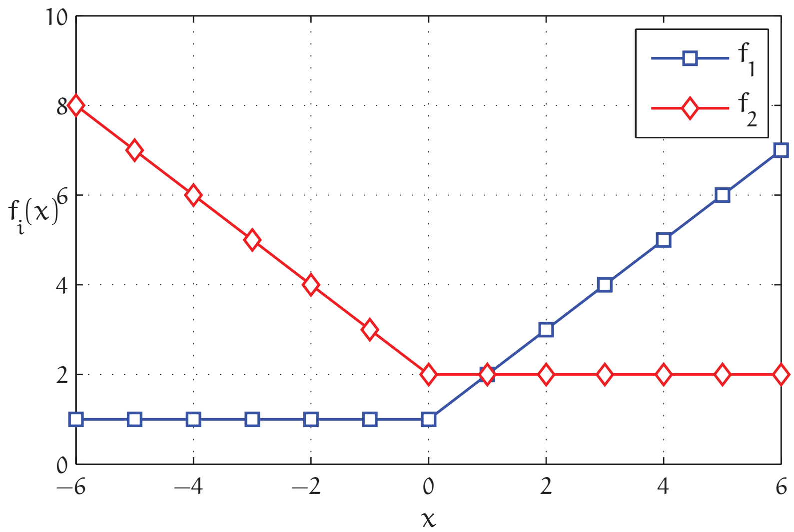

FIGURE 3.2: The two criteria (3.1.4). The feasible set is $X = \mathbb{R} \setminus \{0\}$ and the decision space is $\mathbb{R}$.

First, we identify the feasible set in the criterion space. When $x < 0$ we have $f_1(x) = 1$ and

$f_2(x) = 2 - x$, while for $x > 0$ we have $f_1(x) = x + 1$ and $f_2(x) = 2$. When we substitute y_1 for $f_1(x)$ and y_2 for $f_2(x)$, observe that the feasible set Y in the criterion space $\mathbb{R}^2$ is given by

$$Y = \{(1, y_2) \in \mathbb{R}^2 \mid y_2 > 2\} \cup \{(y_1, 2) \in \mathbb{R}^2 \mid y_1 > 1\}.$$

The feasible set $Y \subseteq \mathbb{R}^2$ in the criterion space is depicted in Figure 3.3. Next, we identify the

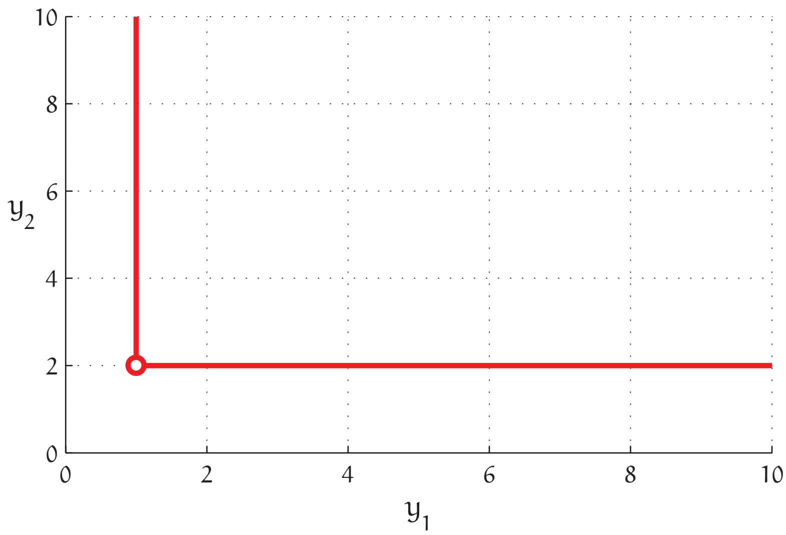

FIGURE 3.3: The feasible set $Y = f(X)$ in the criterion space, where the criteria are given by (3.1.4). Note that $(y_1, y_2) = (1, 2)$ is not feasible since $x = 0$ is not a feasible decision variable.

weakly Pareto optimal, Pareto optimal and proper Pareto optimal set.

Observe from Figure 3.3 that if a feasible point can be improved in y_1 it cannot be improved in y_2 and vice versa. For example, every point $(1, y_2) \in Y$ (where $y_2 > 2$) can be improved (in $f_2(x)$) by the feasible point $\left(1, 2 + \frac{y_2}{2}\right)$. This means that every feasible point is weakly Pareto optimal (weakly nondominated), so

$$X_{wP} = X,$$
$$Y_{wN} = Y.$$

Figure 3.3 also shows that for every feasible point, either y_1 or y_2 can be improved but not both. This means that there are no Pareto optimal or nondominated points, so

$$X_P = \varnothing,$$
$$Y_N = \varnothing.$$

Since there are no Pareto optimal or nondominated points it follows directly from the inclusions (3.1.3) that there are no proper Pareto optimal or proper nondominated points, so

$$X_{pP} = \varnothing,$$
$$Y_{pN} = \varnothing.$$

In Example 3.1 the criteria are not conflicting making it somewhat trivial. However, it shows that it is theoretically possible that the sets $X_{wP} \setminus X_P$ and $Y_{wN} \setminus Y_N$ can be rather large, meaning that there are a lot weakly Pareto optimal points which are not Pareto optimal. In Example 3.1, there are no Pareto optimal points while all feasible points are weakly Pareto optimal.

In the following example we show that it is also possible for the properly Pareto optimal set to be empty while the Pareto optimal set is rather large.

EXAMPLE 3.2. Let $X = (0, \infty)$ and suppose that the criteria $f_1, f_2 : \mathbb{R} \to \mathbb{R}$ are given by:

$$f_1(x) = -x,$$
$$f_2(x) = -\frac{1}{x}. \tag{3.1.5}$$

Similarly as in Example 3.1, the feasible set Y in the criterion space is determined:

$$Y = \{(y_1, y_2) \in \mathbb{R}^2 \mid y_1 < 0,\ y_2 = 1/y_1\}. \tag{3.1.6}$$

Both the criteria and the feasible set Y are visualized in Figure 3.4.

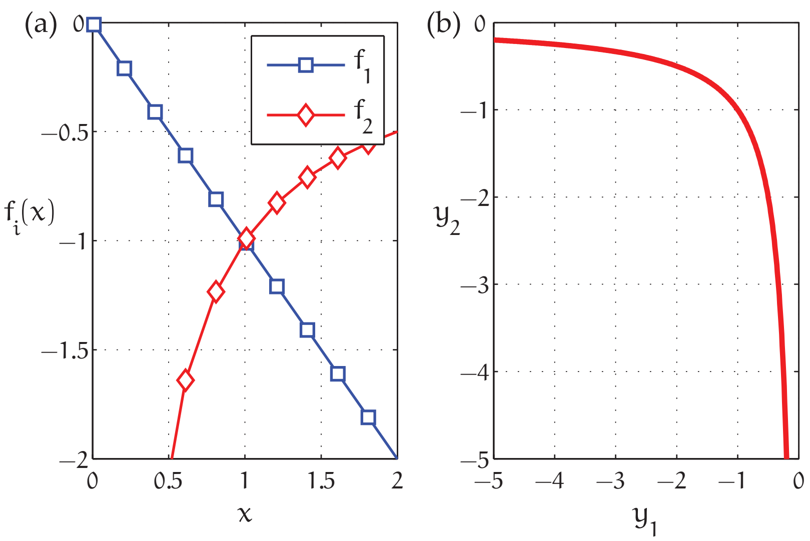

FIGURE 3.4: (a) The two criteria (3.1.5) and (b) the feasible set Y (3.1.6) in the criterion space.

Now, we will identify the optimal sets. In this example, note that f_1 is strictly decreasing and f_2 is strictly increasing on the feasible set $X = (0, \infty)$ (Figure 3.4). Therefore, the Pareto optimal set is X (and the nondominated set is Y). From the inclusions (3.1.3) it then follows that the weak Pareto optimal set is also X (and the weakly nondominated set is Y),

$$X_{wP} = X_P = X,$$
$$Y_{wN} = Y_N = Y.$$

Next, we show that none of the Pareto optimal points $\hat{x} \in X_P$ are properly Pareto optimal. Let $M \in \mathbb{R}_{>0}$ and define $x := (M+1)/\hat{x} \in X$, then we have

$$\Lambda_{1,2}(\hat{x}, x) = \frac{f_1(\hat{x}) - f_1(x)}{f_2(x) - f_2(\hat{x})} = \frac{-\hat{x} + x}{-\frac{1}{x} + \frac{1}{\hat{x}}} = x\hat{x} = M + 1 > M.$$

So for every $M \in \mathbb{R}_{>0}$ we can always find an $x \in X$ such that the trade-off $\Lambda_{1,2}(x, \hat{x})$ is larger than M. We may conclude that there are no proper Pareto optimal points (or proper nondominated points), so

$$X_{pP} = \emptyset,$$
$$Y_{pN} = \emptyset.$$

Example 3.2 shows it is possible to have a lot of Pareto optimal points which are not properly Pareto optimal. However, under certain conditions (including convexity of the criteria), this cannot happen which is shown later on in this chapter. Note that criterion f_2 in Example 3.2 is not convex.

In the next example, almost all Pareto optimal points are also properly Pareto optimal.

EXAMPLE 3.3. Let $X = [0, 1]$ and let the criteria $f_1, f_2 : \mathbb{R} \to \mathbb{R}$ be given by:

$$f_1(x) = 1 - x,$$
$$f_2(x) = 1 - \sqrt{1 - x^2}. \tag{3.1.7}$$

Here, the feasible set Y in the criterion space is a quarter of the unit circle with center $(1, 1)$:

$$Y = \{(y_1, y_2) \in \mathbb{R}^2 \mid (y_1 - 1)^2 + (y_2 - 1)^2 = 1,\ 0 \leqslant y_1, y_2 \leqslant 1\}. \tag{3.1.8}$$

The criteria and the set Y are depicted in Figure 3.5.

Next, we determine the optimal sets beginning with the weakly Pareto optimal set. For the same reason as in Example 3.2 (f_1 is strictly decreasing and f_2 is strictly increasing) we may conclude that the Pareto optimal set is X (and the nondominated set is Y). Combined with the

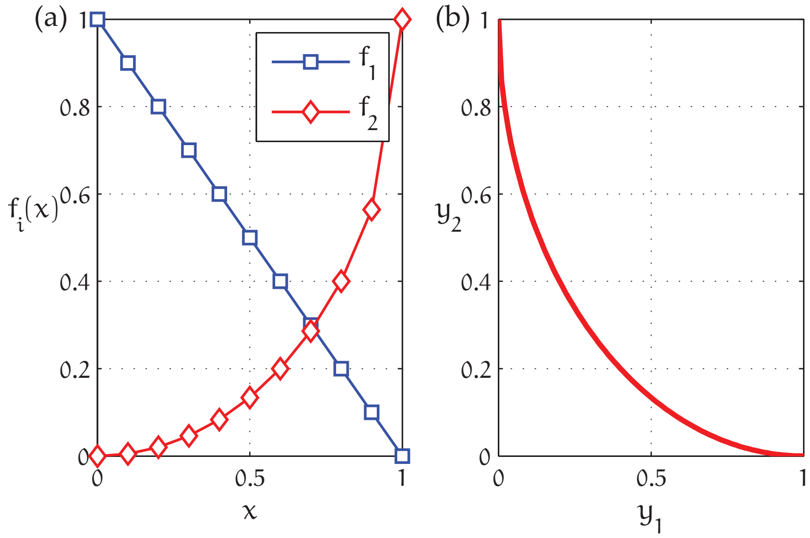

FIGURE 3.5: (a) The two criteria (3.1.7) and (b) the feasible set Y (3.1.8) in the criterion space.

inclusions (3.1.3), we have

$$X_{wP} = X_P = X,$$
$$Y_{wN} = Y_N = Y.$$

More complicated in this example, is identifying the properly Pareto optimal points. All points in $X = [0, 1]$ are candidate points since all of these points are Pareto optimal. Thus, we need to check whether the trade-offs are bounded (see Definition 3.4). Consider the following cases:

- $\hat{x} = 0$, which is not properly Pareto optimal. Let $M \in \mathbb{R}_{>0}$, for $L = M + 1$ define

  $$x := 2L/(L^2 + 1) \in X.$$

  Then the trade-off

$$\begin{aligned}
\Lambda_{1,2}(\hat{x}, x) &= \frac{f_1(\hat{x}) - f_1(x)}{f_2(x) - f_2(\hat{x})} \\
&= \frac{x}{1 - \sqrt{1 - x^2}} \\
&= \frac{2L}{(L^2 + 1)(1 - \sqrt{1 - (\frac{2L}{L^2+1})^2})} \\
&= \frac{2L}{(L^2 + 1)(1 - \frac{L^2-1}{L^2+1})} \\
&= L > M,
\end{aligned}$$

is not bounded by any $M \in \mathbb{R}_{>0}$. We may conclude that $\hat{x} = 0$ is not properly Pareto optimal and $(1,0)$ is not properly nondominated.

- $\hat{x} = 1$ is not properly Pareto optimal either. Let $M \in \mathbb{R}_{>0}$, for $L = M + 1$ define $x := (L^2 - 1)/(L^2 + 1) \in X$. Then the trade-off

$$\begin{aligned}\Lambda_{2,1}(\hat{x}, x) &= \frac{f_2(\hat{x}) - f_2(x)}{f_1(x) - f_1(\hat{x})} \\ &= \frac{\sqrt{1-x^2}}{1-x} \\ &= \frac{\sqrt{1 - (\frac{L^2-1}{L^2+1})^2}}{1 - \frac{L^2-1}{L^2+1}} \\ &= \frac{\frac{2L}{L^2+1}}{\frac{2}{L^2+1}} \\ &= L > M,\end{aligned}$$

is not bounded by any $M \in \mathbb{R}_{>0}$. Consequently, $\hat{x} = 1$ is not properly Pareto optimal and $(0,1)$ is not properly nondominated.

- $0 < \hat{x} < 1$, are all properly Pareto optimal. Fix such a $\hat{x} \in (0,1)$, then we need to verify that the trade-offs $\Lambda_{1,2}$ and $\Lambda_{2,1}$ are bounded.

  To check if $\Lambda_{1,2}$ is bounded, we only need to check those $x \in X$ for which $f_1(x) < f_1(\hat{x})$ and $f_2(\hat{x}) < f_2(x)$ (see Definition 3.4). These inequalities hold for $x \in (\hat{x}, 1]$, see Figure 3.5. So, we need to check if the trade-off

$$\begin{aligned}\Lambda_{1,2}(\hat{x}, x) &= \frac{f_1(\hat{x}) - f_1(x)}{f_2(x) - f_2(\hat{x})} \\ &= \frac{x - \hat{x}}{\sqrt{1-\hat{x}^2} - \sqrt{1-x^2}},\end{aligned}$$

  is bounded for all $x \in (\hat{x}, 1]$. The trade-off $\Lambda_{1,2}$ is well defined for all $x \in (\hat{x}, 1]$, and is a decreasing function of x. The only problem that might occur is that the trade-off becomes unbounded if $x \downarrow \hat{x}$. We thus need to check if this limit exists. With l'Hôpital's rule:

$$\begin{aligned}\lim_{x \downarrow \hat{x}} \Lambda_{1,2}(\hat{x}, x) &= \lim_{x \downarrow \hat{x}} \frac{x - \hat{x}}{\sqrt{1-\hat{x}^2} - \sqrt{1-x^2}} \\ &= \lim_{x \downarrow \hat{x}} \frac{\sqrt{1-x^2}}{x} \\ &= \frac{\sqrt{1-\hat{x}^2}}{\hat{x}}, \quad \text{if } \hat{x} \neq 0.\end{aligned}$$

  So the trade-off $\Lambda_{1,2}$ is bounded by $M = \sqrt{1-\hat{x}^2}/\hat{x}$ provided that $\hat{x} \neq 0$ (which is the case since $\hat{x} \in (0,1)$).

Similarly, we find that $\Lambda_{2,1}$ is bounded by $M = \hat{x}/\sqrt{1-\hat{x}^2}$ provided that $\hat{x} \neq 1$ (which is the case since $\hat{x} \in (0,1)$).

We may conclude that

$$X_{pP} = (0,1),$$
$$Y_{pN} = Y \setminus \{(1,0),(0,1)\}.$$

Note that in the previous 3 examples, the decision space is one-dimensional. In practice, the decision space often is a multi-dimensional interval. Consequently, the feasible sets look differently. Therefore, we give an example where both the decision and criterion space is two-dimensional.

EXAMPLE 3.4. Consider the feasible set $X = [0,20] \times [0,10]$ and criteria $f_1, f_2 : \mathbb{R}^2 \to \mathbb{R}$ given by:

$$\begin{aligned} f_1(x_1,x_2) &= \frac{1}{2}x_1 + x_2 + 1, \\ f_2(x_1,x_2) &= \max\left(2,\ 8 - x_1,\ \frac{1}{2}x_1 - 2\right). \end{aligned} \tag{3.1.9}$$

The criteria are shown in Figure 3.6.

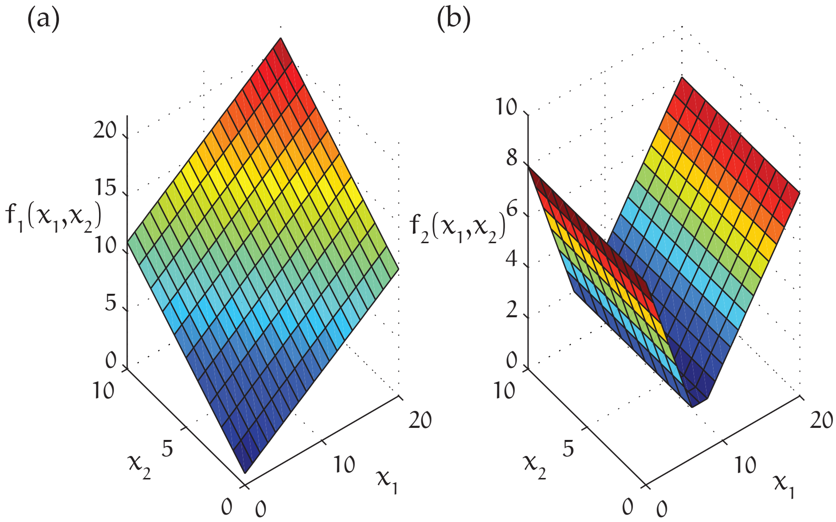

FIGURE 3.6: The two criteria (3.1.9), (a) shows f_1 and (b) shows f_2. The feasible set in the decision space $\mathbb{R}^2$ is given by $X = [0,20] \times [0,10]$.

First, we determine the feasible set Y in the criterion space which is more complicated than in the previous examples. For a fixed $x_2 \in [0,10]$, we eliminate the x_1-variable in the criteria $y_1 = f_1(x_1,x_2)$ and $y_2 = f_2(x_1,x_2)$. Then $x_1 = 2y_1 - 2x_2 - 2$ and $x_1 \in [0,20]$ if and only if $y_1 \in [1+x_2, 11+x_2]$. Substituting x_1 in y_2 gives $y_2 = \max(2, 10 - 2y_1 + 2x_2, y_1 - x_2 - 3)$. So, for a fixed $x_2 \in [0, 10]$ the feasible set Y_{x_2} in the criterion space is given by:

$$Y_{x_2} = \{(y_1, y_2) \in \mathbb{R}^2 \mid y_1 \in [1 + x_2, 11 + x_2],\ y_2 = \max(2, 10 - 2y_1 + 2x_2, y_1 - x_2 - 3)\}.$$

In Figure 3.7, the set Y_{x_2} is depicted in the criterion space for several values of x_2.

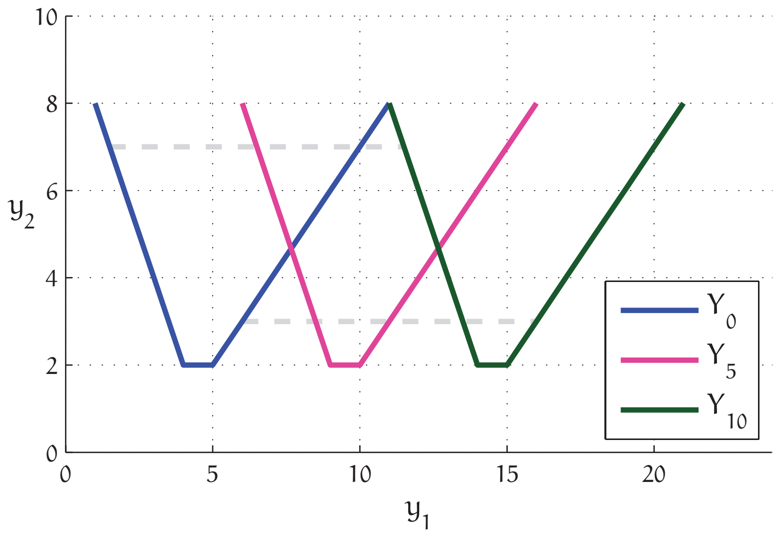

FIGURE 3.7: The sets Y_{x_2} for $x_2 \in \{0, 5, 10\}$. Observe that the set Y_{x_2} shifts horizontally as x_2 increases.

The feasible set Y in the criterion space is then given by the union over $x_2 \in [0, 10]$ of the sets Y_{x_2}:

$$Y = \bigcup_{x_2 \in [0,10]} Y_{x_2},$$

and is shown in Figure 3.8.

Next we identify the (weakly) nondominated set using Figure 3.8. For points on the lower left part of the feasible set Y, it is impossible to improve both criteria. In Figure 3.8, this is on the line segments between the points $(1, 8)$,$(4, 2)$ and $(4, 2)$, $(15, 2)$ in the criterion space. The union of these line segments thus represent the weakly nondominated set Y_{wN}. The nondominated set Y_N, is just the line segment which connects the points $(1, 8)$ and $(4, 2)$ in the criterion space. In set notation:

$$Y_{wN} = \{(y_1, y_2) \in \mathbb{R}^2 \mid y_1 \in [1, 15],\ y_2 = \max(2, 10 - 2y_1)\},$$
$$Y_N = \{(y_1, y_2) \in \mathbb{R}^2 \mid y_1 \in [1, 4],\ y_2 = 10 - 2y_1\}.$$

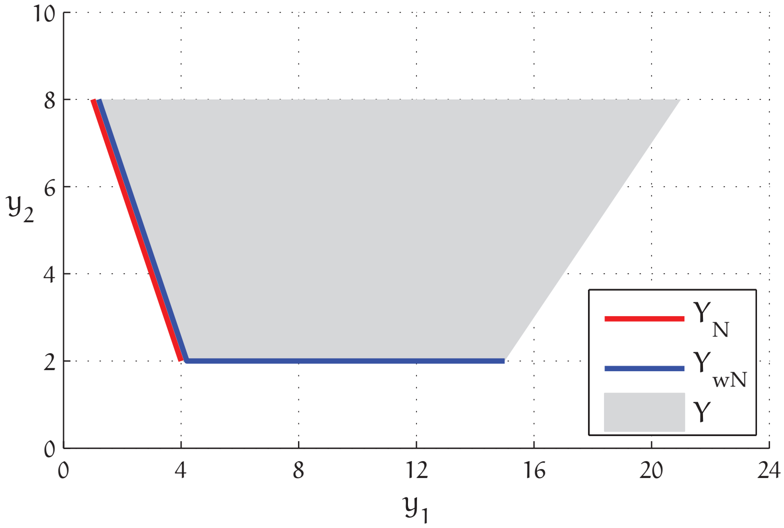

FIGURE 3.8: The feasible set Y in the criterion space. Observe that the set of (weakly) nondominated points is located on the lower left part of the feasible set.

The corresponding (weakly) Pareto optimal points are given by

$$\begin{aligned} X_{wP} &= ([0,6] \times \{0\}) \bigcup \left(\bigcup_{x_2 \in [0,10]} [6,8] \times \{x_2\} \right), \\ X_P &= [0,6] \times \{0\}. \end{aligned}$$

Furthermore, it can be verified that the trade-offs are bounded since both criteria are linear, so all the Pareto optimal points are also properly Pareto optimal:

$$\begin{aligned} X_{pP} &= X_P, \\ Y_{pN} &= Y_N. \end{aligned}$$

Example 3.4 shows that the (weakly) nondominated set is easy to identify once the feasible set Y in the criterion space is known explicitly. Namely, the (weakly) nondominated points are located on the (lower left) edge of Y. Mathematically this means that we expect the weakly nondominated points to be on the *boundary* of Y. Actually, this must be the case. To prove this, it is convenient to represent the (weakly) nondominated set as follows

$$\begin{aligned} Y_{wN} &= \{\hat{y} \in Y \mid \text{there is no } y \in Y \text{ such that } y < \hat{y}\} \\ Y_N &= \{\hat{y} \in Y \mid \text{there is no } y \in Y \text{ with } y \neq \hat{y} \text{ such that } y \leqslant \hat{y}\}. \end{aligned} \tag{3.1.10}$$

Now, the statement can be proven.

PROPOSITION 3.1. $Y_{wN} \subseteq bd\, Y$.

Proof. If $\hat{y} \notin \text{bd } Y = \overline{Y} \setminus \text{int } Y$ then we must have $\hat{y} \in \text{int } Y$. Hence, there is a $\eta > 0$ such that $B(\hat{y}, \eta) \subseteq Y$. Take $h = (\eta/2, \dots, \eta/2) \in B(0, \eta) \cap \mathbb{R}^n_{>0}$ and let $y = \hat{y} - h \in B(\hat{y}, \eta)$. Now, we have found a $y \in Y$ such that $y < \hat{y}$. This means $\hat{y} \notin Y_{wN}$. $\square$

Remark. Immediate consequences of Proposition 3.1 are

1. $Y_N \subseteq \text{bd } Y$, since $Y_N \subseteq Y_{wN}$.

2. $Y_N = Y_{wN} = \varnothing$, if Y is an open set.

We can even say more about the location of (weakly) nondominated points, namely that they are located at the lower left part the feasible set Y. To express this mathematically, it is convenient to introduce the following notation (see also in the Notation section) for integers $N \in \mathbb{N}$:

$$\mathbb{R}^N_{\geqslant 0} := \{x \in \mathbb{R}^N \mid x \geqslant 0\},$$
$$\mathbb{R}^N_{>0} := \{x \in \mathbb{R}^N \mid x > 0\},$$

which are the nonnegative and positive orthants of $\mathbb{R}^N$, see Figure 3.9 for the two-dimensional case. With this notation, stating that the (weakly) nondominated points are located at the lower

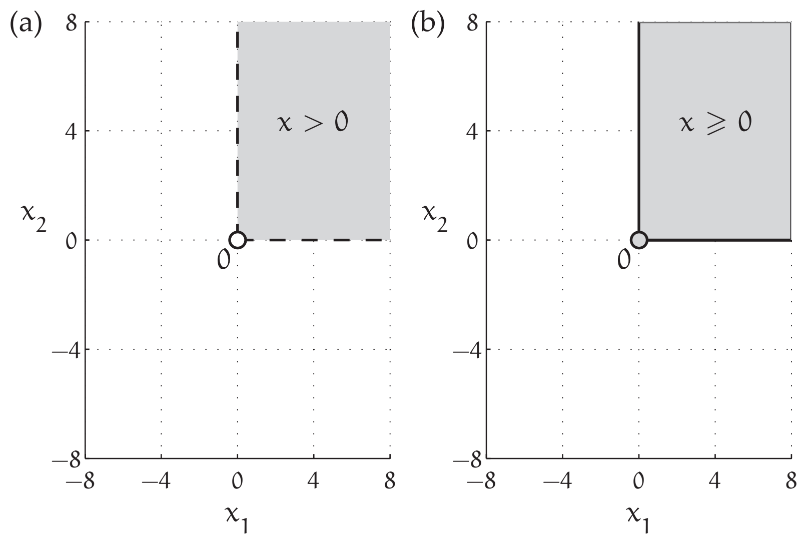

FIGURE 3.9: The nonnegative and positive orthants in $\mathbb{R}^2$. In (a) the set $\mathbb{R}^2_{>0}$ is shown and in (b) the set $\mathbb{R}^2_{\geqslant 0}$ is shown.

left part the feasible set Y can be expressed as follows:

$$Y_{wN} = (Y + \mathbb{R}^n_{>0})_{wN},$$
$$Y_N = (Y + \mathbb{R}^n_{\geqslant 0})_N.$$

Now that we are familiar with the definitions of optimality, we can analyze them further. First, we investigate under which circumstances we can guarantee the existence of (weakly) Pareto optimal points (as we have seen in Example 3.1, this is not trivial). Then, we investigate connectedness properties of the optimal sets.

3.2 Existence of optimal points

In this section, we provide sufficient conditions which guarantee the existence of optimal points for multicriteria optimization problems of the form:

$$\min_{x \in X} f(x).$$

An optimal point for such a multicriteria optimization problem can be interpreted in various ways of which some have been discussed in the last section. Here, the focus is on the existence of weakly Pareto optimal points (Definition 3.2) and Pareto optimal points (Definition 3.1). In other words, we focus on providing conditions that guarantee nonemptyness of the optimal sets X_{wP}, Y_{wN}, X_P and Y_N. Later on in this chapter we also consider the existence of properly Pareto optimal points.

We start with investigating nonemptyness the existence of weakly Pareto optimal points. After that, we do the same for Pareto optimal points.

3.2.1 Existence of weakly Pareto optimal points

Here, we search for conditions that guarantee nonemptyness of the weakly Pareto optimal set and the weakly nondominated set, X_{wP} and Y_{wN}, respectively. It is convenient to consider the set of weakly nondominated points Y_{wN} first. Then, by the basic principles of continuity and compactness (see Chapter 2), results are derived for the Pareto optimal set X_{wP}.

We prove that nonemptyness and compactness of the feasible set Y in the criterion space guarantees the existence of weakly nondominated points.

THEOREM 3.2. *If the feasible set $Y \subseteq \mathbb{R}^n$ in the criterion space is a nonempty compact set then $Y_{wN} \neq \varnothing$.*

Proof. This proof is by contradiction. Obviously, if $Y = \varnothing$ then $Y_{wN} = \varnothing$, which is why we need the condition that Y is nonempty.

Suppose $Y_{wN} = \varnothing$. This means that for every $y' \in Y$ there is a $y \in Y$ such that $y < y'$, so

$$Y \subseteq \bigcup_{y \in Y} (y + \mathbb{R}^n_{>0}). \tag{3.2.1}$$

Since $\mathbb{R}^n_{>0}$ is open (and thus, $y + \mathbb{R}^n_{>0}$ is open for every $y \in Y$), the collection of sets $\{y +$

$\mathbb{R}^n_{>0}\}_{y \in Y}$ in (3.2.1) is an open cover of Y. The compactness of Y implies that there is a $k \in \mathbb{N}$ such that

$$Y \subseteq \bigcup_{i \in [k]} (y^i + \mathbb{R}^n_{>0}), \tag{3.2.2}$$

for some $y^1, \ldots, y^k \in Y$.

Now, fix a $j_0 \in [k]$. We then have $y^{j_0} \in Y$ and so $y^{j_0} \in \bigcup_{i \in [k]}(y^i + \mathbb{R}^n_{>0})$. Certainly, it holds that $y^{j_0} \notin y^{j_0} + \mathbb{R}^n_{>0}$ so there must be at least one $j_1 \in [k] \setminus \{j_0\}$ such that $y^{j_0} \in y^{j_1} + \mathbb{R}^n_{>0}$ which implies $y^{j_1} < y^{j_0}$.

For $j_1 \in [k] \setminus \{j_0\}$ we also have $y^{j_1} \in Y$. The same reasoning as above implies that there must be at least one $j_2 \in [k] \setminus \{j_0, j_1\}$ such that $y^{j_1} \in y^{j_2} + \mathbb{R}^n_{>0}$ and so $y^{j_2} < y^{j_1}$. Due to the finiteness of the set $[k]$, this argument can be repeated and we arrive at the following chain of inequalities:

$$y^{j_k} < y^{j_{k-1}} < \ldots < y^{j_2} < y^{j_1} < y^{j_0}. \tag{3.2.3}$$

But now, $y^{j_k} \in Y$ and $y^{j_k} \notin \bigcup_{i \in [k]}(y^i + \mathbb{R}^n_{>0})$ which contradicts the compactness of Y. □

Now that we have established Theorem 3.2, we impose a continuity assumption on the criterion vector function f to guarantee the existence of weakly Pareto optimal decision vectors.

COROLLARY 3.3. *If the feasible set $X \subseteq \mathbb{R}^m$ in the decision space is a nonempty and compact set and the criterion vector function $f : \mathbb{R}^m \to \mathbb{R}^n$ is continuous, then $X_{wP} \neq \varnothing$.*

Proof. Since X is nonempty, so is $Y = f(X)$. Also Y must be compact due to the compactness of X and continuity of f (Lemma 2.8). Theorem 3.2 now implies that $Y_{wN} = f(X_{wP})$ is nonempty so that $X_{wP} \neq \varnothing$. □

As we have seen in Example 3.1, it may happen that there are a lot of weakly Pareto optimal points while there are no Pareto optimal points. Important to notice (in Example 3.1) is that the feasible set $X = \mathbb{R} \setminus \{0\}$ is not compact, however there are plenty of weakly Pareto optimal points. The condition that the feasible set X is compact in Corollary 3.3 thus is not necessary for the existence of weakly Pareto optimal points. Similarly, the condition that the feasible set Y in the criterion space is compact in Theorem 3.2 is not a necessary condition for the existence of weakly nondominated points.

3.2.2 Existence of Pareto optimal points

We now focus on existence results for Pareto optimal points. Again, we will first derive existence results for the nondominated set Y_N and then impose conditions on the criterion vector function f to obtain existence results for the Pareto optimal set X_P.

Furthermore, once we have found a sufficient condition for the existence of nondominated points we will investigate if we can impose less restrictive sufficient conditions. This has been studied by numerous mathematicians. Here, we present results of Borwein (1983), Hartley (1978) and Corley (1980)†, where Hartley's result is actually a special case of Corley's.

First of all, notice that the proof used in the last section does not work in this case. In order to use the same argument as in the proof of Theorem 3.2, assume $Y_N = \varnothing$ and cover Y as follows,

$$Y \subseteq \bigcup_{y \in Y} (y + \mathbb{R}^n_{\geqslant 0} \setminus \{0\}). \tag{3.2.4}$$

But now, the sets $y + \mathbb{R}^n_{\geqslant 0} \setminus \{0\}$ are not open. So (3.2.4) does not provide us with an *open* cover hence we cannot use the compactness of Y to reduce its coverage by a finite union.

However, the condition that Y is compact and nonempty is still sufficient to guarantee existence of a nondominated point. This is proved in Theorem 3.4.

THEOREM 3.4. *If the feasible set $Y \subseteq \mathbb{R}^n$ in the criterion space is a nonempty compact set then $Y_N \neq \varnothing$.*

Proof. In this proof we use an appropriate continuous mapping and Theorem 2.10.

Define the mapping $U : Y \to \mathbb{R}$ by

$$U(y) = \sum_{i \in [n]} y_i. \tag{3.2.5}$$

Since Y is a nonempty compact set and the mapping (3.2.5) is continuous, we may apply Theorem 2.10. So U attains its minimum $M \in \mathbb{R}$ on the set Y, meaning that there is a $\hat{y} \in Y$ such that $U(\hat{y}) = M$.

We claim that $\hat{y} \in Y_N$. Suppose not, then there is a $y \in Y$ such that $y \leqslant \hat{y}$ and $y_j < \hat{y}_j$ for at least one $j \in [n]$. Consequently

$$\sum_{i \in [n]} y_j < \sum_{i \in [n]} \hat{y}_j,$$

hence $U(y) < U(\hat{y}) = M$. Since $y \in Y$ and M is the minimum of U over Y, we have a contradiction. It thus must be that $\hat{y} \in Y_N$. □

Note that this proof also works for Theorem 3.2. As in the previous section, we can conclude that $X_P \neq \varnothing$ if X is a nonempty compact set and f is continuous.

The remainder of this section is devoted to impose less restrictive sufficient conditions that guarantee existence of Pareto optimal and nondominated points. To do so, we introduce $\mathbb{R}^n_{\geqslant 0}$-*compactness* and $\mathbb{R}^n_{\geqslant 0}$-*semicompactness* for sets which should be seen as weaker forms of compactness.

DEFINITION 3.5 ($\mathbb{R}^n_{\geqslant 0}$-(semi)compactness)**.** *Let $Y \subseteq \mathbb{R}^n$ then Y is called*

1. $\mathbb{R}^n_{\geqslant 0}$-compact *if $(y - \mathbb{R}^n_{\geqslant 0}) \cap Y$ is compact for all $y \in Y$.*

†In these articles, the results are provided in a more general setting.

2. $\mathbb{R}^n_{\geqslant 0}$-semicompact *if every open cover of* Y *of the form*

$$\{O_i\}_{i\in I} = \{\mathbb{R}^n \setminus (y^i - \mathbb{R}^n_{\geqslant 0})\}_{i\in I}$$

has a finite subcover. Here, I *is an index set and* $y^i \in Y$ *for all* $i \in I$.

To get a idea of the relations between these different concepts, consider the next proposition.

PROPOSITION 3.5. *Let* $Y \subseteq \mathbb{R}^n$*, then*

$$Y \textit{ is compact} \quad \Rightarrow \quad Y \textit{ is } \mathbb{R}^n_{\geqslant 0}\textit{-compact} \quad \Rightarrow \quad Y \textit{ is } \mathbb{R}^n_{\geqslant 0}\textit{-semicompact}.$$

Proof. The implications can be proven as follows:

- Suppose Y is compact. Then for all $y \in Y$, the set $(y - \mathbb{R}^n_{\geqslant 0}) \cap Y$ is a closed subset of Y. Lemma 2.7 implies that all of these sets must be compact. Hence Y is $\mathbb{R}^n_{\geqslant 0}$-compact.
- Suppose Y is $\mathbb{R}^n_{\geqslant 0}$-compact. We need to show that every open cover of Y of the form

  $$\{O_i\}_{i\in I} = \{\mathbb{R}^n \setminus (y^i - \mathbb{R}^n_{\geqslant 0})\}_{i\in I}$$

  has a finite subcover. Here, I is an index set and $y^i \in Y$ for all $i \in I$.

  Let $y^k \in Y$ be arbitrary, then

  $$Y \subseteq \bigcup_{i\in I} O_i \quad \text{if and only if} \quad \big((\mathbb{R}^n \setminus O_k) \cap Y\big) \subseteq \bigcup_{i\in I\setminus\{k\}} O_i.$$

  Note $(\mathbb{R}^n \setminus O_k) \cap Y = (y^k - \mathbb{R}^n_{\geqslant 0}) \cap Y$. Since $y^k \in Y$ and Y is $\mathbb{R}^n_{\geqslant 0}$-compact there exists a finite $J \subseteq I$ such that

  $$\big((y^k - \mathbb{R}^n_{\geqslant 0}) \cap Y\big) \subseteq \bigcup_{j\in J} O_j.$$

  Therefore Y can be covered as:

  $$Y \subseteq \bigcup_{j\in J\cup\{k\}} O_j.$$

  We may conclude that Y is $\mathbb{R}^n_{\geqslant 0}$-semicompact.

□

The following result is due to Hartley (1978).

THEOREM 3.6 (Hartley). *If the feasible set* $Y \subseteq \mathbb{R}^n$ *in the criterion space is a nonempty* $\mathbb{R}^n_{\geqslant 0}$*-compact set then* $Y_N \neq \varnothing$.

Proof. The proof is similar to the proof of Theorem 3.4.

Y is nonempty, so we can take a $y \in Y$ and define the set

$$Y' := (y - \mathbb{R}^n_{\geqslant 0}) \cap Y. \tag{3.2.6}$$

Since Y is $\mathbb{R}^n_{\geqslant 0}$-compact we know that Y' is compact. Define the function U as in (3.2.5), only now with domain Y'. We can proceed as in the proof of Theorem 3.4 and may conclude $Y_N \neq \varnothing$. □

Actually, Borwein (1983) states that Theorem 3.6 also holds when you have only one $y \in Y$ for which $(y - \mathbb{R}^n_{\geqslant 0}) \cap Y$ is compact.

THEOREM 3.7 (Borwein). *If the feasible set* $Y \subseteq \mathbb{R}^n$ *in the criterion space is nonempty and there is a* $y \in Y$ *such that* $(y - \mathbb{R}^n_{\geqslant 0}) \cap Y$ *is compact, then* $Y_N \neq \varnothing$.

Proof. Straightforward, the proof given for Theorem 3.6 remains valid with Y' as in (3.2.6). □

So if a nonempty compact subsection of Y can be found, then we may conclude that Y_N is nonempty. It is also possible to guarantee the existence of nondominated points when Y is nonempty and $\mathbb{R}^n_{\geqslant 0}$-semicompact. We will prove this with Zorn's Lemma. As an intermediate result, we show that under these conditions the pair $(Y, \leqslant)$ is inductively ordered.

LEMMA 3.8. *If the feasible set* $Y \subseteq \mathbb{R}^n$ *in the criterion space is a nonempty* $\mathbb{R}^n_{\geqslant 0}$*-semicompact set then* $(Y, \leqslant)$ *is inductively ordered.*

Proof. We prove by contradiction.

Suppose $(Y, \leqslant)$ is not inductively ordered. Then there exists a chain $Y' = \{y^i \mid i \in I\}$ in Y with no lower bound. This implies that

$$\bigcap_{i \in I} \Big((y^i - \mathbb{R}^n_{\geqslant 0}) \cap Y \Big) = \varnothing, \tag{3.2.7}$$

since any element in this set would be a lower bound.

Since the set (3.2.7) is empty, it holds that for every $y \in Y$ there is a $y^i \in Y'$ such that $y \notin y^i - \mathbb{R}^n_{\geqslant 0}$. Define the collection of open sets $\{O_i\}_{i \in I} = \{\mathbb{R}^n \setminus (y^i - \mathbb{R}^n_{\geqslant 0})\}_{i \in I}$ then $\{O_i\}_{i \in I}$ is an open cover of Y,

$$Y \subseteq \bigcup_{i \in I} O_i.$$

Because Y is $R^n_{\geqslant 0}$-semicompact there exists a finite $J \subseteq I$ such that

$$Y \subseteq \bigcup_{j \in J} O_j.$$

Notice that for every two sets in $\{O_i\}_{i\in I}$ we have

$$O_j \subseteq O_k \quad \text{if and only if} \quad y^k \leqslant y^j.$$

Since Y' is totally ordered, $(\{O_i\}_{i\in I}, \subseteq)$ must be as well.

Combining these observations, we know that $(\{O_j\}_{j\in J}, \subseteq)$ is a *finite* totally ordered set so there must be a minimal set, say O_l in $\{O_j\}_{j\in J}$, such that

$$Y \subseteq O_l = \mathbb{R}^n \setminus (y^l - \mathbb{R}^n_{\geqslant 0}).$$

But now, $y^l \notin Y$ while $y^l \in Y'$ which is absurd. $\square$

The crucial part of the proof of Lemma 3.8 is that a finite totally ordered set (nonempty) has a minimal element. The following result is now easily verified and is due to Corley (1980).

THEOREM 3.9 (Corley). *If the feasible set $Y \subseteq \mathbb{R}^n$ in the criterion space is a nonempty $\mathbb{R}^n_{\geqslant 0}$-semicompact set then $Y_N \neq \varnothing$.*

Proof. Lemma 3.8 implies that $(Y, \leqslant)$ is inductively ordered. Zorn's Lemma implies that Y contains a minimal element $\hat{y} \in Y$. It must be that $\hat{y} \in Y_N$ since otherwise there would be a $y \in Y \setminus \{\hat{y}\}$ with $y \leqslant \hat{y}$ contradicting the minimality of $\hat{y}$ in Y. $\square$

Note that the conditions for Theorem 3.9 are less restrictive than the conditions in Theorem 3.4, Theorem 3.6 and Theorem 3.7, but may be harder to check.

As mentioned before, $X_P \neq \varnothing$ if X is a nonempty compact set and f is continuous. However, a less restrictive condition can be imposed on the criteria function f while the result remains true. For this matter, we introduce the concept $\mathbb{R}^n_{\geqslant 0}$-*semicontinuity* for functions.

DEFINITION 3.6 ($\mathbb{R}^n_{\geqslant 0}$-semicontinuity). *A function $f : \mathbb{R}^m \to \mathbb{R}^n$ is called* $\mathbb{R}^n_{\geqslant 0}$-semicontinuous *if the sets*

$$f^{-1}\left(y - \mathbb{R}^n_{\geqslant 0}\right) = \{x \in \mathbb{R}^m \mid f(x) \in y - \mathbb{R}^n_{\geqslant 0}\}$$

are closed for all $y \in \mathbb{R}^n$.

With this concept, a similar statement as Lemma 2.8 can be proven.

LEMMA 3.10. *If the feasible set $X \subseteq \mathbb{R}^m$ in the decision space is a nonempty compact set, and the criterion vector function $f : \mathbb{R}^m \to \mathbb{R}^n$ is $\mathbb{R}^n_{\geqslant 0}$-semicontinuous then the feasible set $Y \subseteq \mathbb{R}^n$ in the criterion space is $\mathbb{R}^n_{\geqslant 0}$-semicompact.*

Proof. This proof is similar to the proof of Lemma 2.8. $\square$

Now, we also have less restrictive conditions that guarantee existence of Pareto optimal points.

COROLLARY 3.11. *If the feasible set* $X \subseteq \mathbb{R}^m$ *in the decision space is a nonempty compact set and the criterion vector function* $f : \mathbb{R}^m \to \mathbb{R}^n$ *is* $\mathbb{R}^n_{\geqslant 0}$*-semicontinuous, then* $X_P \neq \emptyset$.

Proof. By Lemma 3.10, $Y = f(X)$ is $\mathbb{R}^n_{\geqslant 0}$-semicompact. Since Y is also nonempty, we may use Theorem 3.9 which implies that Y_N is nonempty. Hence $X_P \neq \emptyset$. □

Since the inclusions (3.1.3) hold in general, Corollary 3.11 also imposes less restrictive conditions for the existence of weakly Pareto optimal and weakly nondominated points as is mentioned in the next remark.

Remark. If the feasible set $X \subseteq \mathbb{R}^m$ in the decision space is a nonempty compact set and the criterion vector function $f : \mathbb{R}^m \to \mathbb{R}^n$ is $\mathbb{R}^n_{\geqslant 0}$-semicontinuous, then X_{wP}, X_P, Y_{wN} and Y_N are nonempty.

3.3 Connectedness of the optimal sets

In this section, the aim is to obtain results on connectedness of the Pareto optimal and nondominated set. Again, we will first focus on the nondominated set. We investigate to what extent a *weighted sum scalarization* can generate parts of the nondominated set. A *weighted sum scalarization* of a multicriteria optimization problem

$$\min_{x \in X} f(x),$$

is given by

$$\min_{x \in X} \sum_{i \in [n]} \lambda_i f_i(x) = \min_{x \in X} \lambda^T f(x), \tag{3.3.1}$$

with respect to the decision space and given by

$$\min_{y \in Y} \sum_{i \in [n]} \lambda_i y_i = \min_{y \in Y} \lambda^T y, \tag{3.3.2}$$

with respect to the criterion space. Here, $\lambda = (\lambda_1, \ldots, \lambda_n)$ and λ^T denotes its *transpose*.

Since we are minimizing the criteria, it only makes sense to use $\lambda = (\lambda_1, \ldots, \lambda_n) \in \mathbb{R}^n_{\geqslant 0} \setminus \{0\}$. For a geometric interpretation of the single criterion optimization problem (3.3.1), see Figure 4.1. For a fixed $\lambda \in \mathbb{R}^n_{\geqslant 0} \setminus \{0\}$, we define the set

$$WS(\lambda, Y) := \{\hat{y} \in Y \mid \lambda^T \hat{y} \leqslant \lambda^T y \text{ for all } y \in Y\}. \tag{3.3.3}$$

We also define the following sets:

$$
\begin{aligned}
WS(Y) &:= \bigcup_{\lambda \in \mathbb{R}^n_{>0}} WS(\lambda, Y), \\
WS_0(Y) &:= \bigcup_{\lambda \in \mathbb{R}^n_{\geqslant 0} \setminus \{0\}} WS(\lambda, Y).
\end{aligned} \tag{3.3.4}
$$

The sets (3.3.4) turn out to have some key properties that we will need to prove the connectedness of the optimal sets. These properties are given in the next section.

3.3.1 Weighted sum scalarization

The question rises what the relation between the (weakly, properly) nondominated set and the sets $WS(Y)$ and $WS_0(Y)$ is. More specifically:

- Are the points of $WS(Y)$ and $WS_0(Y)$ weakly nondominated, nondominated or even properly nondominated?
- Are all of the weakly nondominated, nondominated or properly nondominated points included in the sets $WS(Y)$ and $WS_0(Y)$?

We start with a simple observation.

LEMMA 3.12. *For the feasible set $Y \subseteq \mathbb{R}^n$, it holds that $WS_0(Y) \subseteq Y_{wN}$.*

Proof. Let $\hat{y} \in Y$. Suppose $\hat{y} \notin Y_{wN}$, then there exists a $y \in Y$ such that $y < \hat{y}$. This implies

$$\sum_{i \in [n]} \lambda_i y_i < \sum_{i \in [n]} \lambda_i \hat{y}_i, \text{ for all } \lambda \in \mathbb{R}^n_{\geqslant 0} \setminus \{0\}.$$

So $\hat{y} \notin WS(\lambda, Y)$ for all $\lambda \in \mathbb{R}^n_{\geqslant 0} \setminus \{0\}$ hence $\hat{y} \notin WS_0(Y)$. □

This means that for every $\hat{y} \in Y$ for which there is a $\lambda \in \mathbb{R}^n_{\geqslant 0} \setminus \{0\}$ so that $\hat{y}$ is the solution to problem (3.3.2), we have $\hat{y} \in Y_{wN}$.

The converse does not need to hold unless we impose a convexity condition on the set Y. Actually, it is sufficient for the lower left part of Y to be convex, a property which is called $\mathbb{R}^n_{\geqslant 0}$-*convexity*.

DEFINITION 3.7 ($\mathbb{R}^n_{\geqslant 0}$-convexity)**.** *Let $Y \in \mathbb{R}^n$ be a set, then Y is called* $\mathbb{R}^n_{\geqslant 0}$-convex *if the set $Y + \mathbb{R}^n_{\geqslant 0}$ is convex.*

Note that if $Y \subseteq \mathbb{R}^n$ is convex then it is definitely $\mathbb{R}^n_{\geqslant 0}$-convex. This follows since both sets Y and $\mathbb{R}^n_{\geqslant 0}$ are convex hence their sum is also convex.

THEOREM 3.13. *If the feasible set $Y \subseteq \mathbb{R}^n$ is $\mathbb{R}^n_{\geqslant 0}$-convex then $Y_{wN} \subseteq WS_0(Y)$.*

Proof. See Ehrgott (2005) for a proof. □

Next, we investigate which conclusions can be drawn if $\lambda \in \mathbb{R}^n_{>0}$. For the set $WS(Y)$, a straightforward observation can be made.

LEMMA 3.14. *For the feasible set* $Y \subseteq \mathbb{R}^n$*, it holds that* $WS(Y) \subseteq Y_N$.

Proof. Let $\hat{y} \in Y$. Suppose $\hat{y} \notin Y_N$ then there is a $y \in Y$ such that $y \leqslant \hat{y}$ and $y_j < \hat{y}_j$ for at least one $j \in [n]$. Consequently,

$$\sum_{i \in [n]} \lambda_i y_i < \sum_{i \in [n]} \lambda_i \hat{y}_i, \text{ for all } \lambda \in \mathbb{R}^n_{>0}.$$

So $\hat{y} \notin WS(\lambda, Y)$ for all $\lambda \in \mathbb{R}^n_{>0}$ hence $\hat{y} \notin WS(Y)$. □

Lemma 3.14 thus means that for every $\hat{y} \in Y$ for which there is a $\lambda \in \mathbb{R}^n_{>0}$ so that $\hat{y}$ is the solution to problem (3.3.2), we have $\hat{y} \in Y_N$. Note the difference with Lemma 3.12. Apparently, if $\lambda > 0$ we can guarantee that solving problem (3.3.2) generates a nondominated point, while solving problem (3.3.2) for some $\lambda \in \mathbb{R}^n_{\geqslant 0} \setminus \{0\}$ only guarantees a weakly nondominated point.

Actually, when $\lambda > 0$ we can guarantee that the solution of problem (3.3.2) is a properly nondominated point.

THEOREM 3.15. *For the feasible set* $Y \subseteq \mathbb{R}^n$*, it holds that* $WS(Y) \subseteq Y_{pN}$.

Proof. For $\hat{y} \in Y$ with $\hat{y} \in WS(Y)$, we know $\hat{y} \in Y_N$ by Lemma 3.14. It thus remains to show that all trade-offs are bounded.

We claim that for an arbitrary $\lambda \in \mathbb{R}^n_{>0}$, all trade-offs are bounded by

$$M_\lambda := (n-1) \max_{k,l \in [n]} \frac{\lambda_k}{\lambda_l}.$$

Note that $M_\lambda > 0$ since $n > 1$ and $\lambda \in \mathbb{R}^n_{>0}$. If M_λ would not be a suitable bound, then there is an $i \in [n]$ and $y \in Y$ with $y_i < \hat{y}_i$ such that for all $j \in [n]$ with $\hat{y}_j < y_j$ we have

$$\frac{\hat{y}_i - y_i}{y_j - \hat{y}_j} > M_\lambda.$$

This implies

$$\begin{aligned}
\hat{y}_i - y_i &> (y_j - \hat{y}_j) M_\lambda \\
&= (n-1)(y_j - \hat{y}_j) \max_{k,l \in [n]} \frac{\lambda_k}{\lambda_l} \\
&\geqslant (n-1)(y_j - \hat{y}_j) \frac{\lambda_j}{\lambda_i}.
\end{aligned}$$

Note that the above does not only hold for those $j \in [n]$ with $\hat{y}_j < y_j$ but for all $j \in [n] \setminus \{i\}$ since $\hat{y}_i - y_i > 0$. So
$$\frac{\lambda_i}{n-1}(\hat{y}_i - y_i) > \lambda_j(y_j - \hat{y}_j), \text{ for all } j \in [n] \setminus \{i\}.$$
Summing up these $n-1$ inequalities leads to

$$\lambda_i(\hat{y}_i - y_i) > \sum_{j \in [n] \setminus \{i\}} \lambda_j(y_j - \hat{y}_j).$$

Or

$$\sum_{i \in [n]} \lambda_i \hat{y}_i > \sum_{i \in [n]} \lambda_i y_i.$$

But then $\hat{y} \notin Y_N$. The bound M_λ is thus suitable and we may conclude $\hat{y} \in Y_{pN}$. □

Again, if the feasible set is also $\mathbb{R}^n_{\geqslant 0}$-convex then the converse of Theorem 3.15 holds as well.

THEOREM 3.16. *If the feasible set $Y \subseteq \mathbb{R}^n$ is $\mathbb{R}^n_{\geqslant 0}$-convex, then $Y_{pN} \subseteq WS(Y)$.*

Proof. See Ehrgott (2005) for a proof. □

Summarizing the above results, if the feasible set $Y \subseteq \mathbb{R}^n$ is $\mathbb{R}^n_{\geqslant 0}$-convex then

$$WS(Y) = Y_{pN} \subseteq Y_N \subseteq Y_{wN} = WS_0(Y). \tag{3.3.5}$$

Another fundamental result that we need is the following.

THEOREM 3.17 (Hartley)**.** *If the feasible set $Y \subseteq \mathbb{R}^n$ is nonempty, $\mathbb{R}^n_{\geqslant 0}$-compact and $\mathbb{R}^n_{\geqslant 0}$-convex, then*
$$WS(Y) \subseteq Y_N \subseteq \overline{WS(Y)}. \tag{3.3.6}$$

Proof. A proof can be found in Hartley (1978). □

Theorem 3.17 implies that for a nonempty, $\mathbb{R}^n_{\geqslant 0}$-compact and $\mathbb{R}^n_{\geqslant 0}$-convex set $Y \subseteq \mathbb{R}^n$ the gap between the sets Y_N and Y_{pN} is not large. In fact, every nondominated point is the limit point of some sequence of properly nondominated points. This also leads to the next result.

COROLLARY 3.18. *If the feasible set $Y \subseteq \mathbb{R}^n$ in the criterion space is a nonempty, $\mathbb{R}^n_{\geqslant 0}$-compact and $\mathbb{R}^n_{\geqslant 0}$-convex set, then $Y_{pN} \neq \varnothing$.*

Proof. Suppose $Y_{pN} = \varnothing$. Since Y is nonempty, $\mathbb{R}^n_{\geqslant 0}$-compact and $\mathbb{R}^n_{\geqslant 0}$-convex we know by Theorem 3.17 that $\varnothing \subseteq Y_N \subseteq \overline{\varnothing}$, so that $Y_N = \varnothing$. The latter is in contradiction with Theorem 3.6, which states $Y_N \neq \varnothing$ since Y is nonempty and $\mathbb{R}^n_{\geqslant 0}$-compact. □

3.3.2 Connectedness of the optimal sets

Before we can introduce the connectedness results, we need conditions for the feasible set X and the criterion function f which assure that $Y = f(X)$ is $\mathbb{R}^n_{\geqslant 0}$-convex, so that we can utilize the results from the last section. We also need another result concerning connected sets which is presented in Warburton (1983).

LEMMA 3.19. *If the feasible set $X \subseteq \mathbb{R}^m$ is convex and the criterion function $f : X \to \mathbb{R}^n$ is given by $f(x) = (f_1(x), \ldots, f_n(x))$, for which $f_i : X \to \mathbb{R}$ is convex for all $i \in [n]$. Then the feasible set $Y \subseteq \mathbb{R}^n$ in the criterion space is $\mathbb{R}^n_{\geqslant 0}$-convex.*

Proof. We need to show that the set $f(X)$ is $\mathbb{R}^n_{\geqslant 0}$-convex, that is, $f(X) + \mathbb{R}^n_{\geqslant 0}$ is convex. Let $z^1, z^2 \in f(X) + \mathbb{R}^n_{\geqslant 0}$, then there are $y^1, y^2 \in f(X)$ and $r^1, r^2 \in \mathbb{R}^n_{\geqslant 0}$ such that

$$\begin{aligned} z^1 &= y^1 + r^1, \\ z^2 &= y^2 + r^2. \end{aligned}$$

Since $y^1, y^2 \in f(X)$ there are $x^1, x^2 \in X$ such that $f(x^1) = y^1$ and $f(x^2) = y^2$. Now

$$\begin{aligned} \alpha z^1 + (1-\alpha)z^2 &= \alpha y^1 + (1-\alpha)y^2 + \alpha r^1 + (1-\alpha)r^2 \\ &= \alpha f(x^1) + (1-\alpha)f(x^2) + \alpha r^1 + (1-\alpha)r^2 \\ &= f(\alpha x^1 + (1-\alpha)x^2) + \big(\alpha f(x^1) + (1-\alpha)f(x^2) - f(\alpha x^1 + (1-\alpha)x^2)\big) \\ &\quad + \big(\alpha r^1 + (1-\alpha)r^2\big). \end{aligned}$$

Since for every $i \in [n]$ the function f_i is convex, we have

$$\alpha f_i(x^1) + (1-\alpha)f_i(x^2) - f_i(\alpha x^1 + (1-\alpha)x^2) \geqslant 0.$$

This implies that $\alpha f(x^1) + (1-\alpha)f(x^2) - f(\alpha x^1 + (1-\alpha)x^2) \in \mathbb{R}^n_{\geqslant 0}$. Also $\alpha r^1 + (1-\alpha)r^2 \in \mathbb{R}^n_{\geqslant 0}$ since $\mathbb{R}^n_{\geqslant 0}$ is a convex set. Define

$$r_\alpha := \big(\alpha f(x^1) + (1-\alpha)f(x^2) - f(\alpha x^1 + (1-\alpha)x^2)\big) + \big(\alpha r^1 + (1-\alpha)r^2\big),$$

and observe that $r_\alpha \in \mathbb{R}^n_{\geqslant 0}$.

So, we have

$$\alpha z^1 + (1-\alpha)z^2 = f(\alpha x^1 + (1-\alpha)x^2) + r_\alpha \in f(X) + \mathbb{R}^n_{\geqslant 0}.$$

We may conclude that $f(X)$ is $\mathbb{R}^n_{\geqslant 0}$-convex. □

Now that we have sufficient conditions for $f(X)$ to be $\mathbb{R}^n_{\geqslant 0}$-convex we state the next theorem from Warburton (1983) concerning connectedness and preimages.

THEOREM 3.20. *Let* $V \subseteq \mathbb{R}^m$ *be compact and* $W \subseteq \mathbb{R}^n$ *be connected. Suppose that* $h : V \times W \to \mathbb{R}$ *is a continuous function and denote for every* $w \in W$ *the set*

$$S(w) := \{\hat{v} \in V \mid h(\hat{v}, w) = \min_{v \in V} h(v, w)\}.$$

If $S(w)$ *is connected for all* $w \in W$ *then*

$$\bigcup_{w \in W} S(w)$$

is connected.

Proof. A proof can be found in Warburton (1983). □

Now, the connectedness results can be presented. We start with the connectedness of the weakly Pareto optimal set.

THEOREM 3.21. *If the feasible set* $X \subseteq \mathbb{R}^m$ *in the decision space is a convex and compact set, and if the criteria* $f_i : \mathbb{R}^m \to \mathbb{R}$ *are convex for all* $i \in [n]$*, then* X_{wP} *is connected.*

Proof. If $X = \emptyset$, this is straightforward. Therefore, assume that we deal with a nonempty feasible set X.

Since the f_i are convex on $\mathbb{R}^m$, they are also continuous on $\mathbb{R}^m$ due to Theorem 2.14. Therefore f is continuous, and since X is compact, we may conclude that $Y = f(X)$ is compact (by Lemma 2.8). Since X is convex and the f_i are convex, it follows that Y is $\mathbb{R}^n_{\geqslant 0}$-convex by Lemma 3.19.

Now, by combining Lemma 3.12 and Theorem 3.13, we conclude that $Y_{wN} = WS_0(Y)$. Or equivalently,

$$X_{wP} = \bigcup_{\lambda \in \mathbb{R}^n_{\geqslant 0} \setminus \{0\}} \{\hat{x} \in X \mid \lambda^T f(\hat{x}) = \min_{x \in X} \lambda^T f(x)\}.$$

The idea is to apply Theorem 3.20 with $V = X$, $W = \mathbb{R}^n_{\geqslant 0} \setminus \{0\}$ and $h : X \times \mathbb{R}^n_{\geqslant 0} \setminus \{0\} \to \mathbb{R}$ given by $h(x, \lambda) = \lambda^T f(x)$. Observe that indeed, X is compact, $\mathbb{R}^n_{\geqslant 0} \setminus \{0\}$ is connected (Example 2.2) and h is continuous. Now we can write

$$X_{wP} = \bigcup_{\lambda \in \mathbb{R}^n_{\geqslant 0} \setminus \{0\}} \{\hat{x} \in X \mid h(\hat{x}, \lambda) = \min_{x \in X} h(x, \lambda)\}.$$

By defining for every $\lambda \in \mathbb{R}^n_{\geqslant 0} \setminus \{0\}$ the set

$$S(\lambda) := \{\hat{x} \in X \mid h(\hat{x}, \lambda) = \min_{x \in X} h(x, \lambda)\},$$

the set of weakly Pareto optimal points can be denoted by

$$X_{wP} = \bigcup_{\lambda \in \mathbb{R}^n_{\geqslant 0} \setminus \{0\}} S(\lambda).$$

Before we can conclude that X_{wP} is connected, we need to verify that the set $S(\lambda)$ is connected for all $\lambda \in \mathbb{R}^n_{\geqslant 0} \setminus \{0\}$. For every such a λ, define the function $\tilde{h}_\lambda : X \to \mathbb{R}$ by

$$\tilde{h}_\lambda(x) = h(x, \lambda) = \lambda^T f(x).$$

Since X is a nonempty compact set, and $\tilde{h}_\lambda$ is continuous, it attains it minimum on X (due to Theorem 2.10). So $S(\lambda)$ is equal to

$$S(\lambda) = \{x \in X \mid h(\hat{x}, \lambda) = \inf_{x \in X} h(x, \lambda)\}.$$

Now, X is closed (by compactness), convex and $\tilde{h}_\lambda$ is convex (by Lemma 2.13), hence Lemma 2.15 implies that $S(\lambda)$ is convex. By Corollary 2.11, $S(\lambda)$ is connected.

All conditions of Theorem 3.20 are now satisfied, hence we may conclude that X_{wP} is connected. □

Next, we prove the connectedness of the properly Pareto optimal set.

COROLLARY 3.22. *If the feasible set $X \subseteq \mathbb{R}^m$ in the decision space is a convex and compact set, and if the criteria $f_i : \mathbb{R}^m \to \mathbb{R}$ are convex for all $i \in [n]$, then X_{pP} is connected.*

Proof. This proof is similar to the proof given for Theorem 3.21. The only difference is that we now apply Theorem 3.15 and Theorem 3.16. Since Y is again $\mathbb{R}^n_{\geqslant 0}$-convex, we may conclude $Y_{pN} = WS(Y)$ or

$$X_{pP} = \bigcup_{\lambda \in \mathbb{R}^n_{>0}} \{\hat{x} \in X \mid \lambda^T f(\hat{x}) = \min_{x \in X} \lambda^T f(x)\}.$$

We again resort to Theorem 3.20, however we now have $W = \mathbb{R}^n_{>0}$. The theorem can still be applied since $\mathbb{R}^n_{>0}$ is convex hence connected (see also Example 2.2). □

Finally, we want to obtain a connectedness result for the Pareto optimal set. We start with the following observation.

LEMMA 3.23. *Suppose $\hat{x} \in X_{wP}$ is the unique solution of* (3.3.1) *for some $\lambda \in \mathbb{R}^n_{\geqslant 0} \setminus \{0\}$ then $\hat{x} \in X_P$.*

Proof. If $\hat{x} \notin X_P$ then there must be a $x \in X$ such that $f(x) \leqslant f(\hat{x})$ and $f_j(x) < f_j(\hat{x})$ for at least one $j \in [n]$. So certainly

$$\lambda^T f(x) \leqslant \lambda^T f(\hat{x}).$$

But now $x \in X$ solves (3.3.1) and $x \neq \hat{x}$ contradicting the uniqueness. Hence $\hat{x} \in X_P$. □

Combining Lemma 3.23 and a more restrictive condition for the criteria, namely strict convexity, we can guarantee that the set of Pareto optimal points is connected.

THEOREM 3.24. *If the feasible set $X \subseteq \mathbb{R}^m$ in the decision space is a convex and compact set, and if the criteria $f_i : \mathbb{R}^m \to \mathbb{R}$ are strictly convex for all $i \in [n]$, then X_P is connected.*

Proof. Since the assumptions in Theorem 3.21 are satisfied, X_{wP} is connected. We show that with the conditions in this theorem, it holds that

$$X_P = X_{wP},$$

which is sufficient to prove connectedness for X_P.

Since it is always holds true that $X_P \subseteq X_{wP}$, we only need to show the other inclusion. To that end, let $\hat{x} \in X_{wP}$. The analog of Theorem 3.13 in the decision space (explicitly given in Theorem 4.1) implies that there must be a $\hat{\lambda} \in \mathbb{R}^n_{\geqslant 0} \setminus \{0\}$ such that $\hat{x} \in X_{wP}$ solves (3.3.1).

Also, the objective function $\hat{\lambda}^T f(x)$ in the weighted sum scalarization (3.3.1) is strictly convex because of the strict convexity of the criteria and Lemma 2.13. Hence, Lemma 2.16 implies that $\hat{x} \in X_{wP}$ uniquely solves (3.3.1).

Combining these observations, we note that Lemma 3.23 is applicable. We may conclude that $\hat{x} \in X_P$ and so, X_P is connected.

□

Now that we have derived connectedness results for the solution concepts in the decision space, we can immediately conclude that the optimal sets in the criterion space must be connected as well.

COROLLARY 3.25. *If the feasible set $X \subseteq \mathbb{R}^m$ in the decision space is a convex and compact set, and if the criteria $f_i : \mathbb{R}^m \to \mathbb{R}$ are convex for all $i \in [n]$, then the sets X_{wP}, X_{pP}, Y_{wN} and Y_{pN} are connected.*

If, in addition, the criteria $f_i : \mathbb{R}^m \to \mathbb{R}$ are strictly convex for all $i \in [n]$, then X_P and Y_N are also connected.

Proof. Since f is continuous (Theorem 2.14) and the image of a connected set under a continuous mapping is again connected (Lemma 2.6), this corollary is justified. □

Actually, for the connectedness of Y_N it is sufficient that the criteria are convex.

COROLLARY 3.26. *If the feasible set $X \subseteq \mathbb{R}^m$ in the decision space is a convex and compact set, and if the criteria $f_i : \mathbb{R}^m \to \mathbb{R}$ are convex for all $i \in [n]$, then Y_N is connected.*

Proof. If $X = \varnothing$, this is straightforward. Therefore, assume $X \neq \varnothing$.

From Corollary 3.25 we have that Y_{pN} is connected. Since Y is a nonempty compact and $\mathbb{R}^n_{\geqslant 0}$-convex set, we may certainly apply Theorem 3.17. This theorem states

$$WS(Y) \subseteq Y_N \subseteq \overline{WS(Y)}.$$

Together with Theorem 3.15 and Theorem 3.16 we have

$$Y_{pN} \subseteq Y_N \subseteq \overline{Y_{pN}},$$

so that the connectedness of Y_N follows from Lemma 2.4. □

Note that from Corollary 3.26 we may not conclude that under the same assumptions the set X_P is connected, since the preimage of a connected set under a continuous function is not necessarily connected.

Notice that all these proofs still work if we replace the convexity condition of the criterion functions $f_i : \mathbb{R}^m \to \mathbb{R}$ by f_i being both (strictly) convex and continuous on $X \subseteq \mathbb{R}^m$ which may be more easily to verify in practice.

3.4 Conclusions on existence and connectedness of the optimal sets

In this chapter we explored the fundamental concepts and properties of multicriteria optimization. More specifically, we investigated multicriteria optimization problems of the form

$$\min_{x \in X} f(x),$$

where $X \subseteq \mathbb{R}^m$ is the feasible set and $f : \mathbb{R}^m \to \mathbb{R}^n$ is the criteria vector function.

The main conclusions for multicriteria optimization problems on existence and connectedness of the weakly Pareto optimal set X_{wP}, weakly nondominated set Y_{wN}, Pareto optimal set X_P, nondominated set Y_N, properly Pareto optimal set X_{pP} and properly nondominated set Y_{pN} are gathered in the next summary.

SUMMARY. If the feasible set $X \subseteq \mathbb{R}^m$ in the decision space is a nonempty convex and compact set, and if either

1. the criteria $f_i : \mathbb{R}^m \to \mathbb{R}$ are convex for all $i \in [n]$ or

2. the criteria $f_i : X \to \mathbb{R}$ are convex and continuous for all $i \in [n]$,

then

I X_{wP}, X_P, X_{pP}, Y_{wN}, Y_N and Y_{pN} are nonempty,

II X_{wP}, X_{pP}, Y_{wN}, Y_N and Y_{pN} are connected,

III X_P is connected if, in addition, all the criteria are strictly convex.

In practice, the most common notion of optimality is Pareto optimality and nondominance. It is desired to have the nonemptyness and connectedness property for both the set of Pareto optimal points and the set of nondominated points (of which the latter is more important). Sufficient conditions for the decision space X and the criteria f_i ($i \in [n]$) have been imposed which ensure these properties. This makes checking upon them worthwhile.

CHAPTER 4

Multicriteria methods

In this chapter, several methods are presented that generate Pareto optimal solutions for a multicriteria optimization problem

$$\min_{x \in X} f(x) = \min_{x \in X} (f_1(x), \dots, f_n(x)).$$

In the literature, for example in Ehrgott (2005) and Mietinnen (1999), plenty of multicriteria methods are mentioned and analyzed. We will focus on a few of these multicriteria methods.

We start with the *weighted sum method* which we already used in Chapter 3 to identify both the weakly and properly nondominated set.

Also, the *ϵ-constraint method* is presented as a multicriteria method. In particular, we present the *2-phase ϵ-constraint (2pϵc) method*, which involves solving a sequence of ϵ-constraint problems. The 2pϵc method is of major importance in this thesis since it is in clinical use at the Erasmus MC - Cancer Institute to automatically generate treatment plans for cancer patients, see Breedveld et al. (2007, 2009). This particular application is discussed in more depth in Chapter 5 and Chapter 6.

Finally, the *reference point method* (RPM) is presented. The RPM was originally developed by Wierzbicki (1986) and is often used as an interactive technique. We do not focus on interactive techniques, but instead use the RPM formulation in Ogryczak and Kozłowski (2009). In Chapter 6, we attempt to configure the RPM for the application in radiation therapy.

Of these methods, the weighted sum and ϵ-constraint method are common approaches for solving multicriteria optimization problems of the form:

$$\min_{x \in X} f(x).$$

The basic idea behind all multicriteria methods is to design a scalarization of the criterion vector function $f : \mathbb{R}^m \to \mathbb{R}^n$, say by a *utility function* $U : \mathbb{R}^n \to \mathbb{R}$. This utility function should represent the preferences of the decision maker (DM) concerning the outcomes in the criterion space. Without loss of generality, we assume that low values of the utility function represent more preferable outcomes than high values of the utility function. Then, the single criterion optimization problem

$$\min_{x \in X} U(f(x)), \tag{4.0.1}$$

is solved to obtain a preferable solution. Assuming that the criteria are convex, we make sure that the optimization problem (4.0.1) is also convex. This means that the single criterion optimization problem (4.0.1) falls into the class *nonlinear convex optimization*, thus having the pleasant properties mentioned in Chapter 2.

The mapping U should be chosen carefully, as we want the solution of minimization problem (4.0.1) to be a (weakly) Pareto optimal point. For utility functions, it is common to introduce additional scalar or vector parameters which generate different Pareto optimal points when adapted.

4.1 Weighted sum method

In this section, the weighted sum method is explained. In Chapter 3 we investigated which optimal points can be found by solving a weighted sum problem:

$$\min_{x \in X} \sum_{i \in [n]} \lambda_i f_i(x), \tag{4.1.1}$$

where $\lambda \in \mathbb{R}^n_{\geqslant 0} \setminus \{0\}$. It turns out that it is convenient for the feasible set Y in the criterion space to be $\mathbb{R}^n_{\geqslant 0}$-convex, a condition that is satisfied when the feasible set X in the decision space is a convex set and the criteria $f_i : X \to \mathbb{R}$ are convex for all $i \in [n]$ (Lemma 3.19). The results are summarized in Theorem 4.1.

THEOREM 4.1. *Suppose that $\hat{x} \in X$ is the optimal solution of* (4.1.1) *then*

- $\hat{x} \in X_{pP}$ *if* $\lambda \in \mathbb{R}^n_{>0}$,
- $\hat{x} \in X_{wP}$ *if* $\lambda \in \mathbb{R}^n_{\geqslant 0} \setminus \{0\}$,
- $\hat{x} \in X_P$ *if* $\lambda \in \mathbb{R}^n_{\geqslant 0} \setminus \{0\}$ *and $\hat{x}$ is the unique optimal solution.*

If in addition, X is convex and $f_i : X \to \mathbb{R}$ is convex for all $i \in [n]$ then

- *there is a $\lambda \in \mathbb{R}^n_{>0}$ such that $\hat{x}$ solves* (4.1.1) *if $\hat{x} \in X_{pP}$,*
- *there is a $\lambda \in \mathbb{R}^n_{\geqslant 0} \setminus \{0\}$ such that $\hat{x}$ solves* (4.1.1) *if $\hat{x} \in X_{wP}$.*

Proof. This is due to Lemma 3.23 and the analogies of Lemma 3.12, Theorem 3.13, Theorem 3.15 and Theorem 3.16 in terms of the decision space. □

The weighted sum method is the most well known scalarization method in multicriteria optimization and also one of the easiest to understand. In Figure 4.1 the basic principle of the weighted sum method is illustrated graphically.

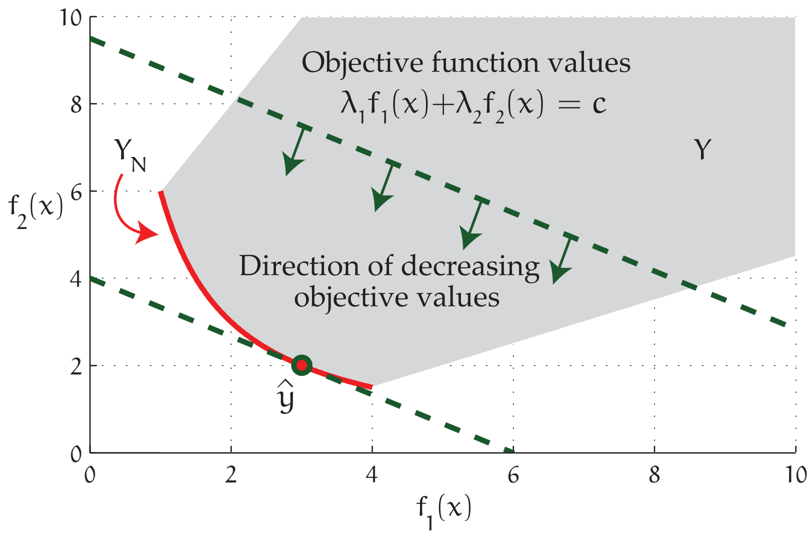

FIGURE 4.1: Illustration of the weighted sum method where $Y \subseteq \mathbb{R}^2$ and $(\lambda_1, \lambda_2) = (2, 3)$. The dotted lines represent the indifference curves of the objective function values. With these parameters, the solution of (4.1.1) is given by $f(\hat{x}) = \hat{y} \in Y_N$.

Without Y being $\mathbb{R}^n_{\geqslant 0}$-convex, the weighted sum method may fail to generate a solution. In Example 3.2 note that Y is not $\mathbb{R}^2_{\geqslant 0}$-convex and that the weighted sum is theoretically unable to find any solution (meaning that $\min_{x \in X} \sum_{i \in [n]} \lambda_i f_i(x) = -\infty$ for all $\lambda \in \mathbb{R}^n_{\geqslant 0} \setminus \{0\}$).

Before applying the weighted sum method in practice, it is thus important that feasible set Y is $\mathbb{R}^n_{\geqslant 0}$-convex. The latter may be hard to verify in practice, however Lemma 3.19 provides a sufficient condition. It namely suffices that the feasible set X in the criterion space is convex as well as all criteria, which can be verified more easily. Applying the weighted sum method for feasible sets Y, which are not $\mathbb{R}^n_{\geqslant 0}$-convex, may result into extremities.

4.2 ϵ-Constraint method

Another multicriteria method is called the ϵ-constraint method. This method focuses on minimizing one of the criteria while keeping the others constrained. For these criteria, upper bounds are provided which are the additional parameters in the ϵ-constraint method.

The main idea of the ϵ-constraint method is that we minimize a criterion f_j for some $j \in [n]$ while providing *feasible upper bounds* ϵ_k for the other criteria. The latter means that

$$\bigcap_{k \in [n] \setminus \{j\}} \{y \in Y \mid y_k \leqslant \epsilon_k\} \neq \varnothing.$$

Then the ϵ-constraint method is formulated as follows:

$$\begin{aligned} \min_{x\in X} \quad & f_j(x) \\ \text{subject to} \quad & f_k(x) \leqslant \epsilon_k \quad k \in [n] \setminus \{j\}. \end{aligned} \tag{4.2.1}$$

The ϵ-constraint method thus can be used when feasible upper bounds are known. Figure 4.2 illustrates the basic principle of the ϵ-constraint method.

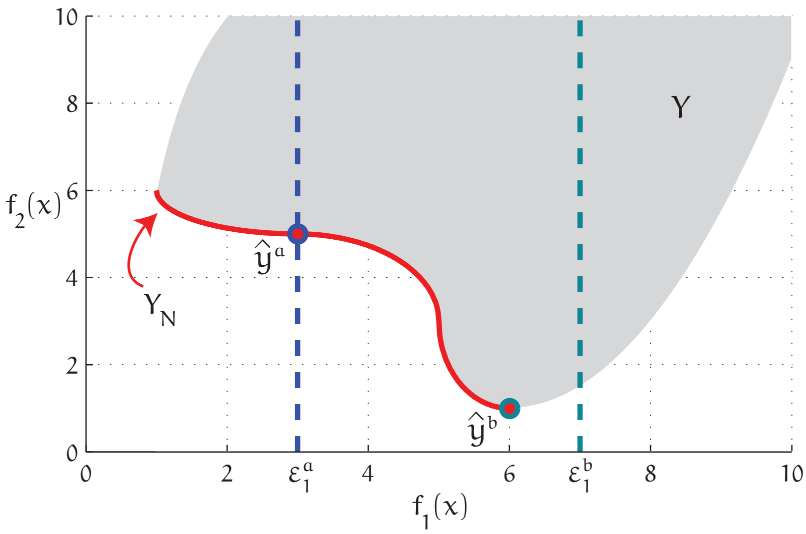

FIGURE 4.2: Illustration of the ϵ-constraint method where $Y \subseteq \mathbb{R}^2$. The nondominated point $\hat{y}^a$ is the solution of minimizing $f_2(x)$ subject to $f_1(x) \leqslant \epsilon_1^a$. Similarly, minimizing $f_2(x)$ subject to $f_1(x) \leqslant \epsilon_1^b$ leads to the nondominated point $\hat{y}^b$.

Solving (4.2.1) generally only leads to a weak Pareto optimal solution of a multicriteria optimization problem. If, in addition, the solution of (4.2.1) is unique then Pareto optimality can be guaranteed.

THEOREM 4.2. *Suppose that $\hat{x} \in X$ is an optimal solution of the ϵ-constraint problem* (4.2.1), *then*

- $\hat{x} \in X_{wP}$,
- $\hat{x} \in X_P$ *if the optimal solution $\hat{x}$ is unique.*

Proof. These results can be proven by contradiction.

- Suppose $\hat{x} \notin X_{wP}$, that is, there is an $x \in X$ such that $f(x) < f(\hat{x})$. We have

$$\begin{aligned} & f_j(x) < f_j(\hat{x}), \\ & f_k(x) \leqslant f_k(\hat{x}) \leqslant \epsilon_k, \text{ for all } k \in [n] \setminus \{j\}, \end{aligned}$$

which contradicts the optimality of $\hat{x}$ in the ϵ-constraint problem (4.2.1). So, $\hat{x}$ must be weakly Pareto optimal.

- Suppose $\hat{x} \notin X_P$ meaning that there is an $x \in X$ such that $f(x) \leqslant f(\hat{x})$ and $f_l(x) < f_l(\hat{x})$ for at least one $l \in [n]$. Consider the next cases.
  - If $l = j$ in (4.2.1), we have

$$\begin{aligned} &f_l(x) < f_l(\hat{x}), \\ &f_k(x) \leqslant f_k(\hat{x}) \leqslant \epsilon_k, \text{ for all } k \in [n] \setminus \{j\}, \end{aligned}$$

    which contradicts the optimality of the solution $\hat{x}$ in (4.2.1).
  - If $l \neq j$ in (4.2.1) then we have

$$\begin{aligned} &f_j(x) \leqslant f_j(\hat{x}), \\ &f_k(x) \leqslant f_k(\hat{x}) \leqslant \epsilon_k, \text{ for all } k \in [n] \setminus \{j, l\}, \\ &f_l(x) < f_l(\hat{x}) \leqslant \epsilon_l. \end{aligned}$$

    So x solves the ϵ-constraint problem (4.2.1). Uniqueness implies that $x = \hat{x}$, but then $f(x) = f(\hat{x})$ which contradicts that there is a $l \in [n]$ with $f_l(x) < f_l(\hat{x})$.

  We may conclude that $\hat{x} \in X_P$.

□

Another way to verify Pareto optimality is the following: if we assume that there is a parameter vector $\epsilon = (\epsilon_1, \dots, \epsilon_n) \in \mathbb{R}^n$ for which an $\hat{x} \in X$ exists such that it solves the ϵ-constraint method (4.2.1) for every $j \in [n]$ then $\hat{x}$ must be Pareto optimal. Actually, these statements are equivalent.

THEOREM 4.3. *Let $\hat{x} \in X$, then $\hat{x} \in X_P$ if and only if there is a parameter vector $\epsilon \in \mathbb{R}^n$ such that $\hat{x}$ solves* (4.2.1) *for every $j \in [n]$.*

Proof. Both implications are proven by contraposition.

"$\Rightarrow$" Suppose that there is a $j \in [n]$ for which $\hat{x}$ does not solve (4.2.1) and note that $\epsilon = f(\hat{x})$ imposes feasible upper bounds. Since $\hat{x}$ does not solve (4.2.1), there must be a $x \in X$ for which $f_j(x) < f_j(\hat{x})$ and $f_k(x) \leqslant \epsilon_k = f_k(\hat{x})$ for all $k \in [n] \setminus \{j\}$, hence $\hat{x} \notin X_P$.

"$\Leftarrow$" Suppose $x \notin X_P$ then there is a $x \in X$ and $j \in [n]$ with $f_j(x) < f_j(\hat{x})$ and $f_k(x) \leqslant f_k(\hat{x})$ for all $k \in [n] \setminus \{j\}$. Now, if $\epsilon \in \mathbb{R}^n$ is a feasible upper bound then $\hat{x}$ does not solve (4.2.1). If $\epsilon \in \mathbb{R}^n$ is a infeasible upper bound then (4.2.1) has no solutions. Either way, $\hat{x}$ can never solve (4.2.1) for $j \in [n]$. □

Appropriately chosen parameters $\epsilon \in \mathbb{R}^n$ thus enable us to find all Pareto optimal solutions without any additional conditions. In particular, the ϵ-constraint method is able to find all Pareto optimal solution when Y is not $\mathbb{R}^n_{\geqslant 0}$-convex (as in Example 3.2) in contrast to the weighted sum method. However, to find the right parameters $\epsilon \in \mathbb{R}^n$ in Theorem 4.3 for generating a Pareto optimal point $\hat{x} \in X_P$ one must set $\epsilon = f(\hat{x})$. In other words, you can only choose the right parameters if you already know the Pareto optimal point you would like to find. So Theorem 4.3 should only be used to check whether an already obtained feasible point $x \in X$ is Pareto optimal or not.

The main advantage of the ϵ-constraint method is that every Pareto optimal point can be found without imposing any additional assumptions. The disadvantage of this method is that it is unclear how to choose feasible upper bounds. This problem can solved by introducing the sequential use of the ϵ-constraint method. An example of such an extension is the 2-phase ϵ-constraint method which, in addition, uses certain predefined thresholds for the criteria that are considered sufficiently low.

4.2.1 2-Phase ϵ-constraint method

The 2-phase ϵ-constraint (2pϵc) method sequentially uses the ϵ-constraint method to solve a multicriteria optimization problem. The basic idea of the 2pϵc method is to steer towards a desired solution. To achieve this, the 2pϵc method assigns predefined goal values (or *aspiration points*) to the criteria and sorts these by priority. The 2pϵc method thus repeatedly solves an optimization problem of the form (4.2.1) and gradually adds feasible upper bounds ϵ_i ($i \in [n]$) for subsequent optimizations.

Before the 2pϵc method can be applied to a multicriteria optimization problem, the criteria need to be prioritized and goal values need to be assigned to each priority. This information is gathered in a prioritized list, which we refer to as a *wish-list*. A general wish-list is given in Table 4.1. Here, $n \leqslant p \in \mathbb{N}$ and $\sigma : [p] \to [n]$ imposes the prioritized structure of the criteria.

TABLE 4.1: General wish-list for the 2pϵc method.

Priority	Criterion	Goal value
1	$f_{\sigma(1)}(x)$	b_1
2	$f_{\sigma(2)}(x)$	b_2
$\vdots$	$\vdots$	$\vdots$
n	$f_{\sigma(n)}(x)$	b_n
$\vdots$	$\vdots$	$\vdots$
p	$f_{\sigma(p)}(x)$	b_p

Every criterion should appear at least once in the wish-list. If the same criterion appears multiple times in Table 4.1, the corresponding goal values should be strictly descending since the criteria are minimized. Obviously, two consecutive priorities always concern different criteria.

The 2pϵc method consists of two phases. In the first phase, the goal values in Table 4.1 are met as well as possible (in order of priority). In the second phase, every criterion is fully minimized (in order of priority) to obtain the final solution.

With Table 4.1, the first phase starts by solving the following ϵ-constraint problem,

$$\min_{x \in X} \quad f_{\sigma(1)}(x). \tag{4.2.2}$$

Suppose that $\hat{x} \in X$ solves (4.2.2). We then define the next upper bound for $f_{\sigma(1)}(x)$,

$$\epsilon_1 := \max(b_1, \delta f_{\sigma(1)}(\hat{x})), \tag{4.2.3}$$

where $\delta \geqslant 1$ is a relaxation parameter. If $\epsilon_1 = b_1$, the goal value b_1 is not only feasible but also leaves sufficient space for the lower prioritized criteria to meet their goal values as well as possible. If, on the other hand, $\epsilon_1 = \delta f_{\sigma(1)}(\hat{x})$ the goal value b_1 was not feasible or did not leave sufficient space for the subsequent priorities.

Depending on the result of the first optimization, a second ϵ-constraint problem is solved

$$\begin{aligned} \min_{x \in X} \quad & f_{\sigma(2)}(x) \\ \text{subject to} \quad & f_{\sigma(1)}(x) \leqslant \epsilon_1. \end{aligned} \tag{4.2.4}$$

Similarly as ϵ_1, the upper bound ϵ_2 for $f_{\sigma(2)}$ is then defined as

$$\epsilon_2 := \max(b_2, \delta f_{\sigma(2)}(\hat{x})), \tag{4.2.5}$$

which depends on the solution $\hat{x} \in X$ of (4.2.4) and goal value b_2. This process is repeated until all p priorities in Table 4.1 have been processed.

In the second phase, the criteria are minimized to their fullest in order of their priorities in Table 4.1. The ϵ-constraint problems in the second phase utilizes the upper bounds obtained from the first phase. The ϵ-constraint problem

$$\begin{aligned} \min_{x \in X} \quad & f_{\sigma(1)}(x) \\ \text{subject to} \quad & f_{\sigma(k)}(x) \leqslant \epsilon_k, \quad k \in [p] \setminus \{1\}. \end{aligned} \tag{4.2.6}$$

is solved to initialize phase two. The solution $\hat{x} \in X$ of (4.2.6) is used to set a new upper bound for $f_{\sigma(1)}$,

$$\bar{\epsilon}_1 := \min(\epsilon_1, \delta f_{\sigma(1)}(\hat{x})). \tag{4.2.7}$$

Note that the new upper bound $\bar{\epsilon}_1$ (4.2.7) cannot be worse than the upper bound ϵ_1, obtained in the first phase (4.2.3).

This process continues till the last ϵ-constraint problem in the 2pϵc method,

$$\begin{aligned} \min_{x \in X} \quad & f_{\sigma(p)}(x) \\ \text{subject to} \quad & f_{\sigma(k)}(x) \leqslant \bar{\varepsilon}_k, \quad k \in [p-1], \end{aligned} \tag{4.2.8}$$

is solved. The solution $\hat{x} \in X$ of (4.2.8) is then the final solution of the 2pϵc method.

Note that Theorem 4.2 and Theorem 4.3 also hold for the 2pϵc method since the last optimization in the 2pϵc method is an ϵ-constraint problem. Also, some ϵ-constraint minimization problems may not be necessary to process. For instance, if the result of previous optimization already turns out to be lower than the implied goal. Also, we ignore a priority if the relaxation already has been applied to the corresponding criterion since we then know that the criterion cannot be improved by much, and may prevent other priorities in meeting their goal values as well as possible.

We conclude this section with an example which illustrates the basic principle of the 2pϵc method graphically.

EXAMPLE 4.1. In this example we consider a simplified version of Example 3.4. Suppose that the feasible set is $X = [0, 20]$ and the criteria $f_1, f_2 : \mathbb{R} \to \mathbb{R}$ are given by

$$\begin{aligned} f_1(x) &= \frac{1}{2}x + 1, \\ f_2(x) &= \max\left(2,\ 8 - x,\ \frac{1}{2}x - 2\right). \end{aligned} \tag{4.2.9}$$

Also, suppose we use the wish-list in Table 4.2.

TABLE 4.2: Wish-list for Example 4.1.

Priority	Criterion	Goal value
1	$f_1(x)$	10
2	$f_2(x)$	4
3	$f_1(x)$	2

With the data in Table 4.2 we can apply the 2pϵc method. In this example, we use $\delta = 1.1$ as a fixed relaxation parameter.

First phase; illustrated in Figure 4.3.

1. The first priority in Table 4.2 is to minimize f_1 to the goal value 10. So, we start by solving

$$\min_{x \in [0,20]} \quad f_1(x). \tag{4.2.10}$$

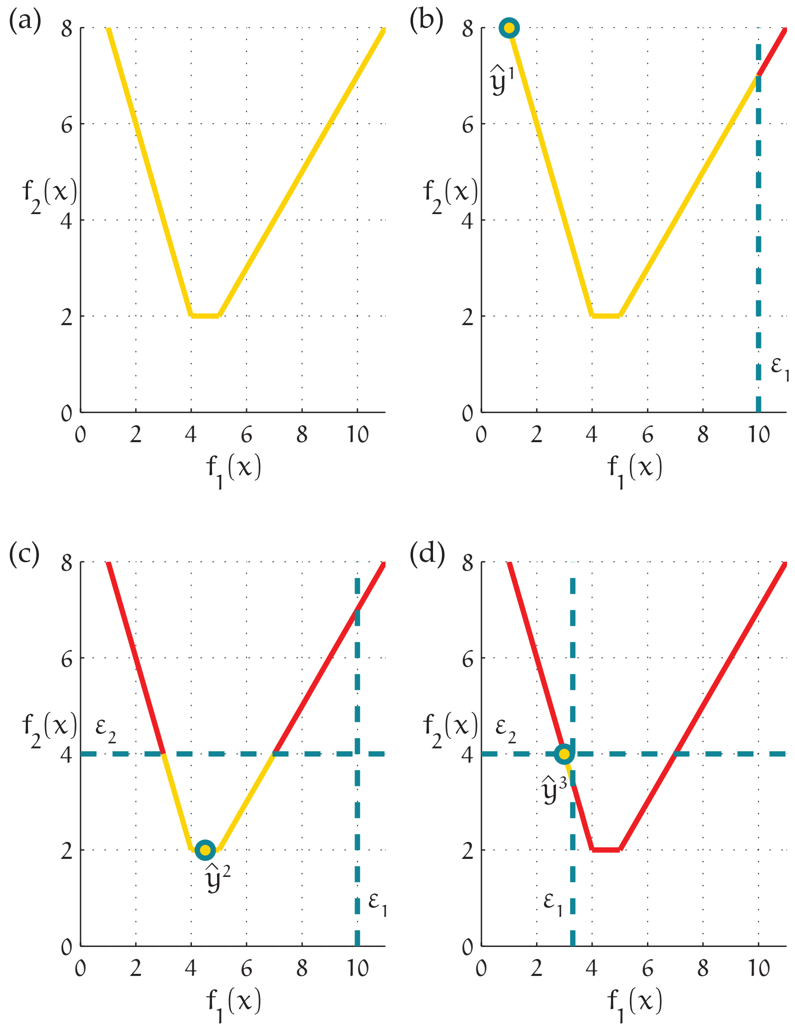

FIGURE 4.3: The first phase of the 2pϵc method. (a) The feasible set Y, (b) after solving (4.2.10) the upper bound $\epsilon_1 = 10$ is added for f_1, (c) the upper bound $\epsilon_2 = 4$ is added for f_2 due to minimization problem (4.2.11) and (d) the upper bound for f_1 is tightened to 3.3 because of minimization problem (4.2.12).

The optimal solution of (4.2.10) is $\hat{x}^1 = 0$ which corresponds to $\hat{y}^1 = (1, 8)$. Criterion f_1 can thus be minimized to 1, but since the goal value is 10, we set the following upper bound:

$$\epsilon_1 = \max(10, 1\delta) = 10.$$

2. According to the wish-list (Table 4.2) the following step is to minimize f_2 to the goal value 4. At the same time, the condition $f_1(x) \leqslant \epsilon_1$ needs to be satisfied. Therefore, we solve

the ϵ-constraint problem

$$\begin{aligned} \min_{x \in [0,20]} \quad & f_2(x) \\ \text{subject to} \quad & f_1(x) \leqslant 10. \end{aligned} \tag{4.2.11}$$

The minimization problem (4.2.11) has multiple optimal solutions, namely $\hat{x}^2 \in [6,8]$ leading to $\hat{y}^2 \in [4,5] \times \{2\}$. Regardless of that optimal solution we set the upper bound

$$\epsilon_2 = \max(4, 2\delta) = 4.$$

3. The last priority is to minimize f_1 to a goal value of 2 while the condition $f_2(x) \leqslant \epsilon_2$ is satisfied. We solve

$$\begin{aligned} \min_{x \in [0,20]} \quad & f_1(x) \\ \text{subject to} \quad & f_2(x) \leqslant 4. \end{aligned} \tag{4.2.12}$$

$\hat{x}^3 = 4$ is the optimal solution of (4.2.12) so that $\hat{y}^3 = (3,4)$. The goal value of 2 for f_1 is thus not feasible. In this case we get a new upper bound for f_1 namely

$$\epsilon_1 = \max(2, 3\delta) = 3.3.$$

Now, the first phase of the 2pϵc method has been processed. As a result we obtained the upper bounds

$$\begin{aligned} \epsilon_1 &= 3.3, \\ \epsilon_2 &= 4, \end{aligned}$$

for f_1 and f_2 respectively. These upper bounds will be utilized in the second phase.

Second phase; illustrated in Figure 4.4.

4. The second phase should start with minimizing f_1 to its fullest. However, this is unnecessary (in this case) since we already applied a relaxation to f_1 (last step in the first phase). Therefore, we skip minimizing f_1 to its fullest.

5. Next, f_2 is minimized to its fullest. The ϵ-constraint problem

$$\begin{aligned} \min_{x \in [0,20]} \quad & f_2(x) \\ \text{subject to} \quad & f_1(x) \leqslant 3.3, \end{aligned} \tag{4.2.13}$$

needs to be solved. This leads to the optimal solution $\hat{x}^5 = 4.6$ so that $\hat{y}^5 = (3.3, 3.4)$. We set the new upper bounds for f_2 of

$$\bar{\epsilon}_2 = \min(\epsilon_2, 3.4\delta) = 3.74.$$

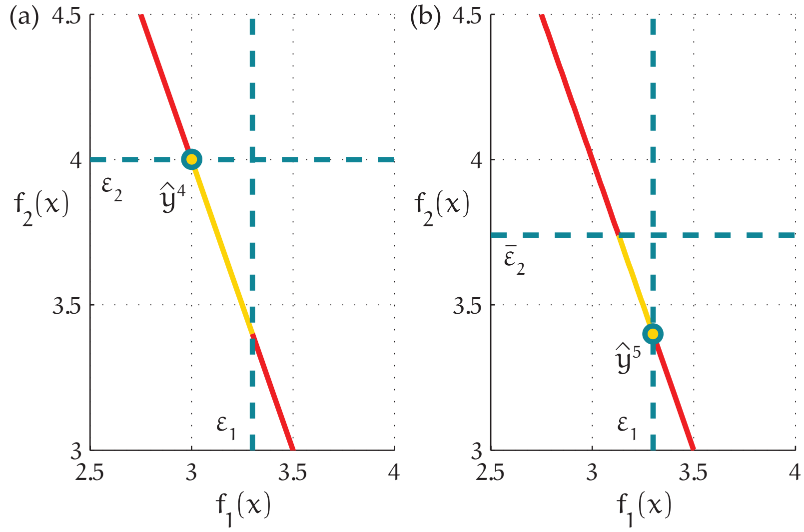

FIGURE 4.4: The second phase of the 2pϵc method. (a) Shows the situation after the first phase and (b) shows the result after minimization problem (4.2.13) which determines the final solution.

6. The last optimization (minimizing f_1 to its fullest) is again redundant, so we have $\hat{y}^6 = \hat{y}^5$.

The 2pϵc method thus produces the Pareto optimal solution $\hat{x} = 4.6$ which corresponds with criterion values $\hat{y} = (3.3, 3.4)$. Four ϵ-constraint problems (thus four optimizations) were needed to obtain the final solution.

4.3 Reference point method

In this section we describe the reference point method (RPM). Originally, the RPM uses a single *reference point* specified by the DM (Wierzbicki, 1986). A reference point is a vector containing aspiration points for each criterion. The reference point may be a feasible or infeasible point in the criterion space, and represents a preferable solution (according to the DM). The RPM then searches for a (weakly) nondominated point close to this reference point.

In Granat and Makowski (2000) and Ogryczak and Kozłowski (2009), the standard RPM is extended by introducing more reference points. In our application (Chapter 6), we will apply the RPM with multiple reference points. Therefore, we discuss the extension of the RPM in this section. First, the principle of the RPM is explained. Then, the corresponding minimization model is presented. Also, the additional parameters in the RPM are analyzed and we will provide an example. Finally, results concerning the (weak) Pareto optimality of the RPM are presented.

4.3.1 Principle of the RPM

For the RPM, the focus is on the feasible set Y in the criterion space. The basic idea is to specify a parametric curve (or *preferred path*) in the criterion space which reflects the preferences of the DM. In the RPM, such a path is constructed by specifying $p \in \mathbb{N}$ reference points in the criterion space. These reference points $r^1, \ldots, r^p \in \mathbb{R}^n$ impose a hierarchy. Reference point r^1 is the most important to attain, thus has the highest priority. If r^1 is attainable, r^2 is the second most important reference point to be attained, thus has the second highest priority. Reference point r^p is the least important point to be attained, thus has the lowest priority. Certainly, the criteria should only improve so $r^p < r^{p-1} < \ldots < r^2 < r^1$.

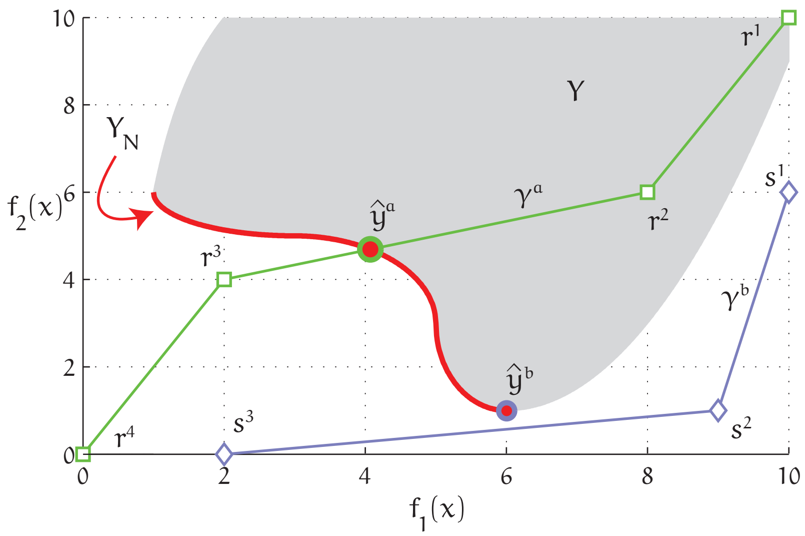

FIGURE 4.5: Illustration of the RPM. Two different paths, γ^a (imposed by reference points r^1, r^2, r^3 and r^4) and γ^b (imposed by reference points s^1, s^2 and s^3), lead to different preferred solutions, $\hat{y}^a$ and $\hat{y}^b$ respectively.

A (two-dimensional) geometric interpretation of the RPM is provided in Figure 4.5. For a set of specified reference points, the preferred path is constructed by linear interpolation between the points as we can observe in Figure 4.5. For path γ^a, the preferred solution $\hat{y}^a$ is just the intersection of path γ^a and the nondominated set Y_N. However, a path does not necessarily intersect Y_N, as is the case of path γ^b in Figure 4.5. In this case, the preferred solution should be one of the extremities of the nondominated set Y_N. This can be achieved by setting the indifference curves as in Figure 4.6.

So, in the RPM a preferred path γ is constructed which reflects the preferences of the DM. For every point on the path γ, the indifference curves are similar as in Figure 4.6. Every point on the path (and thus every indifference curve) corresponds with some value $z \in \mathbb{R}$. For every two points $y^1, y^2 \in \mathbb{R}^n$ with $y^1 < y^2$ on the path we assign values $z_1, z_2 \in \mathbb{R}$ with $z_1 < z_2$. The solution is then a feasible point $\hat{y} \in Y$ for which the value of $z \in \mathbb{R}$ is minimal.

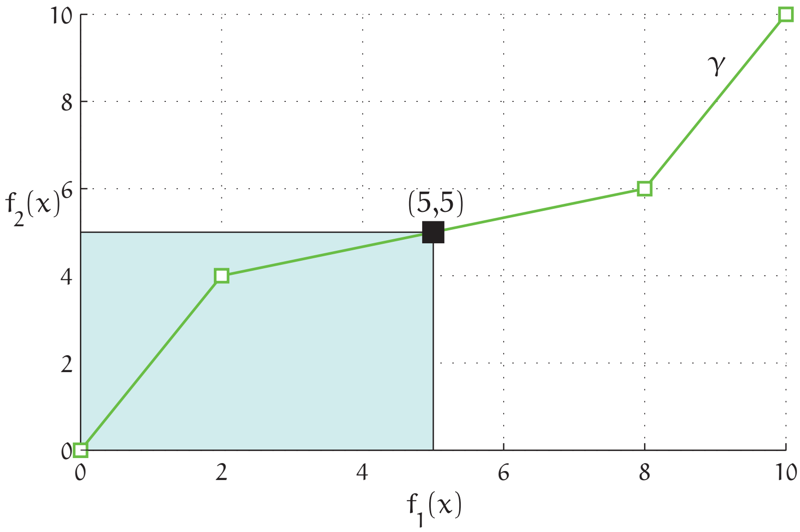

FIGURE 4.6: Indifference curve for the point $(f_1(x), f_2(x)) = (5,5)$ on the preferred path γ. The area under the indifference curve represents the area in which we want to find the solution.

To formalize this basic idea, consider a general *reference list* given in Table 4.3. The preferred

TABLE 4.3: General reference list for the RPM.

Priority	Reference point	$f_1(x)$	$f_2(x)$	$\cdots$	$f_n(x)$
1	r^1	r_1^1	r_2^1	$\cdots$	r_n^1
2	r^2	r_1^2	r_2^2	$\cdots$	r_n^2
$\vdots$	$\vdots$	$\vdots$	$\vdots$		$\vdots$
p	r^p	r_1^p	r_2^p	$\cdots$	r_n^p

path is a parametric curve $\gamma : \mathbb{R} \to \mathbb{R}^n$: every value of $z \in \mathbb{R}$ corresponds to a unique point on the preferred path. Lowering the value of z represents moving from r^1 to r^p in the criterion space, so that all criteria f_i are improved. Path $\gamma(z) = (q_1(z), \ldots, q_n(z))$ is defined (where $q_i : \mathbb{R} \to \mathbb{R}$) as a piecewise continuous curve through reference points r^j ($\gamma(\nu_j) = r^j$):

$$q_i(z) = \begin{cases} r_i^p + \beta_1 g_i^p (z - \nu_p) & z \leqslant \nu_p \\ r_i^j + g_i^j (z - \nu_j) & \nu_j < z \leqslant \nu_{j-1}, \quad j \in [p] \setminus [1] \\ r_i^1 + \beta_2 g_i^2 (z - \nu_1) & \nu_1 < z, \end{cases} \tag{4.3.1}$$

where

$$g_i^j = \frac{r_i^{j-1} - r_i^j}{\nu_{j-1} - \nu_j}, \quad i \in [n],\ j \in [p] \setminus [1]. \tag{4.3.2}$$

and with parameters $0 < \beta_2 \leqslant 1$ and $\beta_1 \geqslant 1$. Here, parameter β_1 represents an additional increase of the DMs satisfaction when better outcomes than r^p are generated. Parameter β_2

represents the dissatisfaction in the case that outcomes are worse than r^1.

For every value of z, we are interested in the feasible points satisfying $f_i(x) \leqslant q_i(z)$ (for example the area in Figure 4.6). For convex programming, the functions $q_i(z)$ need to be concave. This can be achieved by choosing the ν_j in parametrization (4.3.1) such that the g_i^j (4.3.2) decrease, $g_i^p \geqslant \ldots \geqslant g_i^2$. An algorithm to achieve this is to choose an initial pair ν_p and ν_{p-1} ($\nu_p < \nu_{p-1}$), and then choose the other ν_j according to:

$$\nu_{j-1} \geqslant \nu_j + (\nu_j - \nu_{j+1}) \max_{i \in [n]} \frac{r_i^{j-1} - r_i^j}{r_i^j - r_i^{j+1}}, \quad j \in [p-1] \setminus [1]. \tag{4.3.3}$$

Now, we can write

$$q_i(z) = \min_{j \in [p+1]} \left(r_i^j + g_i^j (z - \nu_j) \right),$$

where we introduced $g_i^1 := \beta_2 g_i^2$, $g_i^{p+1} := \beta_1 g_i^p$ for all $i \in [n]$ for convenience. Also, $\nu_{p+1} := \nu_p$ and $r^{p+1} := r^p$. Consequently, we can formulate the convex minimization model:

$$\begin{aligned} &\min_{x \in X} && z \\ &\text{subject to} && f_i(x) \leqslant r_i^j + g_i^j (z - \nu_j) \quad i \in [n],\ j \in [p+1]. \end{aligned} \tag{4.3.4}$$

These are the basics of the RPM. However, the minimization model of the RPM is more general than (4.3.4) which is shown in the next section.

4.3.2 RPM minimization model

In this section, we formally introduce the minimization model of the RPM. As mentioned before, the RPM uses a reference list (Table 4.3) to obtain a preferable solution.

The first step from minimization model (4.3.4) to the minimization model of the RPM is to rewrite the inequalities $f_i(x) \leqslant q_i(z)$ as $s_i(f_i(x)) \leqslant z$. Here, the $s_i : \mathbb{R} \to \mathbb{R}$ are the inverse functions of q_i, which are well defined since the q_i are strictly increasing ($g_i^j > 0$ for all $i \in [n]$ and $j \in [p+1]$). In the RPM the functions s_i are referred to as *partial achievement functions* and can be written as

$$s_i(f_i(x)) = \begin{cases} \nu_p + \alpha_1 w_i^p (f_i(x) - r_i^p) & f_i(x) < r_i^p \\ \nu_j + w_i^j (f_i(x) - r_i^j) & r_i^j < f_i(x) \leqslant r_i^{j-1}, \quad j \in [p] \setminus [1], \\ \nu_1 + \alpha_2 w_i^2 (f_i(x) - r_i^1) & r_i^1 < f_i(x), \end{cases} \tag{4.3.5}$$

where

$$w_i^j = \frac{\nu_{j-1} - \nu_j}{r_i^{j-1} - r_i^j}, \quad i \in [n],\ j \in [p] \setminus [1]. \tag{4.3.6}$$

For convenience, introduce $w_i^1 := \alpha_2 w_i^2$ for an $\alpha_2 \geqslant 1$ and $w_i^{p+1} := \alpha_1 w_i^p$ for a parameter

α_1 with $0 < \alpha_1 \leqslant 1$. The parameters α_1 and α_2 can be interpreted in a similar way as the parameters β_1 and β_2 in the last section. Note that in particular it holds that $s_i(r_i^j) = v_j$ for all $i \in [n]$ and $j \in [p]$ and that the partial achievement functions can be written as

$$s_i(f_i(x)) = \max_{j \in [p+1]} \left(v_j + w_i^j (f_i(x) - r_i^j) \right),$$

where $v_{p+1} := v_p$ and $r^{p+1} := r^p$. An equivalent (convex) minimization model of (4.3.4) is thus given by:

$$\begin{aligned} \min_{x \in X} \quad & z \\ \text{subject to} \quad & v_j + w_i^j (f_i(x) - r_i^j) \leqslant z \quad i \in [n],\ j \in [p+1]. \end{aligned} \tag{4.3.7}$$

Next, we use the partial achievement functions to introduce a small change in the indifference curves (see Figure 4.6). Therefore, let $a_i : \mathbb{R}^m \to \mathbb{R}$ be given by $a_i(x) = s_i(f_i(x))$ for all $i \in [n]$. A *scalarizing achievement function* $S : \mathbb{R}^n \to \mathbb{R}$ is defined as:

$$S(a_1, \dots, a_n) = \max_{i \in [n]} a_i + \sum_{i \in [n]} \rho_i a_i, \tag{4.3.8}$$

where $\rho_i \geqslant 0$ ($i \in [n]$) represent *sensitivity parameters*. The RPM minimizes the scalarizing achievement function subject to the inequalities $a_i(x) \leqslant z$. The corresponding (convex) minimization model for the RPM is given by:

$$\begin{aligned} \min_{x \in X} \quad & z + \sum_{i \in [n]} \rho_i a_i \\ \text{subject to} \quad & a_i \leqslant z \quad && i \in [n] \\ & v_j + w_i^j (f_i(x) - r_i^j) \leqslant a_i \quad && i \in [n],\ j \in [p+1]. \end{aligned} \tag{4.3.9}$$

Note that z represents $\max_{i \in [n]} a_i$ and $a_i(x) = s_i(f_i(x))$. If all criteria are linear, the convex minimization model of the RPM (4.3.9) becomes linear. Notice that the RPM uses predetermined information provided by the DM, similarly as for the 2pϵc method. Whereas the 2pϵc method uses a wish-list, the RPM uses a reference list. A reference list consists of $p \in \mathbb{N}$ reference points $r^1, \dots, r^p$ which are sorted by priority.

The main difference between both methods is that the wish-list prioritizes goal values per criterion, while the reference list prioritizes per reference point (which is a vector). Another difference is that the RPM only needs one optimization instead of several.

The next part explains how the addition of the term $\frac{1}{n} \sum_{i \in [n]} \rho_i a_i$ in the scalarizing achievement functions influences the indifference curve in Figure 4.6.

4.3.3 Sensitivity parameters and trade-offs in the RPM

For a preferred path $\gamma : \mathbb{R} \to \mathbb{R}^n$ given by

$$\gamma(z) = (s_1^{-1}(z), \dots, s_n^{-1}(z)),$$

where s_i^{-1} denotes the inverse of the partial achievement function s_i, the indifference curves for $\hat{z} \in \mathbb{R}$ with no sensitivity parameters ($\rho = 0$) are given by

$$\hat{z} = \max_{i \in [n]} s_i(f_i(x)).$$

See Figure 4.6 as an example.

The addition of $\frac{1}{n} \sum_{i \in [n]} \rho_i a_i$ in the scalarizing achievement function (in 4.3.9) changes the indifference curve, but does not change the preferred path. In Figure 4.7 an example of an indifference curve is shown in a two-dimensional criterion space. In Figure 4.7, the tangents of

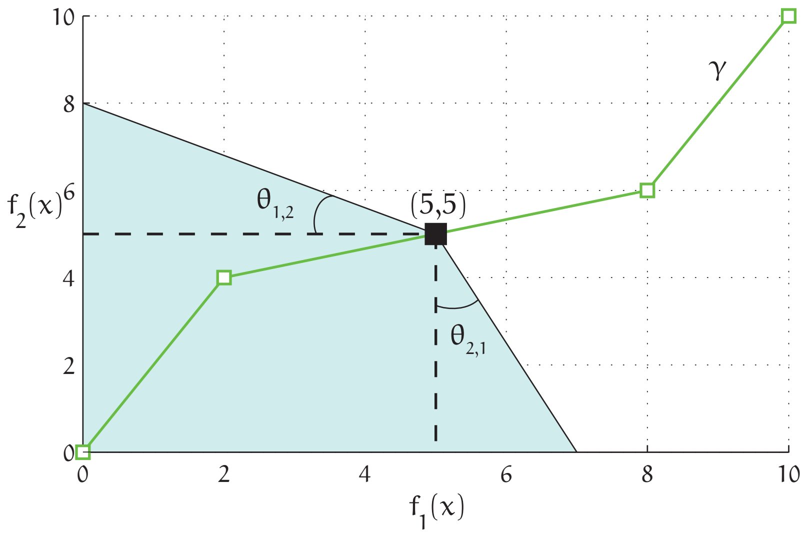

FIGURE 4.7: Indifference curves of (4.3.8) in the criterion space for two criteria. The square point represents a point on the preferred path. For $\rho = 0$ the dashed lines represent the indifference curve, while for $\rho > 0$ the indifference curve is given by the solid lines. Note that the area in which we look for the solution has extended for $\rho > 0$.

angles $\theta_{1,2}, \theta_{2,1}$ can be calculated as follows:

$$\tan(\theta_{1,2}) = \frac{\partial S|_{\{a_1 \leqslant a_2\}}}{\partial f_1} \Big/ \frac{\partial S|_{\{a_1 \leqslant a_2\}}}{\partial f_2}, \qquad \tan(\theta_{2,1}) = \frac{\partial S|_{\{a_1 \geqslant a_2\}}}{\partial f_2} \Big/ \frac{\partial S|_{\{a_1 \geqslant a_2\}}}{\partial f_1}. \tag{4.3.10}$$

The angles do not only depend on ρ but also on the reference points, and thus on the location on the preferred path. More explicitly, for $j \in [p+1]$ we have

$$\tan(\theta^j_{1,2}) = \frac{w^j_1}{w^j_2} \cdot \frac{\rho_1}{1+\rho_2}, \qquad \tan(\theta^j_{2,1}) = \frac{w^j_2}{w^j_1} \cdot \frac{\rho_2}{1+\rho_1} \tag{4.3.11}$$

$$= \begin{cases} \alpha_2 \dfrac{r^{j-1}_2 - r^j_2}{r^{j-1}_1 - r^j_1} \cdot \dfrac{\rho_1}{1+\rho_2} & j = 1, \\ \dfrac{r^{j-1}_2 - r^j_2}{r^{j-1}_1 - r^j_1} \cdot \dfrac{\rho_1}{1+\rho_2} & j = [p] \setminus [1], \\ \alpha_1 \dfrac{r^{j-1}_2 - r^j_2}{r^{j-1}_1 - r^j_1} \cdot \dfrac{\rho_1}{1+\rho_2} & j = p+1, \end{cases} \qquad = \begin{cases} \alpha_2 \dfrac{r^{j-1}_1 - r^j_1}{r^{j-1}_2 - r^j_2} \cdot \dfrac{\rho_2}{1+\rho_1} & j = 1, \\ \dfrac{r^{j-1}_1 - r^j_1}{r^{j-1}_2 - r^j_2} \cdot \dfrac{\rho_2}{1+\rho_1} & j = [p] \setminus [1], \\ \alpha_1 \dfrac{r^{j-1}_1 - r^j_1}{r^{j-1}_2 - r^j_2} \cdot \dfrac{\rho_2}{1+\rho_1} & j = p+1. \end{cases}$$

So, increasing ρ_1 increases the angle $\theta_{1,2}$ which expands the area in which solutions are more in favour of f_1. At the same time, $\theta_{2,1}$ decreases shrinking the area in which f_2 is more favoured.

In general, the indifference curves for $\hat{z} \in \mathbb{R}$ with sensitivity parameters ($\rho \geqslant 0$) are given by

$$\hat{z} = \sum_{i \in [n]} \rho_i s_i(f_i(x)) + \max_{i \in [n]} s_i(f_i(x)).$$

The angles involved can be gathered in a matrix

$$\Theta^j = \begin{pmatrix} \varnothing & \theta^j_{1,2} & \theta^j_{1,3} & \cdots & \theta^j_{1,n} \\ \theta^j_{2,1} & \varnothing & \theta^j_{2,3} & \cdots & \theta^j_{2,n} \\ \theta^j_{3,1} & \theta^j_{3,2} & \varnothing & \cdots & \theta^j_{3,n} \\ \vdots & \vdots & \vdots & \ddots & \vdots \\ \theta^j_{n,1} & \theta^j_{n,2} & \theta^j_{n,3} & \cdots & \varnothing \end{pmatrix}.$$

where $\theta^j_{i,k}$ denotes the angle of f_i with respect to f_k. These satisfy

$$\tan(\theta^j_{i,k}) = \begin{cases} \alpha_2 \dfrac{r^{j-1}_k - r^j_k}{r^{j-1}_i - r^j_i} \cdot \dfrac{\rho_i}{1+\rho_k} & j = 1, \\ \dfrac{r^{j-1}_k - r^j_k}{r^{j-1}_i - r^j_i} \cdot \dfrac{\rho_i}{1+\rho_k} & j = [p] \setminus [1], \\ \alpha_1 \dfrac{r^{j-1}_k - r^j_k}{r^{j-1}_i - r^j_i} \cdot \dfrac{\rho_i}{1+\rho_k} & j = p+1, \end{cases}$$

for $i, k \in [n]$ ($i \neq k$) and $j \in [p+1]$. So in the general case, the reference points $r^1, \dots, r^p$, parameters α_1, α_2 and the sensitivity parameters $\rho_1, \dots, \rho_n$ determine $n(n-1)$ angles per line segment on the preferred path.

Sensitivity can thus be introduced by setting $\rho > 0$, which essentially determines predefined trade-offs between the criteria. The RPM with $\rho > 0$ will deviate from the preferred path when favourable trade-offs are available.

4.3.4 Example of the RPM

In this section, we give an example of a multicriteria optimization problem on which the RPM is applied.

Example 4.2. Suppose that the feasible set is $X = [0, 8]$. Also, suppose that we have two criteria $f_1, f_2 : \mathbb{R} \to \mathbb{R}$ given by:

$$f_1(x) = x\sqrt{x}, \qquad f_2(x) = (x-4)^2 + 2. \tag{4.3.12}$$

In Figure 4.8 the criteria and nondominated set Y_N are illustrated. Note that the Pareto optimal

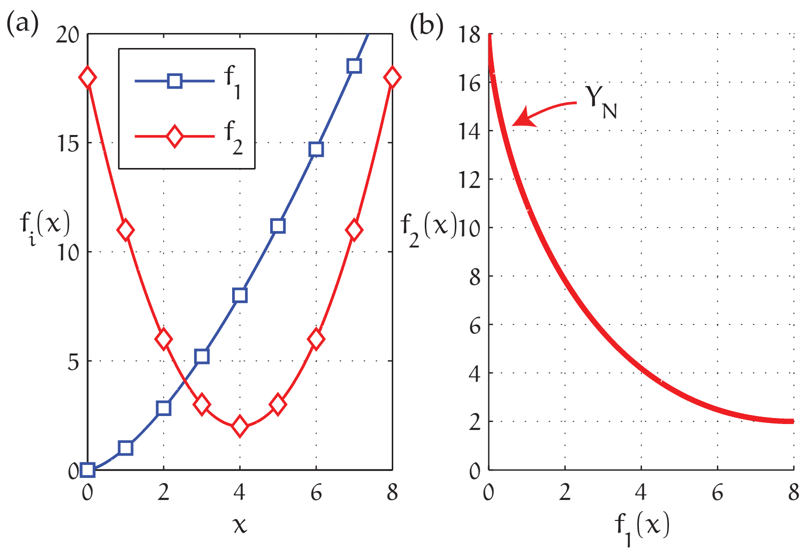

Figure 4.8: (a) The two criteria and (b) the nondominated set Y_N.

points lie in the interval $[0, 4]$. The feasible set Y is the curve

$$Y = \{(y_1, y_2) \in \mathbb{R}^2 \mid 0 \leqslant y_1 \leqslant 16\sqrt{2},\ y_2 = (y_1^{2/3} - 4)^2 + 2\},$$

of which the set of all nondominated solutions Y_N is

$$Y_N = \{(y_1, y_2) \in Y \mid y_1 \in [0, 8]\}.$$

Suppose that we use the reference list in Table 4.4. Reference point $(10, 14)$ has the highest priority, this means that it as important for f_1 to reach a value of 10 as it is for f_2 to reach the value 14. If the first reference point is attainable, the solution is steered to the second reference point $(2, 6)$. This continues until the feasible set Y and infeasible set intersect.

TABLE 4.4: Reference list in Example 4.2.

Priority	Reference point	$f_1(x)$	$f_2(x)$
1	r^1	10	14
2	r^2	2	6
3	r^3	1	2
4	r^4	0	0

The strictly decreasing sequence $(\nu_j)_{j=1}^{p} \in \mathbb{R}$ is initialized by $\nu_p = 0$, $\nu_{p-1} = 1$ and further determined by the algorithm (4.3.3), where we take equality signs. Both α_1 and α_2 are set to 1. In Figure 4.9, the solutions are shown for sensitivity parameters $\rho = (0, 0)$ and $\rho = \left(\frac{1}{2}, 10\right)$ respectively.

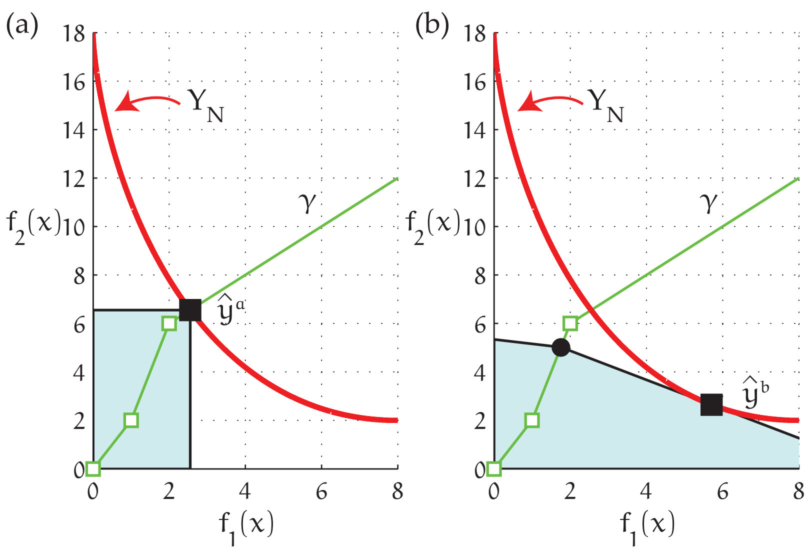

FIGURE 4.9: (a) The nondominated solution $\hat{y}^a$ in case $\rho = (0, 0)$ and (b) the nondominated solution $\hat{y}^b$ when $\rho = \left(\frac{1}{2}, 10\right)$.

The preferred path is constructed based solely on the reference list in Table 4.4. The parameter vector ρ however, can be configured independently of the reference list.

Different choices of ρ can lead to different solutions as shown in Table 4.5. Observe from Table 4.5 that increasing ρ_1 can lead to a lower criterion value of f_1. The same holds for increasing ρ_2. Note that scaling ρ may produce a different solution as can be seen in Table 4.5 for the entries $\left(\frac{1}{2}, \frac{1}{2}\right)$ and $(1, 1)$.

4.3.5 Pareto optimality of the RPM

This section presents results about the (weak) Pareto optimality of the RPM. Essentially, the RPM involves minimizing a scalarizing achievement function $S : \mathbb{R}^n \to \mathbb{R}$ of the form (4.3.13).

TABLE 4.5: Solutions generated by the RPM by varying ρ (and with the reference list in Table 4.4).

ρ	$\hat{y}_1$	$\hat{y}_2$
$(0,0)$	2.55	6.55
$(\frac{1}{2},0)$	2.55	6.55
$(0,\frac{1}{2})$	2.66	6.32
$(\frac{1}{2},\frac{1}{2})$	2.55	6.55
$(1,1)$	2.66	6.32
$(10,\frac{1}{2})$	1	11
$(\frac{1}{2},10)$	5.71	2.65

This function depends on the reference points and the vector parameter ρ,

$$S(y) = \max_{i\in[n]} \left(\max_{j\in[p+1]} \left(\nu_j + w_i^j (y_i - r_i^j) \right) \right) + \sum_{i\in[n]} \rho_i \max_{j\in[p+1]} \left(\nu_j + w_i^j (y_i - r_i^j) \right). \tag{4.3.13}$$

Here, we introduced $w_i^1 := \alpha_2 w_i^1$, $w_i^{p+1} := \alpha_1 w_i^p$, $\nu_{p+1} := \nu_p$ and $r^{p+1} := r^p$ for the sake of notation.

The minimization model of the RPM is then given by

$$\min_{x\in X} \quad S(f(x)). \tag{4.3.14}$$

So the RPM minimization model (4.3.14) is a special case of the more general form

$$\min_{x\in X} U(f(x)).$$

The same can be noted for the weighted sum and the ϵ-constraint method. To prove (weak) Pareto optimality for the RPM it is convenient to consider this general class of minimization models with utility function $U : \mathbb{R}^n \to \mathbb{R}$.

DEFINITION 4.1 (Strictly, strongly increasing). *A utility function* $U : \mathbb{R}^n \to \mathbb{R}$ *is called*

- strictly increasing *if* $U(y^1) < U(y^2)$ *whenever* $y^1 < y^2$ *(*$y^1, y^2 \in \mathbb{R}^n$*),*
- strongly increasing *if* $U(y^1) < U(y^2)$ *whenever* $y^1 \leqslant y^2$ *and* $y_j^1 \neq y_j^2$ *for at least one* $j \in [n]$ *(*$y^1, y^2 \in \mathbb{R}^n$*).*

THEOREM 4.4. *Consider minimization model* (4.0.1)*.*

1. *Let the utility function* $U : \mathbb{R}^n \to \mathbb{R}$ *be strictly increasing. If* $\hat{x} \in X$ *is an optimal solution of minimization model* (4.0.1) *then* $\hat{x} \in X_{wP}$*.*

2. *Let the utility function* $U : \mathbb{R}^n \to \mathbb{R}$ *be strongly increasing. If* $\hat{x} \in X$ *is an optimal solution of minimization model* (4.0.1) *then* $\hat{x} \in X_P$.

Proof. The statements can be proved by contraposition.

1. Suppose $\hat{x} \notin X_{wP}$, then there is an $x \in X$ with $f(x) < f(\hat{x})$. Since $U : \mathbb{R}^n \to \mathbb{R}$ is strictly increasing we have to conclude $U(f(x)) < U(f(\hat{x}))$, that is, $\hat{x} \in X$ is not an optimal solution of minimization model (4.0.1).

2. Suppose $\hat{x} \notin X_P$, then there is a $x \in X$ with $f(x) \leqslant f(\hat{x})$ and $f_j(x) < f_j(\hat{x})$ for at least one $j \in [n]$. Since $U : \mathbb{R}^n \to \mathbb{R}$ is strongly increasing we have $U(f(x)) < U(f(\hat{x}))$, so $\hat{x} \in X$ is not an optimal solution of (4.0.1).

□

Properties of the specific scalarizing achievement function (4.3.13) are gathered in Lemma 4.5.

LEMMA 4.5. *For the scalarizing achievement function* $S : \mathbb{R}^n \to \mathbb{R}$ *given by* (4.3.13) *the following statements hold:*

1. *if* $\rho = 0$*, then* $S(y)$ *is strictly increasing,*

2. *if* $\rho > 0$*, then* $S(y)$ *is strongly increasing.*

Proof. This can be shown using elementary calculus.

1. Let $y^1, y^2 \in \mathbb{R}^n$ with $y^1 < y^2$. Since $w_i^j > 0$ for all $i \in [n]$ and $j \in [p+1]$ we have

$$v_j + w_i^j(y_i^1 - r_i^j) < v_j + w_i^j(y_i^2 - r_i^j), \quad \text{for all } i \in [n] \text{ and } j \in [p+1].$$

Hence

$$\max_{j \in [p+1]} \left(v_j + w_i^j(y_i^1 - r_i^j) \right) < \max_{j \in [p+1]} \left(v_j + w_i^j(y_i^2 - r_i^j) \right), \quad \text{for all } i \in [n],$$

so that

$$\max_{i \in [n]} \left(\max_{j \in [p+1]} \left(v_j + w_i^j(y_i^1 - r_i^j) \right) \right) < \max_{i \in [n]} \left(\max_{j \in [p+1]} \left(v_j + w_i^j(y_i^2 - r_i^j) \right) \right).$$

Since $\rho = 0$, this just reads $S(y^1) < S(y^2)$.

2. Let $y^1, y^2 \in \mathbb{R}^n$ with $y^1 \leqslant y^2$ and $y_k^1 < y_k^2$ for some $k \in [n]$. Then certainly

$$\max_{i \in [n]} \left(\max_{j \in [p+1]} \left(v_j + w_i^j(y_i^1 - r_i^j) \right) \right) \leqslant \max_{i \in [n]} \left(\max_{j \in [p+1]} \left(v_j + w_i^j(y_i^2 - r_i^j) \right) \right),$$

since $w_i^j > 0$ for all $i \in [n]$ and $j \in [p+1]$. Also

$$\rho_i \cdot \max_{j \in [p+1]} \left(\nu_j + w_i^j (y_i^1 - r_i^j) \right) \leqslant \rho_i \cdot \max_{j \in [p+1]} \left(\nu_j + w_i^j (y_i^2 - r_i^j) \right), \quad \text{for all } i \in [n],$$

since $\rho > 0$. Furthermore, for $k \in [n]$ a strict inequality holds:

$$\rho_k \cdot \max_{j \in [p+1]} \left(\nu_j + w_i^j (y_i^1 - r_i^j) \right) < \rho_k \cdot \max_{j \in [p+1]} \left(\nu_j + w_i^j (y_i^2 - r_i^j) \right),$$

because of the assumption $y_k^1 < y_k^2$. Combining these observations, we may conclude $S(y^1) < S(y^2)$.

□

Note that $\rho > 0$ is also a necessary condition for the scalarizing achievement function of the form (4.3.13) to be strongly increasing. A direct consequence is given in Corollary 4.6.

COROLLARY 4.6. *Let* $\hat{x} \in X$ *be the optimal solution of* (4.3.14) *then*

1. $\hat{x} \in X_{wP}$ *if* $\rho = 0$,
2. $\hat{x} \in X_P$ *if* $\rho > 0$.

Proof. Follows directly from Lemma 4.5 and Theorem 4.4. □

Summarized, the RPM is guaranteed to be Pareto optimal if $\rho > 0$, while only weak Pareto optimality can be guaranteed when $\rho = 0$. Actually, when $\rho_k = 0$ for some $k \in [n]$ and $\rho_i > 0$ for the other $i \in [n] \setminus \{k\}$ only weak Pareto optimal solutions can be guaranteed.

Part II

Application in radiation therapy

CHAPTER 5

Multicriteria optimization and Radiation Therapy

In this chapter, we discuss a setting in which we encounter multicriteria optimization problems in radiation therapy. The aim of radiation therapy is to control or destroy the tumour cells while sparing the surrounding healthy tissue as much as possible. As mentioned in Chapter 1, the focus of this thesis is on external beam radiation therapy with X-ray beams (photons).

In external beam radiation therapy, the patient is positioned on a couch and is irradiated from several directions with external X-ray beams. The irradiations from the several directions overlap at the tumour volume so that a sufficient dose (measured in Gray (Gy)) can be delivered while avoiding the surrounding healthy tissue as much as possible. The X-ray beams are generated by a device called a *linear accelerator* (linac), which is placed on an arm (the gantry), which can rotate around the patient. In the linac, electrons are accelerated by subjecting them linearly through a series of oscillating electric potentials. At the end of the linac, the electrons are decelerated by (mostly) a tungsten alloy generating the X-ray beam. Placed after the X-ray is a device called a *collimator*, which shapes the beam of radiation.

For the treatment device, there are two sets of physical parameters that need to be configured:

1. the number of external beams and their directions,
2. the shapes and intensities of their fields.

In case that the intensities are non-uniform (optimized per patient), we refer to the treatment as *intensity modulated radiation therapy* (IMRT). Currently at the Erasmus MC - Cancer Institute, a novel algorithm called *iCycle* is used for determining these two sets of parameters, see Breedveld et al. (2012). The 2-phase ϵ-constraint (2pϵc) method (Section 4.2.1), which can be applied when the number of beams and beam directions are fixed, has a key role in iCycle.

Configuring the treatment device is called *treatment planning*. There are two types of treatment planning:

- *forward* planning (trial-and-error process),
- *inverse* planning (automated planning).

Forward planning is a technique where the dosimetrist manually configures the parameters, such as the number of radiation beams and at which angles these beams are positioned. The computer then performs an optimization to determine the other degrees of freedom resulting in a dose distribution. If the dosimetrist is not satisfied with the dose distribution, the parameters are reconfigured (manually) and a new optimization takes place, resulting into another dose distribution. This process continues until the dosimetrist is satisfied with the treatment plan. The quality of this treatment plan is highly dependent on the experience and skills of the dosimetrist, and the time needed to obtain a satisfying treatment plan is mostly too long .

Inverse planning is a technique in which a treatment plan is generated based on goals set on the criteria, such as target coverage or sparing. An optimization takes place resulting in a dose distribution that meets the predetermined goals as well as possible. If the dose distribution is not to the dosimetrist's liking, the goals are modified and another optimization follows. The dosimetrist, who functions as the decision maker (DM), has the iterative task of determining feasible and optimal goals for the criteria. The wish-list was designed to quantify and automate this task, and thereby allowing fully automated treatment planning.

Our study is to investigate whether the RPM (Section 4.3) can automatically generate treatment plans of similar quality when compared to the treatment plans generated by the 2pϵc method (our focus is thus on inverse planning). To compare these methods, we assume that the number of beams and beam directions are fixed. In our case, configuring the treatment device for an IMRT plan corresponds with optimizing the intensities of the beams (the remaining physical parameters are fixed). The intensity profiles are also called *fluence maps* and are represented by two-dimensional nonnegative functions. The process in which the intensity profiles are optimized is called *fluence map optimization*, which is explained in the next section. This chapter is concluded with a description of tools used to evaluate a treatment plan. We are unable to evaluate the treatment plans ourselves, this can only be done by physicians.

5.1 Fluence map optimization

Here, we explain fluence map optimization into more depth. As the other physical parameters of the treatment device are assumed to be fixed, the fluence map determines the IMRT plan.

In the mathematical model we use a rectangular grid for each of the apertures of the collimator for a fixed beam angle. The number of rectangles on the grid (also called *bixels*) depends on several parameters such as the size of the aperture, beam angle and geometry of the region under the beam. Every bixel is represented as a two-dimensional point. Let $m_i \in \mathbb{N}$ denote the number of bixels for beam i, then we usually have $m_i = \mathcal{O}(10^2)$. If the total number of beams is $N \in \mathbb{N}$, then we have a total number of

$$m = \sum_{i \in [N]} m_i,$$

bixels. Each bixel b_i corresponds to a small intensity element x_i, called a *beamlet*, subdividing the IMRT beam. The fluence map is thus represented by m beamlet intensities or *beamlet weights*. The *fluence vector*

$$x = (x_1, x_2, \ldots, x_m) \in \mathbb{R}^m_{\geqslant 0},$$

consisting of the beamlet weights is the unknown variable which we want to optimize. The feasible set X thus consists of all possible configurations of the beamlet weights.

In order to sufficiently irradiate the tumour while sparing the surrounding healthy tissue as much as possible, we need to calculate the absorbed dose at each location in the patient. The latter is modeled using a CT-scan of the patient, from which the tumour and surrounding healthy organs, called organs at risk (OAR), are delineated. After the delineation, the *region of treatment* (tumour and surrounding healthy tissue which get affected by the irradiation) is discretized into three-dimensional cubes called *voxels*. Each voxel is represented as a three-dimensional point. Let $l \in \mathbb{N}$ denote the number of voxels used to discretize the region of treatment. The absorbed dose of a voxel v_i is denoted as d_i, which depends linearly on the beamlet weights:

$$d_i = \sum_{j \in [m]} h_{ij} x_j, \quad \text{for } i \in [l].$$

In Figure 5.1, the irradiation on a voxel is sketched. Here, h_{ij} represents the (nonnegative) amount of dose absorbed at the i^{th} voxel per unit intensity emission from the j^{th} beamlet. Gathering the doses of the voxels in a vector, the dose calculation formula becomes

$$d = Hx,$$

where

- the vector $d \in \mathbb{R}^l_{\geqslant 0}$ denotes the *dose distribution vector*,
- the matrix $H \in \mathbb{R}^{l \times m}_{\geqslant 0}$ denotes the *dose deposition matrix*,
- the vector $x \in \mathbb{R}^m_{\geqslant 0}$ denotes the fluence vector.

The dose deposition matrix H is calculated with the algorithm in Storchi and Woudstra (1996) and depends on various parameters, for example the beam position.

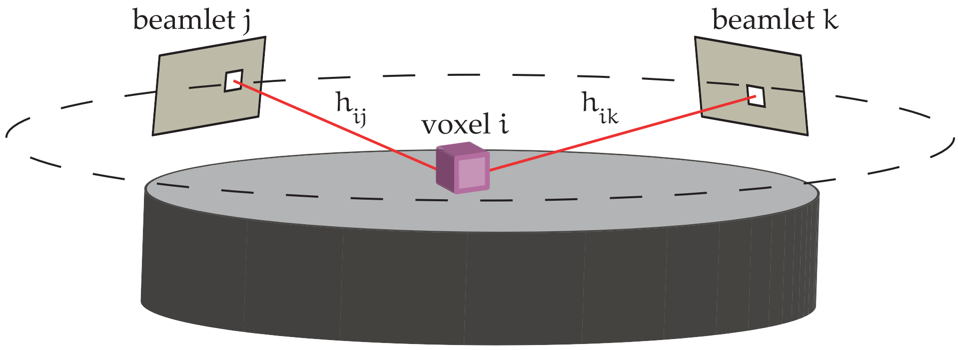

FIGURE 5.1: Irradiation on a voxel. The irradiation on voxel i due to beamlets j and k and corresponding elements h_{ij} and h_{ik} of the dose deposition matrix.

The dose distribution vector d can be utilized to formulate the criteria for fluence map optimization which should be minimized simultaneously. Typical criteria which we will use include

- the *logarithmic tumour control probability* (LTCP) (Breedveld et al. (2012) and Alber and Reemtsen (2007)),
- the maximum dose,
- the minimum dose,
- the mean dose,
- the generalized mean dose.

Suppose $V \subseteq [l]$ is the index set for which the corresponding voxels v_i are in the tumour, OAR or structure at interest. Then, the LTCP, maximum, minimum, mean and generalized mean dose (for $|p| \geqslant 1$) are given by:

$$\mathrm{LTCP}(d) = \frac{1}{M} \sum_{i \in V} \exp\left(-\alpha(d_i - D^p)\right), \tag{5.1.1}$$

$$\mathrm{MAX}(d) = \max_{i \in V} d_i, \tag{5.1.2}$$

$$\mathrm{MIN}(d) = \min_{i \in V} d_i, \tag{5.1.3}$$

$$\mathrm{MEAN}(d) = \frac{1}{M} \sum_{i \in V} d_i, \tag{5.1.4}$$

$$\mathrm{GMEAN}_p(d) = \left(\frac{1}{M} \sum_{i \in V} d_i^p\right)^{\frac{1}{p}}, \tag{5.1.5}$$

where M is the number of elements in V and d_i is the dose delivered to voxel v_i.

In the LTCP, the parameter α is the cell sensitivity and D^p is the prescribed dose. Basically, the LTCP gives an exponential penalty for doses d_i lower than the prescribed dose D^p. Note that the LTCP equals 1 when the doses d_i are equal to the prescribed dose D^p (homogeneous dose distribution). We use the LTCP as criteria for the tumour, and aim for values below 1 giving the tumour a higher dose d_i (than the prescribed dose D^p) which increase the probability of a successful treatment. When generating a treatment plan, minimizing the LTCP has the highest priority.

Note that for $p = 1$ the generalized mean equals the mean dose, for $p = \infty$ it is the maximum dose and for $p = -\infty$ it is the minimum dose. We explicitly mention the mean and maximum/minimum dose since they are commonly used. If the generalized mean is used as a criterion for an OAR or additional structure, it needs to hold that $p \geqslant 1$ (and for the tumour $p \leqslant -1$).

Now, we can formulate a general multicriteria optimization problem which we encounter in radiation therapy. Let $G_1, G_2, \ldots, G_n : \mathbb{R}^l \to \mathbb{R}$ be of the type (5.1.1) - (5.1.5), corresponding to the tumour and OARs. The associated multicriteria optimization problem is then given by

$$\begin{aligned} \min_{x \in X} \quad & (G_1(d)), G_2(d), \ldots, G_n(d)) \\ \text{subject to} \quad & d = Hx. \end{aligned} \tag{5.1.6}$$

Or, in standard form

$$\min_{x \in X} \quad (f_1(x), f_2(x), \ldots, f_n(x)), \tag{5.1.7}$$

where the criteria $f_1, f_2, \ldots, f_n : X \to \mathbb{R}$ are given by $f_i(x) = G_i(Hx)$ ($i \in [n]$). The feasible beamlet weights are bounded so that the feasible set X is a nonempty multi-dimensional interval (and thus compact and convex). The LTCP (5.1.1) and mean dose (5.1.4) are continuous and convex. The generalized mean dose (5.1.5) is also continuous and convex since $d = Hx \geqslant 0$. The maximum (5.1.2) and minimum (5.1.3) can also be represented by continuous and convex functions as follows, when dealing with the maximum dose we add a decision variable, say t, representing the maximum:

$$t = \max_{i \in V} d_i(x),$$

and add the convex inequalities

$$t \geqslant d_i(x), \quad \text{for all } i \in V,$$

to the multicriteria optimization problem (5.1.7). For the minimum dose, we similarly introduce a new decision variable s:

$$s = \min_{i \in V} d_i(x),$$

and add the convex inequalities

$$s \leqslant d_i(x), \quad \text{for all } i \in V,$$

to the multicriteria optimization problem (5.1.7). Note that these inequalities are indeed convex since $d_i(x)$ depends linearly on x.

For the fluence map optimization (5.1.7), where functions (5.1.1) - (5.1.5) are used as criteria, we may conclude that most properties (except connectedness of the Pareto optimal set), summarized in Section 3.4, indeed hold in our application.

5.2 Evaluation treatment plan

Solving the multicriteria optimization problem (5.1.7) results into a set of beamlet weights which configure the treatment device. The question whether these beamlet weights represent a high quality treatment plan is hard to answer. Tools to help evaluating the treatment plan are: Solving the multicriteria optimization problem (5.1.7) results into a set of beamlet weights which configure the treatment device. The question whether these beamlet weights represent a high quality treatment plan is hard to answer. Tools to help evaluating the treatment plan are:

1. the criterion values $f(\hat{x})$ (these are of the type (5.1.1) - (5.1.5)), where $\hat{x} \in X$ is the optimal set of beamlet weights,

2. the cumulative *dose volume histogram* (DVH) associated with the optimal beamlet weights,

3. the dose distribution associated with the optimal beamlet weights.

A cumulative DVH serves to summarize the three-dimensional dose distributions in a two-dimensional plot. In a cumulative DVH, a line is plotted for each volume (tumour, OAR or additional structure), see Figure 5.2 for an example. Along the horizontal axis, the dose is set (in Gray) and the volume (in percentage of the total volume of the structure) is set on the vertical axis. For every structure, the corresponding DVH curve represents the percentage receiving greater than or equal to a certain dose value. For instance, the line for every structure starts at $(0, 100)$, since 100% of the volume receives a dose greater or equal to 0 Gy. This percentage will decrease as the dose increases. The DVH curves monotonically decrease until they intersect the horizontal axis, and the corresponding dose value represents the maximum dose delivered to the associated volume.

We also look at the dose distribution, projected on the CT-slices, since the criterion values and the cumulative DVH do not provide any spatial information. We may know the mean dose delivered to an OAR as well as the cumulative DVH, but we do not know which parts of the organ receive a low or high dose. A dose distribution is a representation of the variation of dose around the tumour, visualized with isodose lines. The tissue on an isodose line receives the same dose. For an example, see Figure 5.3.

To demonstrate these tools, we give an example where we calculate a treatment plan using the 2pϵc method with 3% relaxation (as is done in the current practice).

EXAMPLE 5.1. In this example, we consider a head-and-neck cancer patient with a unilateral (one-sided) tumour. The tumour is irradiated with 6 external beams with fixed angles. To generate a treatment plan, we use the 2pϵc method with 3% relaxation. The wish-list in Table 5.1 is used. In this wish-list, there are also some constraints that exclude undesired sets of beamlet weights from the feasible set X. For example, the maximum dose delivered to the tumour is 49.22 Gy. Additional shells around the tumour have been delineated in the CT-slices for a steep fall-off of the dose outside the tumour (known as *dose conformality*). Furthermore, the maximum dose on the cord should be no more than 48 Gy and for the remaining tissue of the patient (unspecified tissue), the dose should be 49.22 Gy or less. These 5 constraints must be satisfied at all times in contrast to the criteria. The constraints are gathered in the vector inequality $g(x) \leqslant 0$ and are added to the minimization problem. For the treatment plan, the highest priority is to lower the LTCP value of the tumour to 0.5. The other priorities involve surrounding OARs, namely the salivary glands (both parotids glands and the submandibular glands (SMGs)). Saving the saliva production of these glands is highly important. Therefore, the second highest priority is to reduce the mean dose delivered to the right parotid gland to 39 Gy. This process continues until we obtain a Pareto optimal solution.

For the tumour, a LTCP value of 0.5 is also sufficient which means that a maximum of 0.5 is set in the case that lower values are feasible. The results of applying the 2pϵc method are gathered in Table 5.2. Observe that the goal value for the LTCP of 0.5 is attained for the tumour. The most important OAR (the right parotid gland) is likely to be spared since it receives a mean dose of only 3.43 Gy. One the left side, which is where the tumour is located, the mean dose delivered to the OAR is higher (23.52 Gy to the left parotid gland and 39.79 Gy to the left SMG). The right SMG is irradiated with a mean dose of 10.96 Gy.

Next, we compute the cumulative DVH associated with the treatment plan. The DVH is shown in Figure 5.2. Note that in the DVH, it is desirable that the curves corresponding to the OARs are as steep as possible since the intersection of this curve with the dose-axis represents the maximum dose delivered to that OAR. The curve corresponding with the tumour should be horizontal as long as possible before rapidly decreasing to the dose-axis, since we want to irradiate the whole tumour (100% of its volume) with a high dose while limiting the maximum dose at the same time.

For the spatial information, we consider Figure 5.3 which depicts the dose distribution. Note that the volume close to the tumour receives high doses while the volume further away from the tumour receives a lower dose.

TABLE 5.1: Wish-list for the head-and-neck cancer patient.

Constraints

Number	Volume	Type	Limit	
1	Tumour	max	49.22 Gy	
2	Tumour Shell 1 cm	max	34.5 Gy	
3	Tumour Shell 4 cm	max	36 Gy	
4	Cord	max	48 Gy	
5	Unspecified Tissue	max	49.22 Gy	

Criteria

Priority	Volume	Type	Goal value	
1	Tumour	LTCP	0.5	(also a sufficient value)
2	Parotid (R)	mean	39 Gy	
3	Parotid (L)	mean	39 Gy	
4	SMG (R)	mean	39 Gy	
5	SMG (L)	mean	39 Gy	
6	Parotid (R)	mean	20 Gy	
7	Parotid (L)	mean	20 Gy	
8	SMG (R)	mean	20 Gy	
9	SMG (L)	mean	20 Gy	
10	Parotid (R)	mean	10 Gy	
11	Parotid (L)	mean	10 Gy	
12	SMG (R)	mean	10 Gy	
13	SMG (L)	mean	10 Gy	

TABLE 5.2: Criterion values of the treatment plan generated with the 2pϵc method.

Volume	Type	2pϵc method
Tumour	LTCP	0.5
Parotid (R)	mean	3.43 Gy
Parotid (L)	mean	23.52 Gy
SMG (R)	mean	10.96 Gy
SMG (L)	mean	39.79 Gy

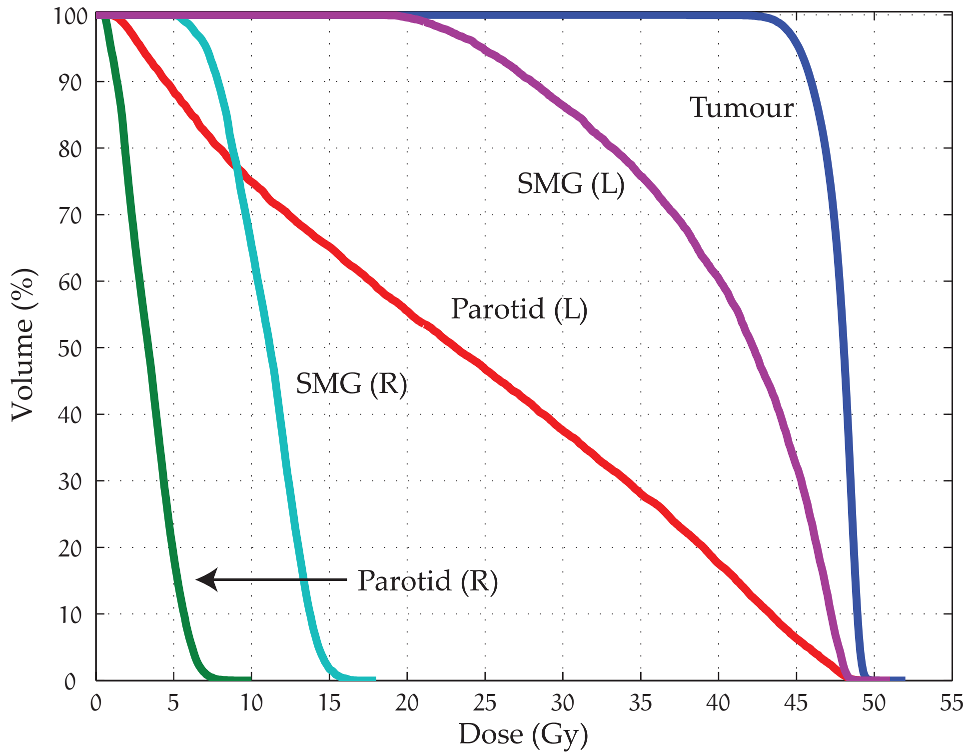

FIGURE 5.2: The cumulative DVH of the treatment plan generated by the 2pϵc method.

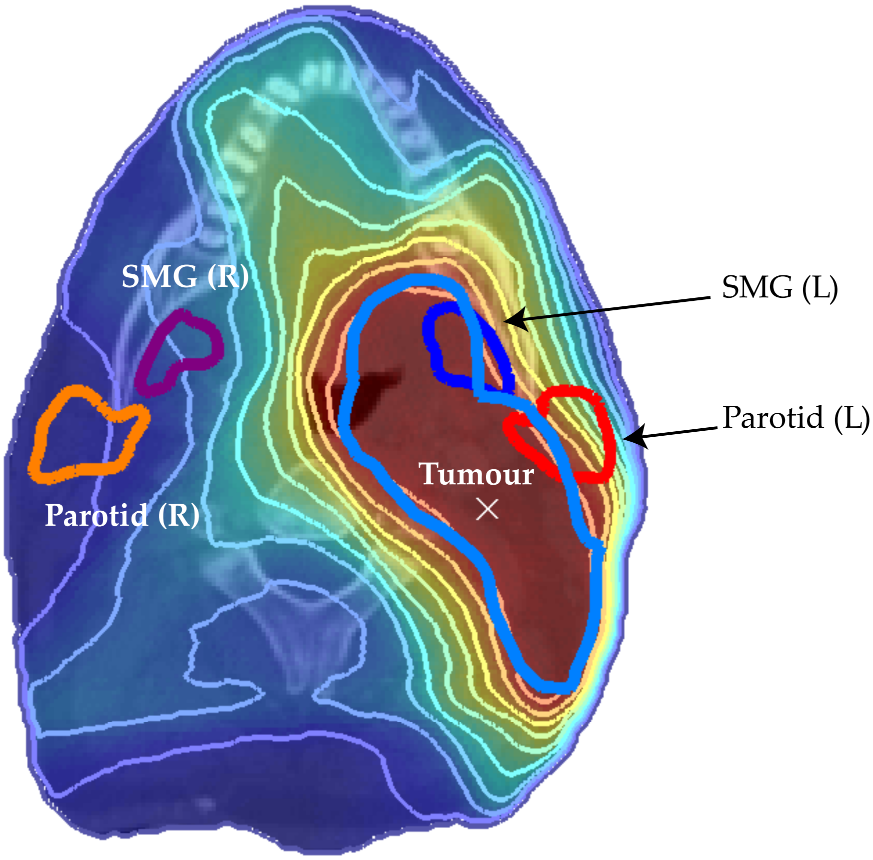

FIGURE 5.3: The dose distribution in a CT-slice of the patient. Here, blue corresponds with low doses and red with high doses. The thin lines represent isodose lines and the thick lines are the delineations of the OARs and the tumour. Since the tumour is positioned at the left side, the left parotid gland and left SMG are much harder to spare than the glands at the right side (note that in medical imaging, the left side of the patient is at the right side of the CT-slice and vice versa).

CHAPTER 6

Configuring the RPM for treatment planning

In this chapter we configure the RPM for the fluence map optimization (Section 5.1). Currently, the 2-phase ϵ-constraint (2pϵc) method (Section 4.2.1) with $\delta = 1.03$ is in clinical use at the Erasmus MC - Cancer Institute to generate treatment plans (Breedveld et al. (2007, 2009)). Per patient group, such as prostate or head-and-neck cancer patients, a wish-list is constructed to generate a Pareto optimal treatment plan. Our aim is to mimic the 2pϵc method with the reference point method (RPM), as described in Section 6.3.

As a side-note, our intention is not to obtain the same treatment plan but to configure the RPM in such a way that the treatment plan found is of similar quality (judged by physicians) when compared to the treatment plan generated by the 2pϵc method. Also, the weighted sum method (Section 4.1) is not suitable for treatment planning, as different patients in the same patient group need different parameters $\lambda \in \mathbb{R}^n_{\geqslant 0} \setminus \{0\}$ for a high quality treatment plan (the trade-offs in a high quality treatment plan can differ significantly between patients).

Difficulties that arise when attempting to mimic the 2pϵc method with the RPM are the relaxation parameter and the fact that the location and shape of the nondominated set Y_N is different for each patient (also for patients in the same patient group). This is because of differences in

1. the size, shape and location of the tumour,

2. the size, shape and location of the surrounding organs,

3. the number of beams and their directions.

For example, some head-and-neck cancer patients have a unilateral (one-sided) tumour while others have a bilateral (two-sided) tumour (extensions in the lymph nodes).

For a specific configuration of the RPM, which we refer to as the *lexicographic reference point method* (LRPM), the information in the wish-list is utilized to construct a suitable reference list. Also, the sensitivity parameters in the RPM method are used, where we intend to use a uniform set of parameters per patient group.

6.1 Comparing the 2pϵc method and the RPM

In this section we compare the principles of the 2pϵc method with those of the RPM. In Example 4.1 and Example 4.2 these principles are depicted.

Although we know how the solution is steered in the criterion space for both methods, there are some differences between the methods. The first observation that should be made is that the input data differs, as the 2pϵc method uses a wish-list (Table 4.1) while the RPM uses a reference list (Table 4.3). In other words, the 2pϵc method prioritizes goal values per criterion while the RPM prioritizes vectors (reference points), in which goal values are specified for each criterion. Secondly, we should note that both methods use different parameters. The 2pϵc method uses a relaxation parameter $\delta \geqslant 1$, while the RPM uses parameters $0 < \alpha_1 \leqslant 1 \leqslant \alpha_2$ and $\rho = (\rho_1, \dots, \rho_n) \geqslant 0$.

Because of these differences, it turns out to be difficult to mimic the 2pϵc method with the RPM. In the 2pϵc method, it is crucial to note that it is impossible to know beforehand for which priorities the relaxation will be applied. In fact, the 2pϵc method needs to perform multiple optimizations to detect if a certain criterion needs to be relaxed or not in the subsequent optimizations. However, this cannot be done in the RPM since this method consists of a single optimization in which all reference points need to be specified, the reference points cannot be changed while the optimization is in progress.

The 2pϵc can be interpreted in the same way as the RPM (Figure 4.5 and Figure 4.6). The path belonging to the 2pϵc method consists of horizontal and vertical parts since we optimize per criterion while keeping the others constrained. However, it is not clear where these horizontal and vertical parts will be located since this depends on the relaxation parameter and the nondominated set Y_N. However, when no relaxation is used ($\delta = 1$) the path of the 2pϵc method is always the same (meaning it does not depend on Y_N). To illustrate this, consider the wish-list in Table 6.1. Additionally, suppose that we have the constraints

$$\begin{aligned} f_1(x) &\leqslant 11, \\ f_2(x) &\leqslant 8. \end{aligned}$$

For the wish-list in Table 6.1, the paths with and without relaxation of the 2pϵc method in the criterion space for two different nondominated sets are depicted in Figure 6.1.

Only if $\delta = 1$, the 2pϵc method can be interpreted as a uniform path (the same for every

TABLE 6.1: Example of a simple wish-list.

Priority	Criterion	Goal value
1	$f_1(x)$	10
2	$f_2(x)$	6
3	$f_1(x)$	1
4	$f_2(x)$	2

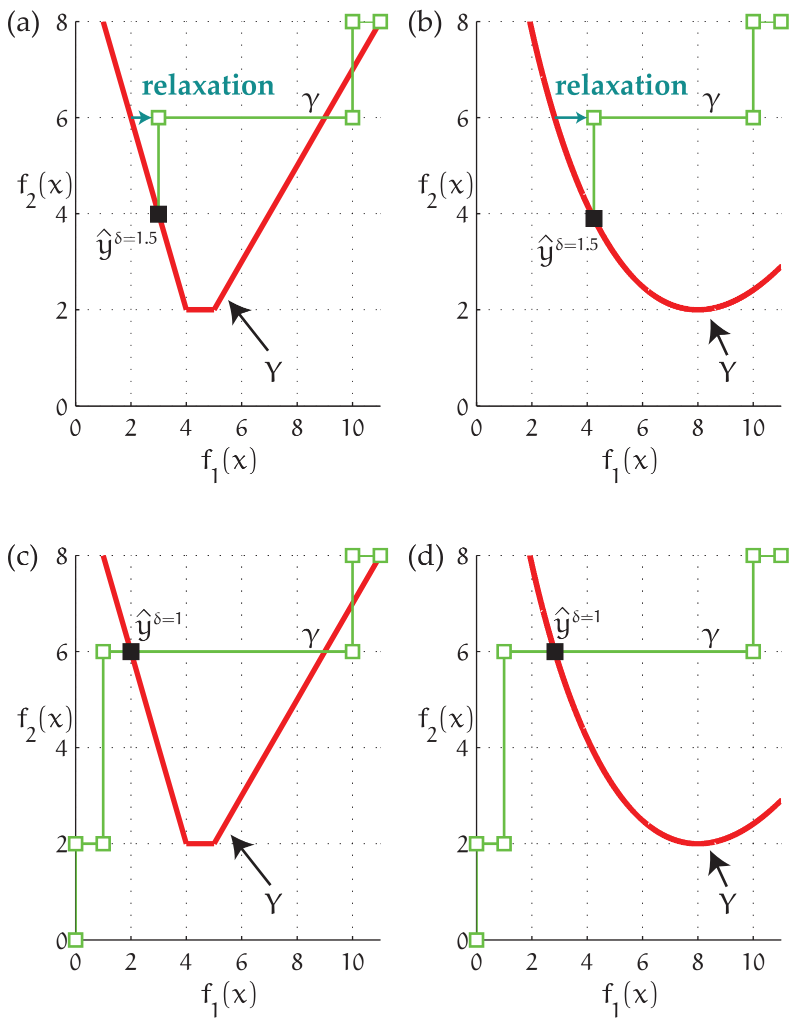

FIGURE 6.1: Illustration of the paths with and without relaxation using the wish-list in Table 6.1. In (a) and (b) the paths with relaxation parameter $\delta = 1.5$ are illustrated for two different nondominated sets while (c) and (d) show the paths with no relaxation for these cases. Note that the paths in (a) and (b) are different while the paths in (c) and (d) are the same.

nondominated set Y_N). Therefore, our first attempt to configure the RPM is based on this uniform path, which we describe in the next section. Recall that in practice, the 2pϵc method is applied with a 3% relaxation ($\delta = 1.03$).

6.2 Approximation non relaxed 2pϵc method with the RPM

In this section, we attempt to approximate the 2pϵc method (without relaxation) with the RPM. To mimic the constraints

$$f_i(x) \leqslant \epsilon_i, \quad \text{for } i \in [n],$$

we set $\rho = 0$ in the RPM (so that the indifference curves are as in Figure 4.6).

Also, we make the following assumptions in the remainder of this section for convenience.

A.1 Every criterion is bounded over the feasible set $X \subseteq \mathbb{R}^m$ (the beamlet weights).

A.2 The wish-list for the 2pϵc method is given by

TABLE 6.2: Wish-list for the 2pϵc method.

Priority	Criterion	Goal value
1	$f_1(x)$	b_1
2	$f_2(x)$	b_2
3	$f_3(x)$	b_3
$\vdots$	$\vdots$	$\vdots$
$n-2$	$f_{n-2}(x)$	b_{n-2}
$n-1$	$f_{n-1}(x)$	b_{n-1}
n	$f_n(x)$	b_n

We thus consider the case that the criteria only appear once in the wish-list (Table 6.2). We can thus choose bounds for the criteria, $f_i^{min}, f_i^{max} \in \mathbb{R}$ for $i \in [n]$, satisfying

$$f_i^{min} \leqslant b_i \leqslant f_i^{max},$$

and

$$f_i^{min} \leqslant \min_{x \in X} f_i(x),$$
$$\max_{x \in X} f_i(x) \leqslant f_i^{max}.$$

In our application, the criteria are of the form (5.1.1) - (5.1.5) so we can take a minimum value of 0 or $f_i^{min} = 0$ for all $i \in [n]$. f_i^{max} can be set to a maximum constraint for the associated criterion or to the maximum allowed tumour dose.

TABLE 6.3: Ideal reference list for the RPM. Here, the *value levels* $(v_j)_{j=1}^{2n}$ suffice $v_{2n} > v_{2n-1}$ and the condition given by (4.3.3).

Priority	Value level	Reference point	$f_1(x)$	$f_2(x)$	$f_3(x)$	$\cdots$	$f_{n-2}(x)$	$f_{n-1}(x)$	$f_n(x)$
1	v_1	r^1	b_1	f_2^{max}	f_3^{max}	$\cdots$	f_{n-2}^{max}	f_{n-1}^{max}	f_n^{max}
2	v_2	r^2	b_1	b_2	f_3^{max}	$\cdots$	f_{n-2}^{max}	f_{n-1}^{max}	f_n^{max}
3	v_3	r^3	b_1	b_2	b_3	$\cdots$	f_{n-2}^{max}	f_{n-1}^{max}	f_n^{max}
$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\ddots$	$\vdots$	$\vdots$	$\vdots$
$n-2$	v_{n-2}	r^{n-2}	b_1	b_2	b_3	$\cdots$	b_{n-2}	f_{n-1}^{max}	f_n^{max}
$n-1$	v_{n-1}	r^{n-1}	b_1	b_2	b_3	$\cdots$	b_{n-2}	b_{n-1}	f_n^{max}
n	v_n	r^n	b_1	b_2	b_3	$\cdots$	b_{n-2}	b_{n-1}	b_n
$n+1$	v_{n+1}	r^{n+1}	f_1^{min}	b_2	b_3	$\cdots$	b_{n-2}	b_{n-1}	b_n
$n+2$	v_{n+2}	r^{n+2}	f_1^{min}	f_2^{min}	b_3	$\cdots$	b_{n-2}	b_{n-1}	b_n
$n+3$	v_{n+3}	r^{n+3}	f_1^{min}	f_2^{min}	f_3^{min}	$\cdots$	b_{n-2}	b_{n-1}	b_n
$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\ddots$	$\vdots$	$\vdots$	$\vdots$
$2n-2$	v_{2n-2}	r^{2n-2}	f_1^{min}	f_2^{min}	f_3^{min}	$\cdots$	f_{n-2}^{min}	b_{n-1}	b_n
$2n-1$	v_{2n-1}	r^{2n-1}	f_1^{min}	f_2^{min}	f_3^{min}	$\cdots$	f_{n-2}^{min}	f_{n-1}^{min}	b_n
$2n$	v_{2n}	r^{2n}	f_1^{min}	f_2^{min}	f_3^{min}	$\cdots$	f_{n-2}^{min}	f_{n-1}^{min}	f_n^{min}

The ideal reference list, which produces the same solution as the 2pϵc method with no relaxation, is given in Table 6.3. We set α_1 and α_2 to 1 in the RPM. These parameters are irrelevant since the last reference point r^{2n} in Table 6.3 can never be improved and the first reference point r^1 is always attainable for $f_2, \ldots, f_n$. The idea is that the first n reference points $(r^1, \ldots, r^n)$ mimic the first phase of the 2pϵc method and the last n reference points $(r^{n+1}, \ldots, r^{2n})$ mimic the second phase of the 2pϵc method.

Unfortunately, the RPM cannot be applied with the ideal reference list in Table 6.3 since $r^{j+1} \not< r^j$ for $j \in [2n-1]$. One way to get around this issue is to perturb the ideal reference list. To achieve this, choose values $f_i^{\min}, f_i^{\max} \in \mathbb{R}$ for $i \in [n]$ and $\xi > 0$ small with

$$\begin{aligned} f_i^{\min} + (n-1)\xi &< b_i, \\ b_i + (n-1)\xi &< f_i^{\max}, \\ f_i^{\min} &\leqslant \min_{x \in X} f_i(x), \\ \max_{x \in X} f_i(x) &\leqslant f_i^{\max}. \end{aligned}$$

Now, we can construct the reference list in Table 6.7, which can be used in the RPM. The reference list in Table 6.7 approximates the wish-list in Table 6.2 of the 2pϵc method. Note that in general, we have p priorities in the wish-list and n criteria which results in $p+n$ reference points to approximate the wish-list. The approximation should improve as $\xi \to 0$.

We illustrate this approximation with an example in radiation therapy.

EXAMPLE 6.1. Consider the same patient as in Example 5.1, only now with the wish-list in Table 6.4. Since we have already seen in Example 5.1 that a LTCP value of 0.5 is feasible for the tumour, we can use this as a constraint instead (including the LTCP in combination with the RPM results into difficulties, see Section 6.4). The associated reference list is given by Table 6.5. Here, $f_i^{\max} = 49.22$ is set to the maximum tumour dose and $f_i^{\min} = 0$ is the ideal mean dose delivered to each OAR (note that the ideal situation in which $f(x) = 0$ is always infeasible). In the RPM, we set α_1 and α_2 to 1 and $\rho = 0$. The value levels are determined by algorithm (4.3.3) initialized by $\nu_{16} = 0$ and $\nu_{15} = 1$.

The resulting criterion values are summarized in Table 6.6. Observe from Table 6.6 that the treatment plan generated by the RPM improves for smaller ξ as it gets closer to the criterion values of the treatment plan generated by the 2pϵc method (with no relaxation). For $\xi = 2$, the treatment plan of the RPM and the 2pϵc method are nearly identical.

However, if ξ is taken smaller than 2 in the reference list (Table 6.5), the solver has difficulty solving the corresponding minimization model of the RPM (4.3.9). This is an issue since the clinical wish-lists at the Erasmus MC - Cancer Institute consist of even more criteria (mostly between 10-25) and more priorities (mostly between 10-30). To understand why we encounter this problem, consider the simple multicriteria optimization problem in Example 6.2.

TABLE 6.4: Wish-list for the head-and-neck patient.

Constraints

Number	Volume	Type	Limit
1	Tumour	max	49.22 Gy
2	Tumour Shell 1 cm	max	34.5 Gy
3	Tumour Shell 4 cm	max	36 Gy
4	Cord	max	48 Gy
5	Unspecified Tissue	max	49.22 Gy
6	Tumour	LTCP	0.5

Criteria

Priority	Volume	Type	Goal value
1	Parotid (R)	mean	39 Gy
2	Parotid (L)	mean	39 Gy
3	SMG (R)	mean	39 Gy
4	SMG (L)	mean	39 Gy
5	Parotid (R)	mean	20 Gy
6	Parotid (L)	mean	20 Gy
7	SMG (R)	mean	20 Gy
8	SMG (L)	mean	20 Gy
9	Parotid (R)	mean	10 Gy
10	Parotid (L)	mean	10 Gy
11	SMG (R)	mean	10 Gy
12	SMG (L)	mean	10 Gy

TABLE 6.5: Reference list constructed from the wish-list in Table 6.4.

Priority	Reference point	Parotid (R)	Parotid (L)	SMG (R)	SMG (L)
1	r^1	$39+3\xi$	49.22	$49.22+\xi$	$49.22+2\xi$
2	r^2	$39+2\xi$	$39+3\xi$	49.22	$49.22+\xi$
3	r^3	$39+\xi$	$39+2\xi$	$39+3\xi$	49.22
4	r^4	39	$39+\xi$	$39+2\xi$	$39+3\xi$
5	r^5	$20+3\xi$	39	$39+\xi$	$39+2\xi$
6	r^6	$20+2\xi$	$20+3\xi$	39	$39+\xi$
7	r^7	$20+\xi$	$20+2\xi$	$20+3\xi$	39
8	r^8	20	$20+\xi$	$20+2\xi$	$20+3\xi$
9	r^9	$10+3\xi$	20	$20+\xi$	$20+2\xi$
10	r^{10}	$10+2\xi$	$10+3\xi$	20	$20+\xi$
11	r^{11}	$10+\xi$	$10+2\xi$	$10+3\xi$	20
12	r^{12}	10	$10+\xi$	$10+2\xi$	$10+3\xi$
13	r^{13}	3ξ	10	$10+\xi$	$10+2\xi$
14	r^{14}	2ξ	3ξ	10	$10+\xi$
15	r^{15}	ξ	2ξ	3ξ	10
16	r^{16}	0	0	0	0

TABLE 6.6: Criterion values of several treatment plans.

Volume	Type	2pϵc method ($\delta = 1$)	RPM ($\xi = 3$)	RPM ($\xi = 2$)
Parotid (R)	mean	4.27 Gy	4.85 Gy	4.27 Gy
Parotid (L)	mean	24.05 Gy	25.89 Gy	24.02 Gy
SMG (R)	mean	13.53 Gy	13.56 Gy	13.54 Gy
SMG (L)	mean	39.00 Gy	38.64 Gy	39.02 Gy

TABLE 6.7: Input list for the RPM approximating the 2pϵc method with the prioritized list in Table 6.2. Here, the *value levels* $(\nu_j)_{j=1}^{2n}$ suffice $\nu_{2n} > \nu_{2n-1}$ and the condition given by (4.3.3).

Priority	Value level	Reference point	$f_1(x)$	$f_2(x)$	$f_3(x)$	$\cdots$	$f_{n-2}(x)$	$f_{n-1}(x)$	$f_n(x)$
1	ν_1	r^1	$b_1+(n-1)\xi$	f_2^{max}	$f_3^{max}+\xi$	$\cdots$	$f_{n-2}^{max}+(n-4)\xi$	$f_{n-1}^{max}+(n-3)\xi$	$f_n^{max}+(n-2)\xi$
2	ν_2	r^2	$b_1+(n-2)\xi$	$b_2+(n-1)\xi$	f_3^{max}	$\cdots$	$f_{n-2}^{max}+(n-5)\xi$	$f_{n-1}^{max}+(n-4)\xi$	$f_n^{max}+(n-3)\xi$
3	ν_3	r^3	$b_1+(n-3)\xi$	$b_2+(n-2)\xi$	$b_3+(n-1)\xi$	$\cdots$	$f_{n-2}^{max}+(n-6)\xi$	$f_{n-1}^{max}+(n-5)\xi$	$f_n^{max}+(n-4)\xi$
$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\ddots$	$\vdots$	$\vdots$	$\vdots$
$n-2$	ν_{n-2}	r^{n-2}	$b_1+2\xi$	$b_2+3\xi$	$b_3+4\xi$	$\cdots$	$b_{n-2}+(n-1)\xi$	f_{n-1}^{max}	$f_n^{max}+\xi$
$n-1$	ν_{n-1}	r^{n-1}	$b_1+\xi$	$b_2+2\xi$	$b_3+3\xi$	$\cdots$	$b_{n-2}+(n-2)\xi$	$b_{n-1}+(n-1)\xi$	f_n^{max}
n	ν_n	r^n	b_1	$b_2+\xi$	$b_3+2\xi$	$\cdots$	$b_{n-2}+(n-3)\xi$	$b_{n-1}+(n-2)\xi$	$b_n+(n-1)\xi$
$n+1$	ν_{n+1}	r^{n+1}	$f_1^{min}+(n-1)\xi$	b_2	$b_3+\xi$	$\cdots$	$b_{n-2}+(n-4)\xi$	$b_{n-1}+(n-3)\xi$	$b_n+(n-2)\xi$
$n+2$	ν_{n+2}	r^{n+2}	$f_1^{min}+(n-2)\xi$	$f_2^{min}+(n-1)\xi$	b_3	$\cdots$	$b_{n-2}+(n-5)\xi$	$b_{n-1}+(n-4)\xi$	$b_n+(n-3)\xi$
$n+3$	ν_{n+3}	r^{n+3}	$f_1^{min}+(n-3)\xi$	$f_2^{min}+(n-2)\xi$	$f_3^{min}+(n-1)\xi$	$\cdots$	$b_{n-2}+(n-6)\xi$	$b_{n-1}+(n-5)\xi$	$b_n+(n-4)\xi$
$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\vdots$	$\ddots$	$\vdots$	$\vdots$	$\vdots$
$2n-2$	ν_{2n-2}	r^{2n-2}	$f_1^{min}+2\xi$	$f_2^{min}+3\xi$	$f_3^{min}+4\xi$	$\cdots$	$f_{n-2}^{min}+(n-1)\xi$	b_{n-1}	$b_n+\xi$
$2n-1$	ν_{2n-1}	r^{2n-1}	$f_1^{min}+\xi$	$f_2^{min}+2\xi$	$f_3^{min}+3\xi$	$\cdots$	$f_{n-2}^{min}+(n-2)\xi$	$f_{n-1}^{min}+\xi(n-1)$	b_n
$2n$	ν_{2n}	r^{2n}	f_1^{min}	f_2^{min}	f_3^{min}	$\cdots$	f_{n-2}^{min}	f_{n-1}^{min}	f_n^{min}

EXAMPLE 6.2. Consider the settings in Example 4.2, that is, with feasible set $X = [0, 8]$ and criteria

$$f_1(x) = x\sqrt{x}, \qquad f_2(x) = (x-4)^2 + 2.$$

Suppose we use the wish-list in Table 6.8. Let $f_2^{\max} = 14$ and $f_i^{\min} = 0$ for $i \in [2]$. Then we can construct the reference list in Table 6.9 for the RPM. The associated paths are depicted in Figure 6.2.

TABLE 6.8: The wish-list used for the 2 criteria.

Priority	Criterion	Goal
1	$f_1(x)$	10
2	$f_2(x)$	10
3	$f_1(x)$	2
4	$f_2(x)$	2

TABLE 6.9: Reference list.

Priority	Reference point	$f_1(x)$	$f_2(x)$
1	r^1	$10+\xi$	14
2	r^2	10	$10+\xi$
3	r^3	$2+\xi$	10
4	r^4	2	$2+\xi$
5	r^5	ξ	2
6	r^6	0	0

For the RPM, we set α_1 and α_2 to 1, $\rho = 0$ and determine the value levels by algorithm (4.3.3) initialized by $v_6 = 0$ and $v_5 = 1$. The 2pϵc method ($\delta = 1$) results in the nondominated point $(f_1(\hat{x}), f_2(\hat{x})) = (2, 7.82)$, and the results of the RPM for different values of ξ are presented in Table 6.10. Observe that the solutions generated by the RPM approximate the solution of the 2pϵc method very well and that they improve as $\xi \to 0$. However, the number of iterations needed for the optimization tends to grow rapidly for smaller ξ. We quantify the complexity of the problem beforehand with parameter Δ defined by

$$\Delta := \left(\max_{\substack{i\in[2]\\ j\in[7]}} w_i^j\right) \Bigg/ \left(\min_{\substack{i\in[2]\\ j\in[7]}} w_i^j\right). \tag{6.2.1}$$

The reason that Δ increases as $\xi \to 0$ is that for every two consecutive reference points r^j and r^{j+1}, there is an criterion f_i for which $r_i^j - r_i^{j+1} = \xi$. Looking at the algorithm for the value

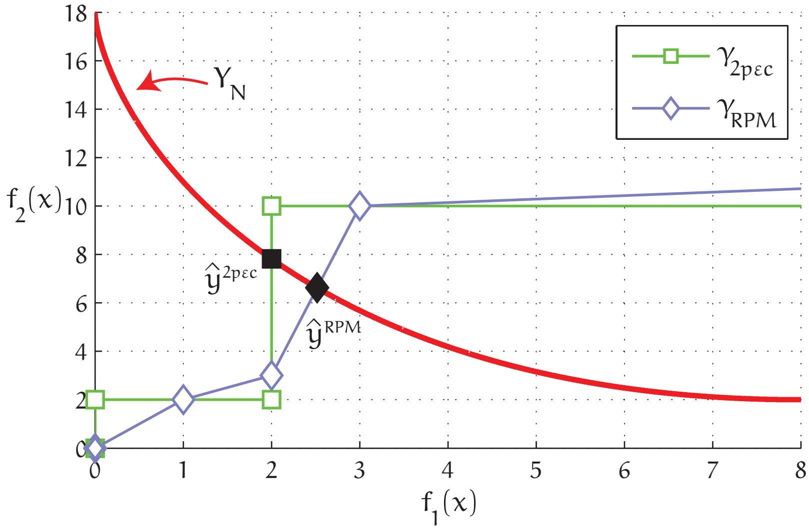

FIGURE 6.2: The paths of both the non relaxed 2pϵc method ($\gamma_{2p\epsilon c}$) and the RPM (γ_{RPM} with $\xi = 1$). The corresponding nondominated solutions are $\hat{y}^{2p\epsilon c}$ and $\hat{y}^{RPM}$ respectively.

TABLE 6.10: Solutions of the RPM for different values of ξ with the reference list in Table 6.9.

ξ	$f_1(x)$	$f_2(x)$	Δ	Iterations
1	2.52	6.62	$2.94 \cdot 10^2$	21
0.9	2.48	6.70	$5.82 \cdot 10^2$	32
0.8	2.44	6.78	$1.22 \cdot 10^3$	31
0.7	2.40	6.87	$2.72 \cdot 10^3$	36
0.6	2.35	6.97	$6.70 \cdot 10^3$	32
0.5	2.31	7.08	$1.89 \cdot 10^4$	54
0.4	2.25	7.21	$6.50 \cdot 10^4$	36
0.3	2.20	7.34	$3.07 \cdot 10^5$	46
0.2	2.14	7.48	$2.60 \cdot 10^6$	196
0.1	2.07	7.64	$9.25 \cdot 10^7$	17657
0.09	2.06	7.66	$1.58 \cdot 10^8$	8334
0.08	2.06	7.68	$2.88 \cdot 10^8$	63426
0.07	2.05	7.70	$5.68 \cdot 10^8$	78
0.06	2.04	7.71	$1.24 \cdot 10^9$	50582
2pϵc	2	7.82		

levels, (4.3.3), we note that these grow rapidly. As a result we see that for the values w_i^j (4.3.6), the ratio of the largest and smallest of the w_i^j becomes large as well.

This configuration of the RPM causes the solver to have numerical/convergence issues. Even for a simple multicriteria optimization problem as in Example 6.2 we encounter these issues, making this configuration of the RPM unsuitable for our application. Summing up the issues:

1. the path in the criterion space alters in (almost) vertical and (almost) horizontal parts. Therefore, there is too much focus on minimizing one of the criteria which can result into bad trade-offs,

2. we approximate the 2pϵc method with no relaxation while in practice we use $\delta = 1.03$,

3. the minimization model of the RPM (4.3.9) requires a lot of computation time or cannot be handled by the optimizer at all. This is caused by the many sharp turns in the preferred path which causes the weights w_i^j (4.3.6) to grow too rapidly.

We may conclude that the configuration of the RPM explained in this section is not applicable in radiation therapy. The optimizer is generally unable to handle the associated minimization model (4.3.9). Even if the optimizer does converge towards a treatment plan, there is a significant risk of having undesired trade-offs. In the next section, we adapt the path in the criterion space in order to deal with these issues.

6.3 Lexicographic reference point method

In order to improve the configuration of the RPM, a smoother preferred path of the RPM is needed. In this section, we describe a specific configuration of the RPM, called the *lexicographic reference point method* (LRPM), which smooths out the preferred path of the RPM described in Section 6.2. Also, the LRPM utilized the sensitivity parameters $\rho = (\rho_1, \ldots, \rho_n)$ of the RPM (Section 4.3.3).

To illustrate the smoothing of the preferred path, we reconsider Example 6.2.

EXAMPLE 6.3. We use the same settings as in Example 6.2. However, we now construct the preferred path of the LRPM which is a smoother path than the one in Example 6.2. The path of the LRPM is depicted in Figure 6.3. The corresponding reference list that we applied here is given in Table 4.4 and actually, we already analyzed this path of the LRPM in Example 4.2. The value for Δ (6.2.1) for the preferred path γ_{LRPM} is 4 (independent of the value for ρ) which is low when compared to the values in Table 6.10.

The preferred path of the LRPM should be able to deal with large-scale problems, and also maintain the prioritized structure (lexicographic ordering) induced by the wish-list. The algorithm that selects the reference points which lead to a smooth preferred path can be generalized in the case of n criteria. In our application, we also want to assign the same priority to different criteria. These demands are processes in Algorithm 6.1, which automatically determines the reference list from a predetermined wish-list. Basically, Algorithm 6.1 consists of three main loops:

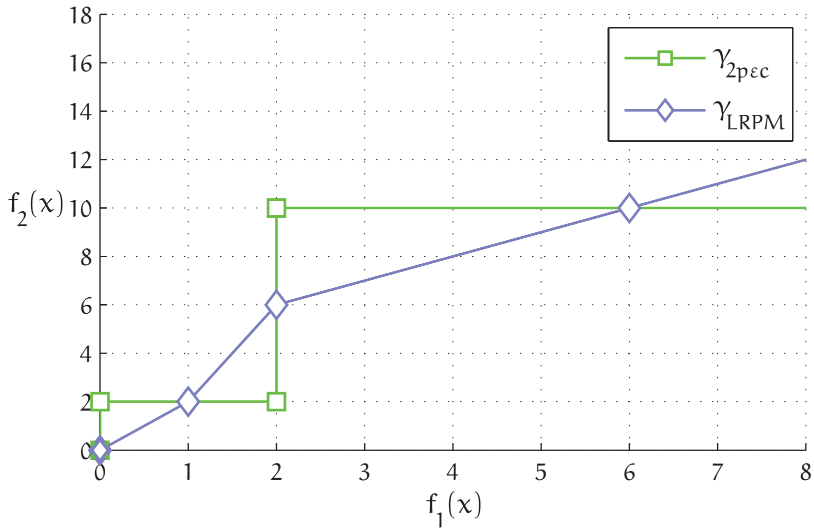

FIGURE 6.3: The paths of both the non relaxed 2pεc method ($\gamma_{2p\epsilon c}$) and the LRPM (γ_{LRPM}). The path of the LRPM uses the midpoints of the linear segments of $\gamma_{2p\epsilon c}$ as reference points.

1. In the first loop, the goal values of the wish-list are used as aspiration points. Each different priority in the wish-list adds a reference point to the reference list. At the end of the loop, a row of zeros is added representing full minimization of the criteria (in our application).

2. In the second loop, aspiration points in between already defined aspiration points are filled in by linear interpolation.

3. In the third loop, the remaining undefined aspiration points are filled in. These are located at the upper triangle of the reference list. These aspiration points are determined by putting them on the linear line of the two largest reference points which are already defined after the second loop.

It should be mentioned that the choice of value levels $v_1, v_2, \ldots$ does not affect the optimal criterion values $f(\hat{x}) \in Y$, as long as the convexity condition (4.3.3) is satisfied. The value levels should thus not be seen as parameters in the RPM, but rather as scalars that assure convexity of minimization model (4.3.9).

Note that in Algorithm 6.1, we do not take upper bounds f_i^{max} into account which reduces the number of reference points. Moreover, the number of inequalities of the form

$$v_j + w_i^j (f_i(x) - r_i^j) \leqslant a_i,$$

in the minimization model of the RPM (4.3.9) is reduced as well as the complexity of the model. The LRPM thus uses a smooth preferred path with a small number of reference points while retaining the lexicographic ordering. Therefore, the LRPM is suitable for the large-scale problems

Algorithm 6.1: Reference list of the LRPM.

Data: The wish-list with $p \in \mathbb{N}$ priorities and $n \in \mathbb{N}$ $(n > 1)$ criteria;
Result: Reference list $R := (r_i^j)_{i,j}$;

```
R := ∅;
i := 1;
while i ⩽ p do
    add new row j of length n to reference list R;
    gather entries with the same priority i in index set K;
    for k ∈ K do
        set r_k^j := b_k, where b_k is the goal value of priority k in the wish-list;
    end
    set i := i + length(K);
end
add row of zeros of length n to reference list R;
for i ∈ [n] do
    for every empty aspiration point r_i^j do
        if there are nonempty aspiration points r_i^{j1} and r_i^{j2} with r_i^{j2} < r_i^j < r_i^{j1} then
            fill in r_i^j by linear interpolation between r_i^{j1} and r_i^{j2};
            set w := (j2 − j)/(j2 − j1) then r_i^j := w r_i^{j1} + (1 − w) r_i^{j2};
        end
    end
end
for i ∈ [n] do
    for every empty aspiration point r_i^j do
        find largest entry r_i^{j1} in the column;
        set r_i^j on the linear interpolation line between r_i^{j1} and r_i^{j1+1};
        r_i^j := r_1^{j1} + (j1 − j)(r_i^{j1} − r_i^{j1+1});
    end
end
```

which we encounter in practice.

Concerning the other parameters that configure the RPM:

1. α_1 and α_2 are set to 1 in the LRPM since the preferred path does not need an additional bend below the last reference point (the origin) or above the first reference point r^1,
2. $\rho = (\rho_1, \dots, \rho_n)$ are set manually, although chosen uniformly per patient group.

Next, we apply the LRPM on an example in radiation therapy.

EXAMPLE 6.4. Here, we use the same settings as in Example 6.1 but now with the LRPM. The constraints in the wish-list (Table 6.4) are added to the RPM minimization model (4.3.9) as $g(x) \leqslant 0$. For the criteria we construct the reference list by applying Algorithm 6.1.

After the first loop in Algorithm 6.1 and adding the row of zeros, the reference list is as in Table 6.11. The second loop in Algorithm 6.1 then fills in the aspiration points in between

TABLE 6.11: Reference list after first loop.

Priority	Reference point	Parotid (R)	Parotid (L)	SMG (R)	SMG (L)
1	r^1	39	$\varnothing$	$\varnothing$	$\varnothing$
2	r^2	$\varnothing$	39	$\varnothing$	$\varnothing$
3	r^3	$\varnothing$	$\varnothing$	39	$\varnothing$
4	r^4	$\varnothing$	$\varnothing$	$\varnothing$	39
5	r^5	20	$\varnothing$	$\varnothing$	$\varnothing$
6	r^6	$\varnothing$	20	$\varnothing$	$\varnothing$
7	r^7	$\varnothing$	$\varnothing$	20	$\varnothing$
8	r^8	$\varnothing$	$\varnothing$	$\varnothing$	20
9	r^9	10	$\varnothing$	$\varnothing$	$\varnothing$
10	r^{10}	$\varnothing$	10	$\varnothing$	$\varnothing$
11	r^{11}	$\varnothing$	$\varnothing$	10	$\varnothing$
12	r^{12}	$\varnothing$	$\varnothing$	$\varnothing$	10
13	r^{13}	0	0	0	0

already defined aspiration points, see Table 6.12. Finally, the third loop in Algorithm 6.1 com-

TABLE 6.12: Reference list after second loop.

Priority	Reference point	Parotid (R)	Parotid (L)	SMG (R)	SMG (L)
1	r^1	39	$\varnothing$	$\varnothing$	$\varnothing$
2	r^2	34.25	39	$\varnothing$	$\varnothing$
3	r^3	29.5	34.25	39	$\varnothing$
4	r^4	24.25	29.5	34.25	39
5	r^5	20	24.25	29.5	34.25
6	r^6	17.5	20	24.25	29.5
7	r^7	15	17.5	20	24.25
8	r^8	12.5	15	17.5	20
9	r^9	10	12.5	15	17.5
10	r^{10}	7.5	10	12.5	15
11	r^{11}	5	20/3	10	12.5
12	r^{12}	2.5	10/3	5	10
13	r^{13}	0	0	0	0

pletes the reference list in Table 6.13. Due to assigning aspiration points on the same linear

TABLE 6.13: Complete reference list.

Priority	Reference point	Parotid (R)	Parotid (L)	SMG (R)	SMG (L)
1	r^1	39	43.75	48.5	53.25
2	r^2	34.25	39	43.75	48.5
3	r^3	29.5	34.25	39	43.75
4	r^4	24.25	29.5	34.25	39
5	r^5	20	24.25	29.5	34.25
6	r^6	17.5	20	24.25	29.5
7	r^7	15	17.5	20	24.25
8	r^8	12.5	15	17.5	20
9	r^9	10	12.5	15	17.5
10	r^{10}	7.5	10	12.5	15
11	r^{11}	5	20/3	10	12.5
12	r^{12}	2.5	10/3	5	10
13	r^{13}	0	0	0	0

segment as others, some of the inequalities

$$v_j + w_i^j(f_i(x) - r_i^j) \leqslant a_i,$$

are the same. In this example, we only need to implement 19 of these inequalities and the value for Δ (6.2.1) is 27.436. Consequently, the solver did not have any issues when solving the corresponding minimization model (4.3.9).

Next, we demonstrate that the LRPM is capable of approximating the criterion values for both the relaxed ($\delta = 1.03$) and non relaxed ($\delta = 1$) 2pϵc method, which are gathered in Table 6.14.

TABLE 6.14: Criterion values for the 2pϵc method with and without relaxation.

Volume	Type	2pϵc method ($\delta = 1.03$)	2pϵc method ($\delta = 1$)
Parotid (R)	mean	3.43 Gy	4.27 Gy
Parotid (L)	mean	23.52 Gy	24.05 Gy
SMG (R)	mean	10.96 Gy	13.53 Gy
SMG (L)	mean	39.79 Gy	39.00 Gy

Applying the LRPM for different sensitivity parameters,

$$\rho^1 = (3,\ 2,\ 3.5,\ 0.5),$$
$$\rho^2 = (0.5,\ 3,\ 0.5,\ 2.5),$$

results into the criterion values in Table 6.15. For different sensitivity parameters, the LRPM is

TABLE 6.15: Criterion values of the treatment plan generated with the 2pϵc method.

Volume	Type	LRPM (with ρ^1)	LRPM (with ρ^2)
Parotid (R)	mean	3.35 Gy	4.19 Gy
Parotid (L)	mean	23.49 Gy	24.01 Gy
SMG (R)	mean	11.05 Gy	13.34 Gy
SMG (L)	mean	39.81 Gy	39.02 Gy

able to generate nearly identical treatment plans as the 2pϵc method. This indicates that the choice of sensitivity parameters is important for the treatment plan.

6.4 Discussion of the 2pϵc method and the LRPM

In this section, we discuss some of the characteristics of both the 2pϵc method and the LRPM in order to provide a quick overview of both methods. Difficulties with applying the LRPM arise when sufficient conditions are given to the criteria.

First, some key characteristics of the 2pϵc method:

- n criteria with a wish-list,
- multiple optimizations to generate a Pareto optimal treatment plan,
- fixed relaxation parameter δ,
- different criteria should have different priorities,
- repeated feedback with automated DM (wish-list) after each optimization,
- integration of sufficient goals.

Next, we look at the characteristics of the LRPM:

- n criteria with a reference list (constructed with the wish-list and Algorithm 6.1),
- single optimization to generate a Pareto optimal treatment plan,
- sensitivity parameters $\rho_1, \ldots, \rho_n$ (manually chosen),

- different criteria can have the same priority,
- no feedback,
- no integration of sufficient goals.

The most important similarity between both methods is that the wish-list is utilized as input. Another similarity is that both methods produce a Pareto optimal treatment plan. As a consequence, we cannot deterministically tell which of the treatment plans is better. A gain in one criteria (for example, a lower mean dose for the parotid glands) means a deterioration in at least one of the other criteria (for example, a higher mean dose for the submandibular glands).

The main differences between both methods are the number of optimizations needed to generate the treatment plan and the additional parameters of the method. Because the 2pϵc method optimizes per criterion, it can be verified whether the goal value is feasible or not. Depending on the result, a suitable constraint is set (feedback) before processing to subsequent optimizations. When the goal value is infeasible, the relaxation parameter is applied to set a suitable constraint. The LRPM on the other hand, only consist of one optimization and therefore no feedback from the wish-list can be provided. This is also the reason why the LRPM has different parameters $(\rho_1, \dots, \rho_n)$, which introduce sensitivity in a different manner than the 2pϵc method (see Section 4.3.3 for the interpretation of the sensitivity parameters of the RPM).

For the LRPM, it is easy to implement the same priority for different criteria (see first loop in Algorithm 6.1), the goal values are just set in the same reference point. In the 2pϵc method however, there is no good way to integrate the same priority for different criteria since it is based on the ϵ-constraint method (Section 4.2). Currently, we perform a weighted sum optimization with equal weights instead of an ϵ-constraint optimization when we encounter such a situation. However, there are no good heuristics to incorporate equal priorities in the 2pϵc method.

If, after performing an optimization in the 2pϵc method, the goal value turns out feasible it can also be decided to set a sufficient constraint. For example, if a sufficient value of 0.5 is given for the LTCP of the tumour (criterion f_1) and 0.4 turns out to be feasible (after solving an ϵ-constraint problem), then a constraint of $f_1(x) \leqslant 0.5$ is set. In the LRPM, sufficient values for criteria cannot be integrated. If we want to incorporate a sufficient value for 0.5 for f_1, then we would ideally set all r_1^j to 0.5 upward of a certain $j \in \mathbb{N}$. However, subsequent aspiration points for a criterion cannot be the same in the RPM (explained in Section 4.3.1). This can be approximated by setting $r_1^j = 0.5$ and $r_1^{j+k} = 0.5 - k\xi$, for $k \in \mathbb{N}$ and $\xi > 0$ small. This again leads to a large ratio (6.2.1) of the largest and smallest of the values w_i^j (4.3.6) (if the partial achievement function s_1 remains convex). Another possibility would be to simply add the constraint

$$f_1(x) \geqslant 0.5,$$

however the minimization problem looses its convexity when adding this constraint (since the LTCP (5.1.1) is a nonlinear convex function).

In the clinical wish-lists however, the first priority is often to minimize the LTCP to some value (say 0.5) which is also sufficient. Since this is the first priority, we can "solve" this issue by doing the following:

1. First we solve the ϵ-constraint problem

$$\begin{aligned} \min_{x \in X} \quad & f_1(x). \\ \text{subject to} \quad & g(x) \leqslant 0 \end{aligned} \tag{6.4.1}$$

   Depending on the optimal solution $\hat{x} \in X$ we set $\epsilon_1 = \max(b_1, \delta f_1(\hat{x}))$ where b_1 is the goal value and $\delta = 1.03$.

2. For the remaining criteria we construct the minimization model (4.3.9) of the LRPM (as discussed in Section 6.3). Furthermore, we add the constraints

$$\begin{aligned} g(x) &\leqslant 0, \\ f_1(x) &\leqslant \epsilon_1, \end{aligned}$$

   to minimization model (4.3.9), where ϵ_1 is obtained from step 1.

So, we first replicate the first optimization of the 2pϵc method and, depending on this results, we construct the minimization model of the LRPM for the remaining criteria with the addition of a constraint for the first criterion.

Of course, we could also construct a linear partial achievement function for the LTCP of the tumour. However, a small difference in the LTCP (say 0.1) can lead to a significant difference for the quality of tumour irradiation. By replicating the first optimization in the 2pϵc method, we ensure the same quality of tumour irradiation when generating the Pareto optimal treatment plans.

CHAPTER 7

Results

In this chapter, we apply the lexicographic reference point method (LRPM) (Section 6.3) as an alternative for the 2-phase ϵ-constraint (2pϵc) method for automated treatment planning. Treatment plans generated by the 2pϵc method are considered the golden standard, and will be compared to the treatment plans generated by the LRPM with the evaluation tools explained in Section 5.2 (criterion values, cumulative dose volume histograms and dose distributions).

We consider two patient groups:

1. prostate cancer patients,

2. head-and-neck cancer patients.

For both patient groups, we want to apply the LRPM with uniformly chosen sensitivity parameters $\rho_1, \ldots, \rho_n$. It turns out that this is feasible for the group of prostate cancer patients. However, the variety in size and location of tumours in the head-and-neck region (Voet et al., 2013) makes it hard to choose a uniform set of sensitivity parameters for that whole patient group. For example, in case of a unilateral (one-sided) tumour, either the left or right salivary glands can be spared with high probability while for bilateral (two-sided) tumours, both the left and right salivary glands should have the same probability (more or less) to be spared. It thus depends on the location of the tumour which trade-offs are favourable in a treatment plan. In our study, we consider head-and-neck cancer patients with a bilateral tumour.

To enable comparison of the treatment plans we use the same beam setup (number of beams and beam angles) for all patients. We use 23 beams placed in an equi-angular setup to mimic VMAT-like (*volumetric modulated arc therapy*) dose distributions. Per beam angle, the number of beamlets is $\mathcal{O}(10^2)$. For all patients, VMAT plans have been calculated with both the 2pϵc method and the LRPM. In VMAT, the patient is continuously irradiated by a single arc rotation of the treatment device.

7.1 Prostate cancer patients

For our study on the group of prostate cancer patients, we have randomly selected a sample of 30 prostate cancer patients. For these patients, the same wish-list is used. The VMAT plans generated by the 2pϵc method with a 23 equi-angular beam setup were regarded as high quality (Voet et al., 2014).

The wish-list, used to automatically generate the treatment plans with the 2pϵc method, in Table 7.1 was established by physicians, dosimetrists and physicists (Voet et al., 2014).

TABLE 7.1: Wish-list for prostate cancer patients.

Constraints

Number	Volume	Type	Limit
1	Tumour (prostate)	max	104% of prescribed dose
2	Tumour (seminal vesicles)	max	104% of prescribed dose
3	Tumour Shell 50 mm	max	60% of prescribed dose
4	Rectum	max	104% of prescribed dose
5	Hips (L + R)	max	40 Gy
6	Unspecified Tissue	max	104% of prescribed dose
7	Tumour (prostate)	LTCP	0.5
8	Tumour (seminal vesicles)	LTCP	0.5

Criteria

Priority	Volume	Type	Goal value
1	Rectum	gmean_{12}	40% of prescribed dose
2	Rectum	gmean_{8}	25% of prescribed dose
3	Rectum	mean	33% of prescribed dose
4	External Ring	max	40% of prescribed dose
5	Tumour Shell 5 mm	max	93% of prescribed dose
6	Anus	mean	10% of prescribed dose
7	Tumour Shell 15 mm	max	70% of prescribed dose
8	Tumour Shell 25 mm	max	50% of prescribed dose
9	Bladder	mean	60% of prescribed dose
10	Hip (L + R)	mean	25% of prescribed dose
11	Unspecified Tissue	mean	10 Gy

For prostate cancer patients, the tumour has two different dose prescriptions:

– the part of the tumour located in the prostate,

– the part of the tumour located in the seminal vesicles.

The part of the tumour in the prostate is prescribed a higher dose (78 Gy) than the part of the tumour in the seminal vesicles (72.2 Gy), see Voet et al. (2014). In practice, it feasible to constrain both the LTCPs of the tumour to 0.5 (so the LTCPs of the tumour are no criteria) due to the 23 equi-angular beam setup and the maximum constraints in the wish-list (Table 7.1). Looking at the criteria in the wish-list, the highest priority is to minimize the generalized mean for the rectum which should lead to a minimal amount of volume of the rectum that receives high doses. Minimizing on the external ring structure serves to minimize the *entrance dose* (the dose absorbed below the surface of the skin). The tumour shells (5, 15 and 25 mm around the tumour) are added to achieve a large decrease in dose outside the tumour. Other criteria involve the anus, bladder, hips and the other unspecified tissue (body). Note that the hips (left and right) are given the same priority in the wish-list and that the last priority serves to remove as much of the unnecessary dose inside the patient as possible.

Next, we test both the 2pϵc method and the LRPM on a patient with prostate cancer. For the resulting treatment plans, we compare the criterion values, DVHs and visualize the dose distributions. Then, we present the results for the sample of 30 prostate cancer patients. For the VMAT plans generated by the LRPM (as described in Section 6.3), we used a uniform set of sensitivity parameters.

7.1.1 Example prostate cancer patient

Here, we consider a prostate cancer patient for whom two VMAT plans have been calculated, one is generated by the 2pϵc method and the other by the LRPM. Both methods utilize the wish-list in Table 7.1.

The criterion values for the VMAT plans are presented in Table 7.2. Observe that both the gmean_{12} and gmean_8 of the rectum are in favour of the LRPM. Also, the maximum dose delivered to the external ring and the 5 and 15 mm tumour shells are in favour of the LRPM. The mean doses delivered to both the rectum and the anus are in favour of the 2pϵc method. There is also a noticeable difference in the mean doses of the hips, which are in favour of the 2pϵc method.

Remember that both treatment plans are Pareto optimal, so the improvement for the LRPM in some of the criteria must lead to a deterioration somewhere else. For instance, the LRPM gives a better result for the generalized mean of the rectum but the mean dose of the rectum, anus and the hips are in favour of the 2pϵc method. The LRPM offers a different trade-off between the criteria than the 2pϵc method.

Next, we compare the cumulative DVHs of both treatment plans, see Figure 7.1. Notice that for both treatment plans, the DVH curves of the tumour (prostate and seminal vesicles) are nearly identical, which is due to the constraints in the wish-list (Table 7.1). In the DVHs, it

TABLE 7.2: The criterion values for the prostate cancer patient.

Volume	Type	2pϵc method	LRPM
Rectum	gmean_{12}	62.2 Gy	61.7 Gy
Rectum	gmean_{8}	57.6 Gy	57.0 Gy
Rectum	mean	27.9 Gy	28.1 Gy
External Ring	max	28.7 Gy	26.6 Gy
Tumour Shell 5 mm	max	76.1 Gy	75.6 Gy
Anus	mean	21.6 Gy	22.2 Gy
Tumour Shell 15 mm	max	59.8 Gy	59.0 Gy
Tumour Shell 25 mm	max	49.2 Gy	49.4 Gy
Bladder	mean	39.3 Gy	38.9 Gy
Hip (L)	mean	18.9 Gy	19.7 Gy
Hip (R)	mean	17.0 Gy	19.1 Gy
Unspecified Tissue	mean	8.0 Gy	8.2 Gy

becomes clear what the differences between both treatment plans are. The high doses delivered to the rectum (high priority) are less for the LRPM than for the 2pϵc method, however there is also a clear deterioration in the mean doses of the hips (low priority).

Finally, to visualize which dose is delivered to which part of an organ at risk (OAR), we depict the dose distributions in Figure 7.2. The dose distribution explain why it is difficult to lower the generalized mean dose delivered to the rectum: the rectum is close to the tumour. The isodose lines are relatively close to each other between the rectum and the tumour which represents a steep dose fall-off (high dose conformality). The main visible differences between the dose distributions in Figure 7.2 are the isodose lines around the rectum, bladder and hips. From the dose distributions, we may conclude that the mean dose received by the rectum and hips are slightly in favour of the treatment plan generated by the 2pϵc method, and the mean dose received by the bladder is slightly in favour of the treatment plan generated by the LRPM. The dose distributions show, in addition, which part of the OARs receive a high or low dose. For example, the volume of the rectum closest to the tumour gets irradiated the most while the volume of the rectum further away from the tumour receives a lower dose.

7.1.2 Sample of 30 prostate cancer patients

For a uniform set of sensitivity parameters, the LRPM is applied to generate VMAT plans for 30 prostate cancer patients. Also, the VMAT plans were calculated for the 2pϵc method (golden standard) in order to compare the results.

We will not show the DVHs and dose distributions for all these patients, instead we present the results in several plots in which evaluation criteria are shown for both the 2pϵc method and the LRPM. The selected evaluation criteria of interest:

1. rectum V_{75Gy}, the amount of volume (%) of the rectum receiving at least 75 Gy,
2. rectum V_{60Gy}, the amount of volume (%) of the rectum receiving at least 60 Gy,
3. rectum mean dose,
4. anus mean dose,
5. tumour $V_{95\%}$ (prostate), the amount of volume (%) of the prostate receiving at least 95% of the prescribed dose,
6. tumour $V_{95\%}$ (seminal vesicles), the amount of volume (%) of the seminal vesicles receiving at least 95% of the prescribed dose,
7. bladder V_{65Gy},
8. bladder mean dose,
9. tumour shell 15 mm maximum dose,
10. tumour shell 25 mm maximum dose,
11. left hip maximum dose,
12. right hip maximum dose.

The evaluation criteria are shown in Figure 7.3, Figure 7.4 and Figure 7.5.

A point in each of these plots represents a criterion value for the two treatment plans: the value on the horizontal axis corresponds to the evaluation criterion of the treatment plan generated by the 2pϵc method. Similarly, the value on the vertical axis corresponds to the LRPM for a particular evaluation criterion. Points under the solid line (identity line) are in favour of the treatment plan generated by the LRPM and for points above the solid line, the 2pϵc method has a better result.

From Figure 7.3 we observe that the volume of the rectum receiving high dose is less for the LRPM since the points in the V_{75Gy}- and V_{60Gy}-plots are below the identity line. This is no coincidence, as we tuned the sensitivity parameters so that the highest priority in the wish-list (Table 7.1) are in favour of the LRPM. For the rectum, the LRPM reduces the V_{75Gy} by 0.52 ± 0.24, where 0.52 is the mean of the differences and 0.24 is the standard deviation. The mean $\bar{y}$ is defined as

$$\bar{y} := \frac{1}{n} \sum_{i \in [n]} y_i,$$

and the standard deviation as

$$\mathrm{std}(y) := \sqrt{\frac{1}{n-1} \sum_{i \in [n]} (y_i - \bar{y})}.$$

The LRPM also reduces the rectum V_{60Gy} by 0.54 ± 0.31. The mean dose of the rectum however, is sometimes in favour of the 2pϵc method and sometimes in favour of the LRPM. The LRPM differed by -0.08 ± 0.53 for the mean dose of the rectum (the 2pϵc method gives better results on average). Also for the mean dose of the anus, the LRPM differed by -0.16 ± 0.49 making the results of the 2pϵc method slightly better on average.

In Figure 7.4 it is shown that the quality of the irradiation on the tumour is high for both plans. For most patients, the prostate tumour $V_{95\%}$ is slightly improved for the LRPM (namely 0.05 ± 0.05). Looking at the scale of the axis, we observe that all patients have a prostate tumour $V_{95\%}$ of at least 99.1%. This means that for all patients, 99.1% of the prostate tumour received at least 95% of the prescribed dose. For 10 patients, the tumour had two different dose prescriptions (prostate and seminal vesicles tumour, see Section 7.1). For these patients, the $V_{95\%}$ for the seminal vesicles is at least 99.1%. The LRPM slightly improved the $V_{95\%}$ of the seminal vesicles by 0.02 ± 0.05. For the bladder, we observe that in most cases, both the V_{65Gy} and mean dose are in favour of the 2pϵc method. The LRPM differed by -1.38 ± 1.29 for the bladder V_{65Gy} and -1.90 ± 1.79 for the mean dose of the bladder.

In Figure 7.5 the differences for the tumour shells are sometimes in favour of the 2pϵc method and sometimes in favour of the LRPM. The LRPM differed by -0.13 ± 2.13 for the maximum dose of the 15 mm shell and -1.12 ± 2.37 for the maximum dose of the 25 mm shell. Keep in mind that the tumour shells serve to realize a steep dose fall-off outside the tumour (dose conformality), and are not actual organs. The differences for the maximum dose on the hips tend to be in favour of the 2pϵc method and are sometimes quite large. The LRPM differed by -0.88 ± 1.74 for the maximum dose of the left hip and -1.00 ± 1.89 for the maximum dose of the right hip.

We kept track of the computation times for all 30 patients. We observed that, on average, the LRPM reduces the computation time from 34.9 to 3.0 minutes. This is an average speed-up factor of nearly 12.

All treatment plans were found clinically acceptable. For all patients, the tumour irradiation for both the 2pϵc method and the LRPM were of similar high quality. For high prioritized criteria, the LRPM performed better while the 2pϵc method gives better results for the lower prioritized criteria. These differences were found neither clinically nor statistically relevant (Heijmen et al., 2014). Furthermore, the computation time of the LRPM is nearly 12 times faster (on average) when compared to the 2pϵc method.

7.2 Head-and-neck cancer patients

In this section we consider 2 head-and-neck cancer patients. As mentioned before, generating a treatment plan for head-and-neck cancer patients is complex due to the differences in tumour size and location as well as the sizes of the surrounding organs. For this reason, we selected two patients with a bilateral tumour. We again use a 23 equi-angular beam setup combined with a fixed wish-list (Voet et al., 2013), for which the treatment plans generated by the 2pϵc method are of high quality.

The wish-list used is similar to the one in Table 7.3. Observe that, in contrast to the wish-list

TABLE 7.3: Wish-list for head-and-neck patients.

Constraints

Number	Volume	Type	Limit
1	Tumour	max	107% of the prescribed dose
2	Cord	max	38 Gy
3	Unspecified Tissue	max	107% of the prescribed dose

Criteria

Priority	Volume	Type	Goal value	
1	Tumour	LTCP	0.4	(also a sufficient value)
2	Parotids/SMGs	mean	39 Gy	
3	Parotids/SMGs	mean	20 Gy	
4	Oral cavity	mean	39 Gy	
5	Cord/Brainstem	max	38 Gy	
6	External Ring	max	90% of the prescribed dose	
7	Larynx/swallowing muscles	mean	75% of the prescribed dose	
8	Tumour Shell 1 cm	max	75% of the prescribed dose	
9	Parotids/SMGs	mean	10 Gy	
10	Tumour Shell 4 cm	max	40% of the prescribed dose	
11	Parotids/SMGs	mean	2 Gy	

for prostate cancer patients (Table 7.1), the LTCP of the tumour is added as a criterion instead of a constraint. Due to the complexity of the head-and-neck cases, it cannot be guaranteed that the goal value of 0.4 is feasible (because of other constraints and the overlap of the tumour with surrounding organs). A way to deal with the first priority in the LRPM is explained in Section 6.4, namely to first perform an ϵ-constraint optimization on the LTCP and, depending on the results, add an extra constraint in the minimization model of the LRPM (4.3.9), which then optimizes the other criteria. For head-and-neck cancer patients, the LRPM thus needs 2 optimizations (instead of 1) to generate a treatment plan. Other features in the wish-list for head-and-neck cancer patients (Table 7.3), is that the same criteria (same volume and type) appears multiple times and that there are several equal priorities involved.

A high priority is to spare the salivary glands (parotid glands and submandibular glands (SMGs)). Other criteria involve the oral cavity, cord, brainstem, larynx and shell structures. We also consider 4 swallowing muscles:

1. musculus constrictor superior (MCS),
2. musculus constrictor medius (MCM),
3. musculus constrictor inferior (MCI),
4. musculus constrictor cricopharyngeus (MCP).

For the 2 patients, the criterion values for both treatment plans (of the 2pϵc method and the LRPM) are shown in Table 7.4. Both patients were treated with 46 Gy prescribed to the tumour. Note that for patient I, less OARs are given as criteria than for patient II. A certain OAR can be outside the region of treatment (depending on the location and size of the tumour) or, a large part of the OAR overlaps with the tumour so that the OAR cannot be spared anyhow. Observe that the differences for the criteria can be quite large, especially for lower prioritized criteria. For both patients, the mean dose delivered to the parotid glands is less for the 2pϵc method but within a margin of 2 Gy. In return, the LRPM has generated a treatment plan for patient I with a lower maximum dose/generalized mean dose on the tumour shells plus additional sparing on both the cord and brainstem. The maximum dose of the cord is reduced with almost 8 Gy, and the maximum dose of the brainstem with more than 10 Gy. For Patient II, the LRPM gives an improvement of more than 5 Gy in mean dose for the right SMG as well as improvements for the cord, larynx, swallowing muscles, esophagus and right cochlea. The maximum dose of the cord is reduced with more than 6 Gy, the mean dose of the larynx is reduces by 4 Gy and the mean doses of the swallowing muscles (MCS, MCM, MCI and MCP) is reduced significantly (7 Gy for the MCM, 11 Gy for the MCI and 14 Gy for the MCP). Also the mean dose delivered to the esophagus is halved, so that the mean dose is only 18 Gy. At last, the maximum dose on the right cochlea is improved by more than 7 Gy.

For both patients, the generated treatment plans are quite different. A slight deterioration (less than 2 Gy) in the mean dose of the parotid glands (highest priority) leads to major improvements for lower prioritized criteria. We thus expect to observe significant differences in both the cumulative DVHs and dose distributions.

For patient I, the DVHs are shown in Figure 7.6 and the dose distributions in Figure 7.7.

For the DVHs of patient I (Figure 7.6), we observe that the parotid glands and left SMG are in favour of the 2pϵc method (which is confirmed in Table 7.4). The LRPM gives better results for the other OARs in Figure 7.6. For the OARs not shown in Figure 7.6, the differences in DVH

TABLE 7.4: The criterion values for the 2 head-and-neck cancer patients.

		Patient I		Patient II	
Volume	Type	2pϵc method	LRPM	2pϵc method	LRPM
Tumour	LTCP	0.4	0.4	0.4	0.4
Parotid (L)	mean	16.1 Gy	17.3 Gy	28.5 Gy	30 Gy
Parotid (R)	mean	17.4 Gy	18.9 Gy	22.4 Gy	24.2 Gy
SMG (L)	mean	34.1 Gy	35.1 Gy	44.0 Gy	43.8 Gy
SMG (R)	mean	35.6 Gy	35.1 Gy	37.7 Gy	32.6 Gy
Tumour Shell 0.5 cm	max	43.7 Gy	41.9 Gy	43.7 Gy	42.8 Gy
Tumour Shell 1.5 cm	max	35.6 Gy	33.1 Gy	36.8 Gy	34.6 Gy
Tumour Shell 3 cm	gmean_{15}	20.5 Gy	18.3 Gy	21.3 Gy	22.5 Gy
Tumour Shell 4 cm	gmean_{15}	16.1 Gy	15.2 Gy	16.2 Gy	18.9 Gy
Oral cavity	mean	27.9 Gy	28.1 Gy	29.8 Gy	25.1 Gy
Cord	max	24.6 Gy	16.4 Gy	26.7 Gy	20.6 Gy
Brainstem	max	17.7 Gy	7.2 Gy	30 Gy	29.4 Gy
External Ring	max	34.1 Gy	29.3 Gy	39.1 Gy	33.6 Gy
Larynx	mean	∅	∅	34.7 Gy	30.4 Gy
MCS	mean	∅	∅	47.8 Gy	47.3 Gy
MCM	mean	∅	∅	41.6 Gy	34.6 Gy
MCI	mean	∅	∅	34.6 Gy	23.3 Gy
MCP	mean	∅	∅	34.6 Gy	20.1 Gy
Esophagus	mean	∅	∅	36.1 Gy	18.0 Gy
Cochlea (L)	max	∅	∅	30 Gy	30 Gy
Cochlea (R)	max	∅	∅	30 Gy	22.8 Gy
Unspecified Tissue	mean	10.0 Gy	10.1 Gy	9.3 Gy	9.4 Gy

curves were minimal. The DVH curves for the tumour are nearly identical for both treatment plans.

For patient I, observe from the dose distributions of both treatment plans (Figure 7.7) that the isodose lines near the parotid glands are more favourable for the 2pϵc method. It can also be observed that the mean dose of the oral cavity is in favour of the LRPM (more blue, less red) and that the cord is more spared in the dose distribution of the LRPM.

For patient II, the dose distributions for both plans are depicted in Figure 7.8 and the DVHs are shown in Figure 7.9 and Figure 7.10.

For patient II, both plans are quite different as may be expected from the criterion values in Table 7.4. For the dose distributions (Figure 7.8), observe that the differences around the cord and MCM are significant. The dose distribution for the LRPM leads to less irradiation on the cord and MCM while still irradiating the tumour sufficiently.

Not only the dose distributions of both plans are quite different, also the DVHs show an interesting trade-off. In Figure 7.9, both parotid glands receive a slightly higher mean dose for the LRPM. However, both SMGs (especially the right SMG) are more spared in the treatment plan generated by the LRPM. Also, the DVH curves of the cord and oral cavity are in favour of the LRPM. Figure 7.9 also shows that the DVH curves for the tumour are nearly identical. Most differences in the DVH curves in Figure 7.10 are significant. Only the DVH curve of the tumour shell (4 cm) is in favour of the 2pϵc method which can also be observed from the dose distributions in Figure 7.8. The DVH curves of the larynx, esophagus, right cochlea and swallowing muscles are all in favour of the LRPM, mostly with a significant improvement.

For patient I, the plans were found to be of similar quality and for patient II, the treatment plan of the LRPM was favoured. The LRPM reduced the computation time from 133.2 to 42.1 minutes (speed-up factor of 3.2) for patient I, and from 294.6 to 67.0 minutes (speed-up factor of 4.4) for patient II.

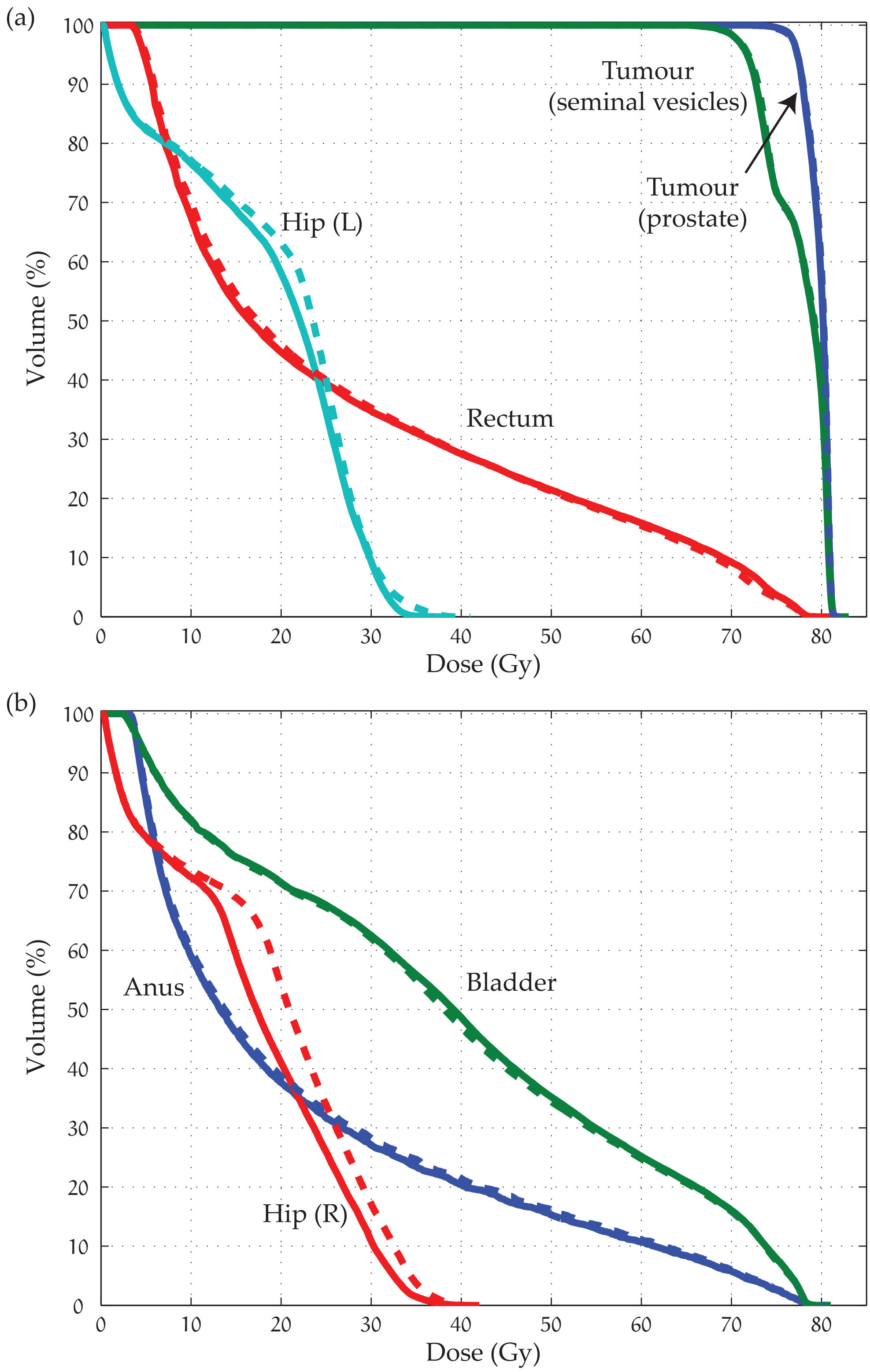

FIGURE 7.1: The DVHs of both the 2pϵc method (solid lines) and the LRPM (dashed lines). (a) shows the tumour, rectum and left hip and in (b) the anus, bladder and right hip are shown. The differences for the other criteria in the DVH were minimal.

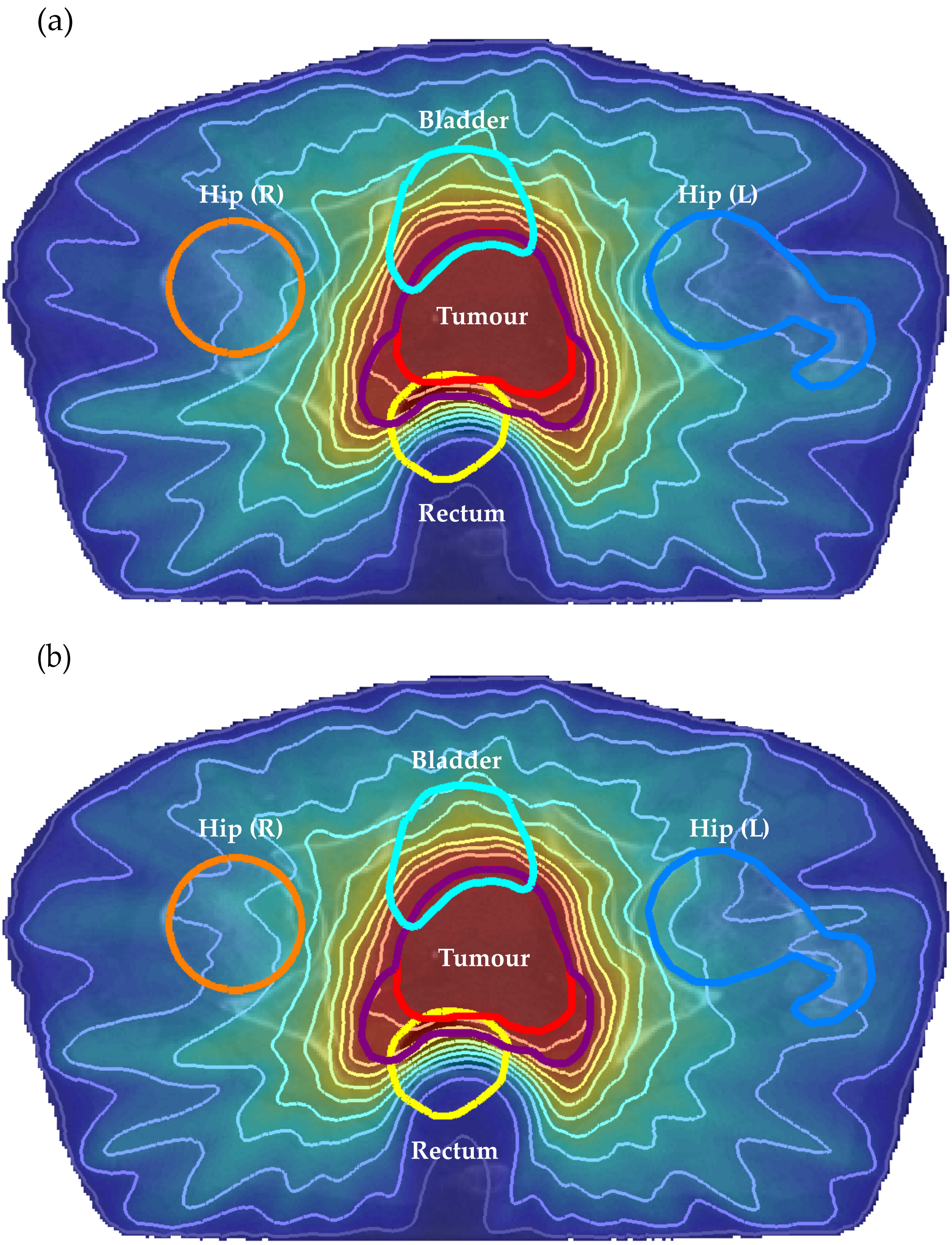

FIGURE 7.2: The dose distributions of the treatment plans generated by (a) the 2pεc method and (b) the LRPM. The thick solid lines are delineations of the OARs and additional structures. The thin solid lines represent isodose lines. Blue corresponds with low doses and red with high doses.

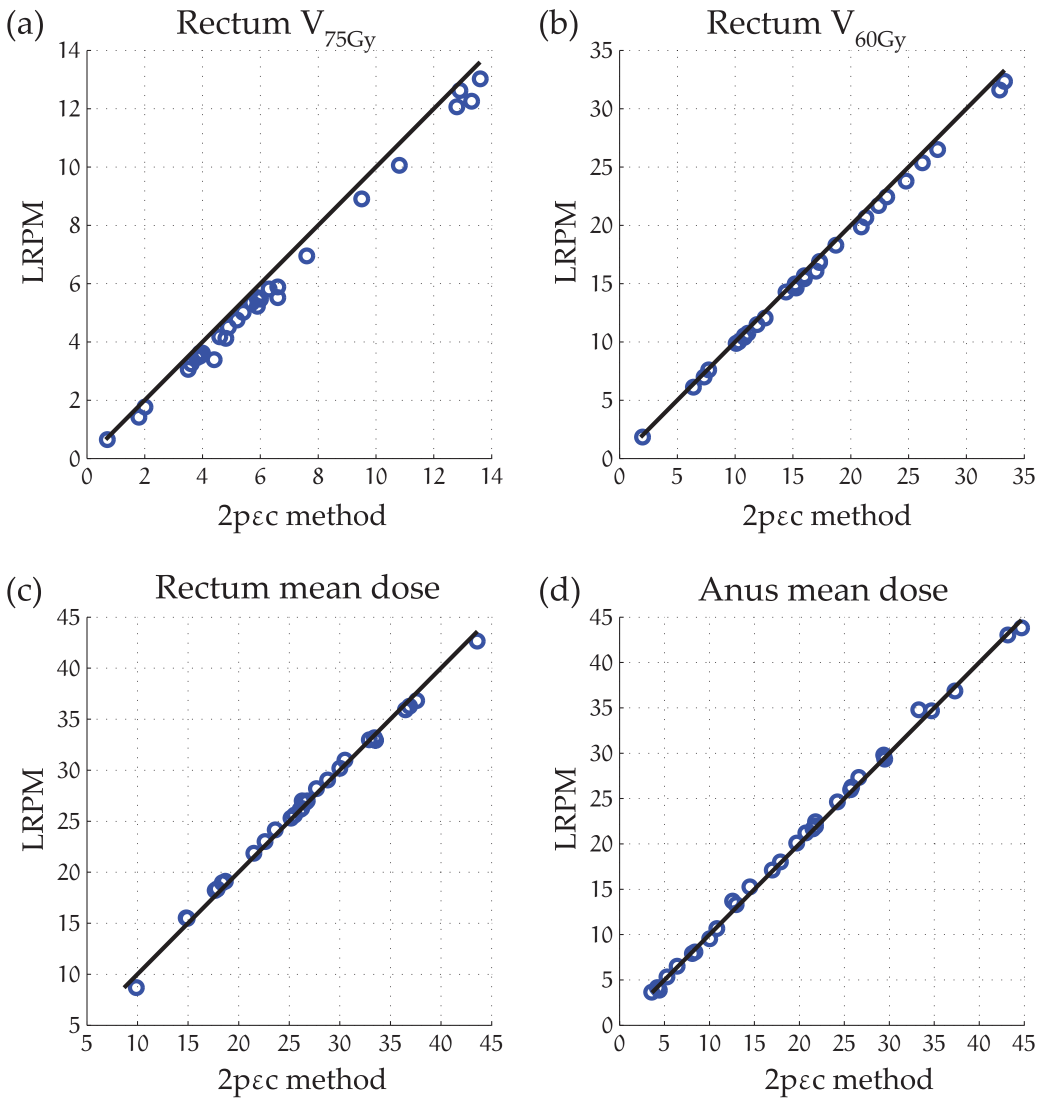

FIGURE 7.3: Evaluation criteria of the 2pεc method plotted against the LRPM. (a) shows the rectum V_{75Gy}, (b) the rectum V_{60Gy}, (c) the rectum mean dose and (d) the anus mean dose.

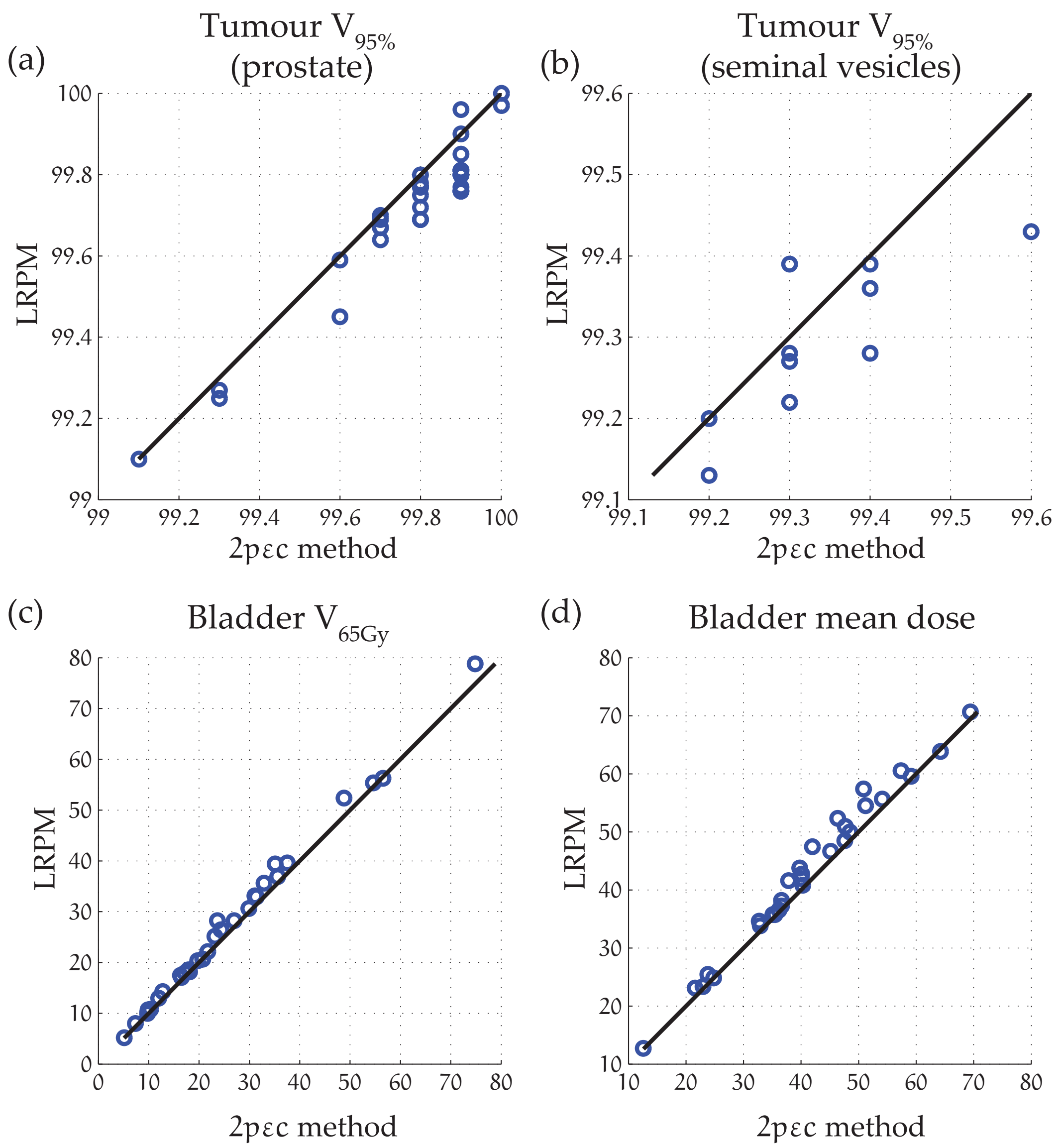

FIGURE 7.4: Evaluation criteria of the 2pεc method plotted against the LRPM. (a) shows the tumour $V_{95\%}$ for the prostate, (b) the tumour $V_{95\%}$ for the seminal vesicles, (c) the bladder V_{65Gy} and (d) the bladder mean dose.

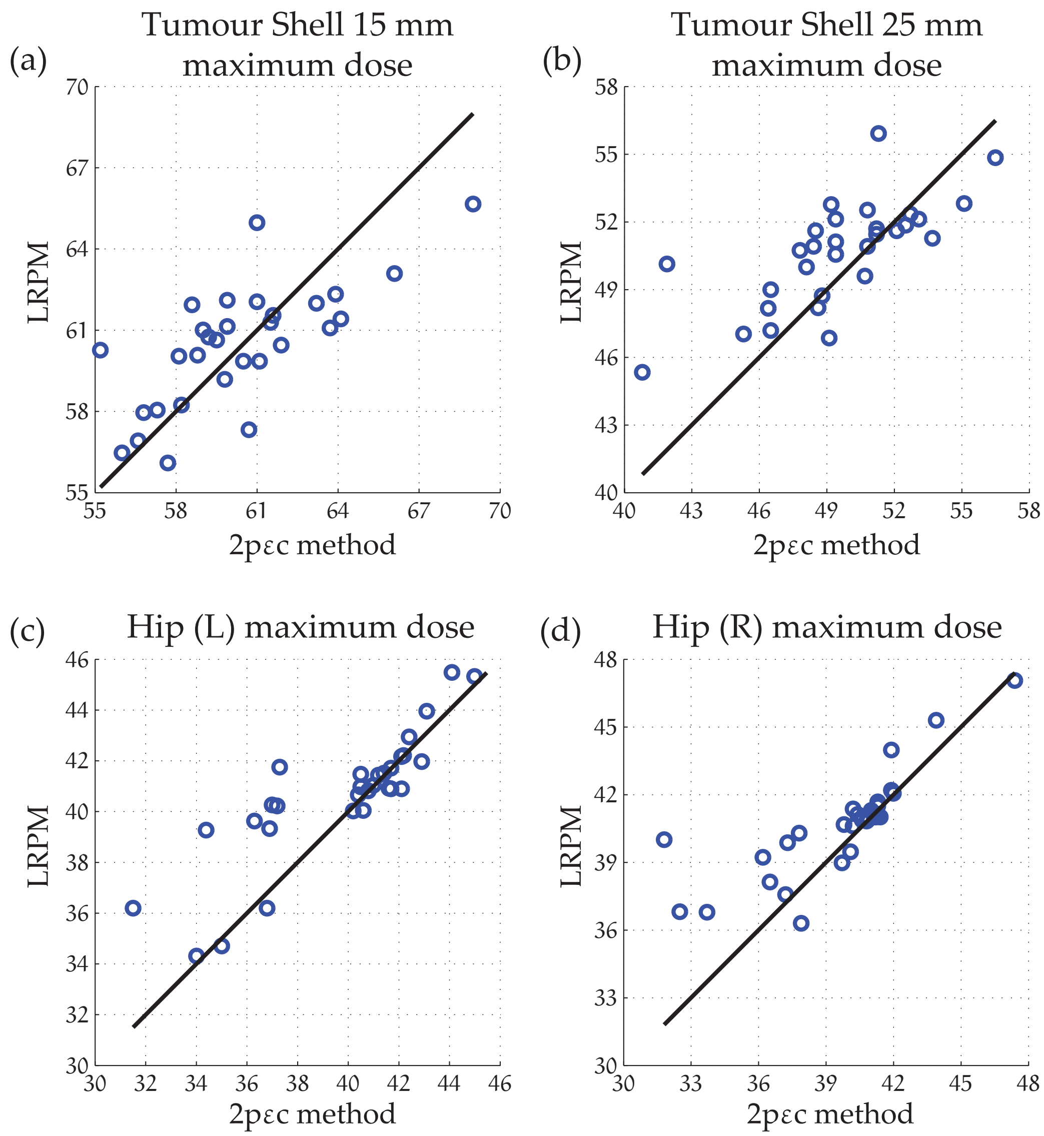

FIGURE 7.5: Evaluation criteria of the 2pεc method plotted against the LRPM. (a) shows the tumour shell 15 mm maximum dose, (b) the tumour shell 25 mm maximum dose, (c) the left hip maximum dose and (d) the right hip maximum dose.

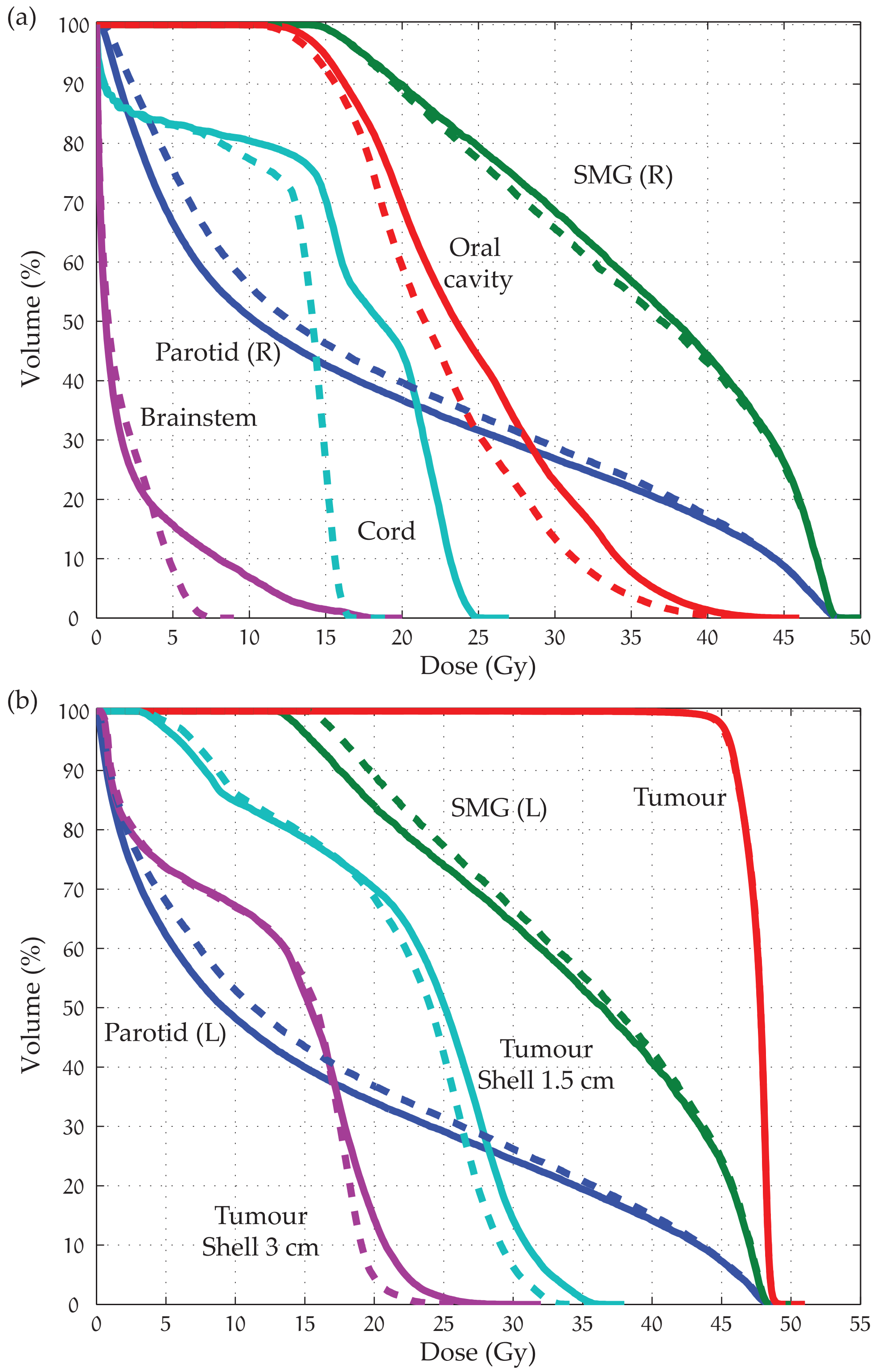

FIGURE 7.6: The DVHs of both the 2pεc method (solid lines) and the LRPM (dashed lines) for head-and-neck cancer patient I. (a) shows the right salivary glands, oral cavity, cord and brainstem and (b) shows the left salivary glands and the tumour (shells) .

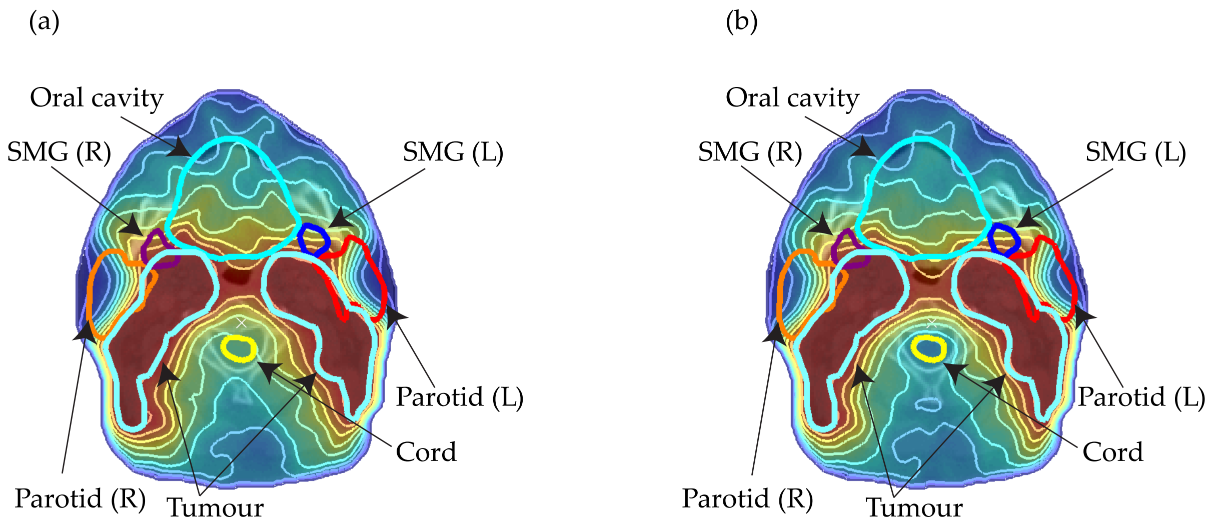

FIGURE 7.7: Dose distribution of both treatment plans for head-and-neck cancer patient I. In (a) the dose distribution of the 2pεc method is shown and (b) shows the dose distribution of the LRPM.

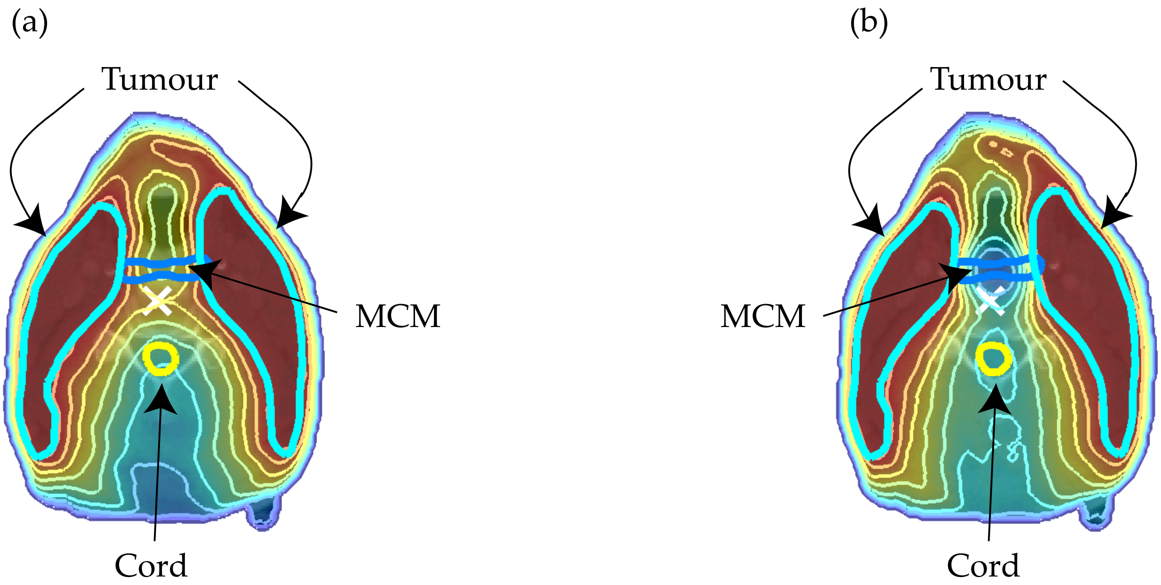

FIGURE 7.8: Dose distribution of both treatment plans for head-and-neck cancer patient II. In (a) the dose distribution of the 2pεc method is shown and (b) shows the dose distribution of the LRPM. Note the difference near the MCM.

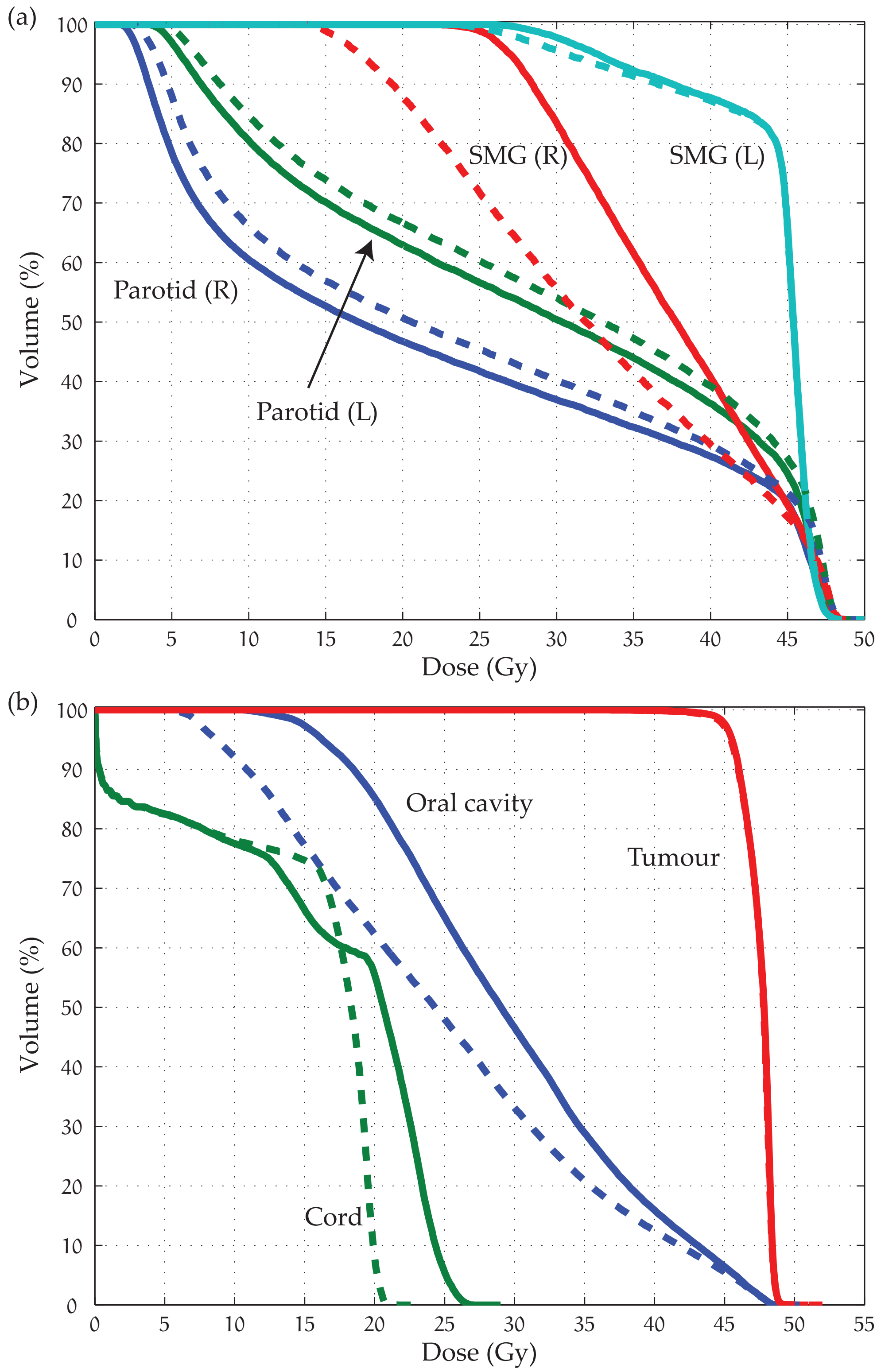

FIGURE 7.9: The DVHs of both the 2pεc method (solid lines) and the LRPM (dashed lines) for head-and-neck cancer patient II. (a) shows the salivary glands and in (b) the tumour, oral cavity and cord are shown.

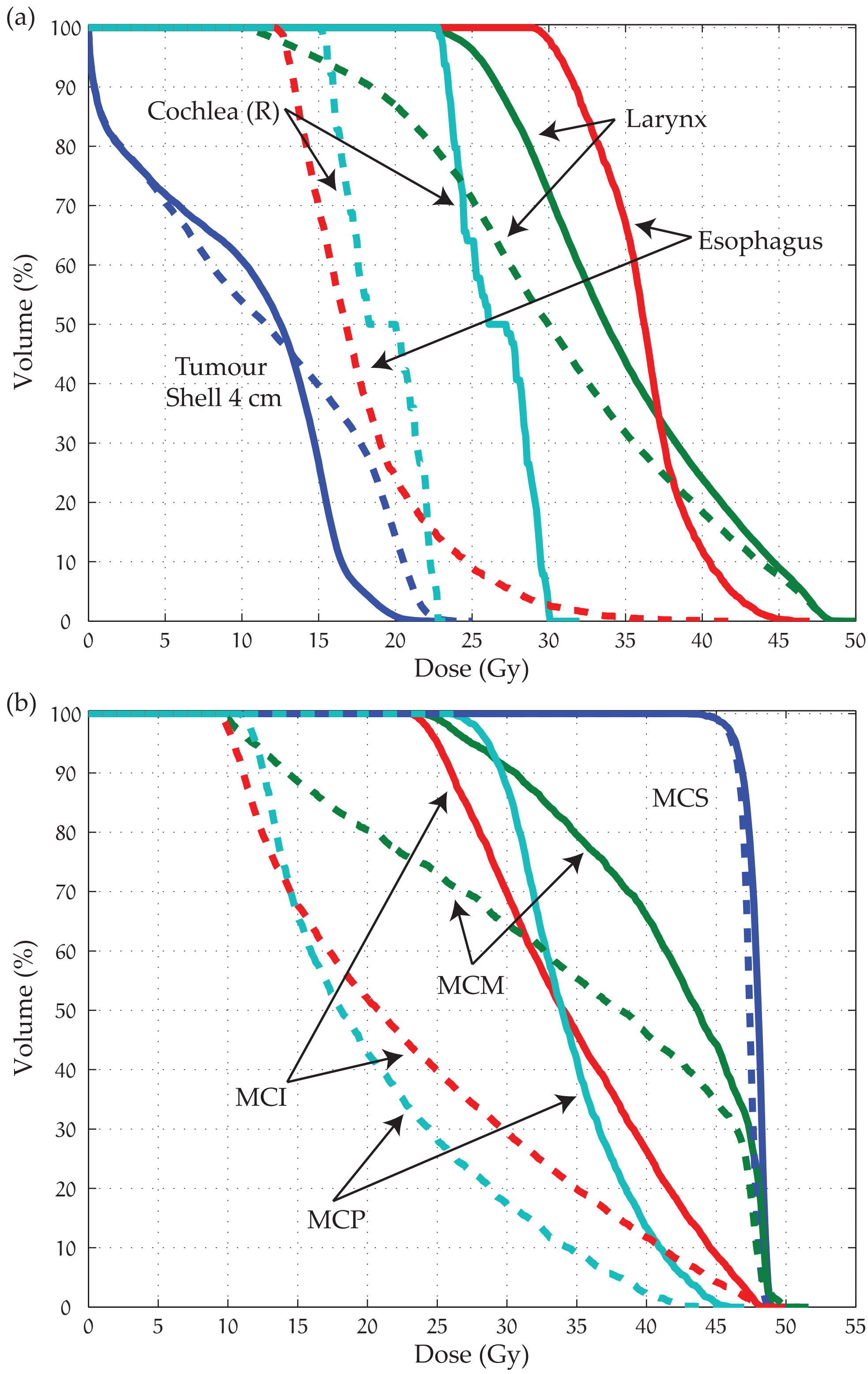

FIGURE 7.10: The DVHs of both the 2pεc method (solid lines) and the LRPM (dashed lines) for head-and-neck cancer patient II. In (a) the tumour shell (4 cm), larynx, esophagus and right cochlea are shown, and (b) shows the swallowing muscles.

CHAPTER 8

Conclusions and further research

In this chapter, we first summarize the results of the theory (Part I), then we answer the research question about the applicability of the reference point method (RPM) in radiation therapy. Finally, we discuss further research on this work.

8.1 Summary of the theory

In Part I of this thesis, the concept of multicriteria optimization was introduced. In a multicriteria optimization problem, multiple real-valued functions need to be optimized simultaneously. These functions (or criteria) often conflict, meaning that optimizing a single criterion results in non-optimal solutions for the other criteria. Mathematically, there is often a whole set of Pareto optimal solutions. Deciding whether a particular Pareto optimal solution is better than another is of subjective nature.

The analysis of general multicriteria optimization problems was done in Chapter 3. The main findings concerned existence and connectedness of Pareto optimal and nondominated points. Both properties can be guaranteed if the decision space is a nonempty compact set and the criteria are continuous and convex, although the criteria need to be strictly convex for the connectedness of Pareto optimal points.

In Chapter 4, multicriteria methods are discussed. These are methods, which often have additional parameters, that generate a Pareto optimal point by solving a single criterion optimization problem. Our focus was on the weighted sum method, ϵ-constraint method and the RPM. The weighted sum method can generate every Pareto optimal point by varying the parameters of the method, provided that the feasible set in the criterion space is $\mathbb{R}^n_{\geqslant 0}$-convex. When this property is missing, the weighted sum method should not be applied. The ϵ-constraint method minimizes one criterion while keeping the others constrained. An extension of this method, the 2-phase ϵ-constraint (2pϵc) method allows to steer the solution, by assigning goal values to the criteria and sorting these by priority (gathered in the wish-list), towards a desired part of the nondominated front. The 2pϵc method solves a sequence of ϵ-constraint problems to obtain the final Pareto optimal solution. Additional steering of the solution is done with a relaxation parameter. Finally, we investigated the RPM which also imposes a prioritized structure of the criteria. Instead of assigning goal values to certain criteria, aspiration points are specified for every criterion per priority (gathered in the reference list). In contrast to the 2pϵc method, the RPM needs a single optimization to obtain a Pareto optimal solution. The RPM connects the reference points creating a preferred path in the criterion space. This path is followed until we intersect the infeasible set. At the same time, the additional sensitivity parameters serve to locate Pareto optimal solutions with desired trade-offs.

8.2 Research question

In Part II, it is shown that treatment planning in radiation therapy involves solving a multi-criteria optimization problem, known as fluence map optimization. In the current practice at the Erasmus MC - Cancer Institute, the 2pϵc method is applied to obtain an optimal fluence map. Per patient group (such as prostate cancer patients), a uniform wish-list, constructed by physicians, dosimetrists and physicists, is used together with the 2pϵc method (with a fixed relaxation of 3%) to generate high quality treatment plans.

In our study, we investigated the applicability of the RPM to generate high quality treatment plans in radiation therapy. The RPM reduces the computation time since it requires a single optimization instead of several. This brings us to our research question:

> *Can the reference point method be configured so that it generates treatment plans that are of similar clinical quality when compared to the treatment plans generated by the 2-phase ϵ-constraint method, and how much reduction in computation time can be realized?*

In Section 6.2, it becomes clear that we can theoretically approximate the wish-list by a reference list in the case that the 2pϵc method is used without relaxation. Solving the associated minimization model of the RPM however, turned out to be rather difficult. Even for a one-dimensional decision space, a two-dimensional criterion space and a short wish-list (Example 6.2), the minimization models of the RPM were hard to solve. Also, the relaxation in the 2pϵc method is essential for the quality of the treatment plan, so the configuration of the RPM in Section 6.2 did not suffice.

Smoothing the preferred path in Section 6.2 led to a minimization model for the RPM suitable for long wish-lists while still maintaining the prioritized structure. This was introduced in Section 6.3, where we presented the lexicographic reference point method (LRPM). The LRPM automatically generates a reference list (Algorithm 6.1) for a fixed wish-list. The sensitivity parameters for the LRPM were configured manually and have an essential role for the quality of the treatment plan.

In Chapter 7, we tested the LRPM for 30 prostate cancer patients and 2 head-and-neck cancer patients. For all test cases, both the 2pϵc method and the LRPM were applied to generate treatment plans. As both plans are Pareto optimal but different, a trade-off between the criteria must have been made.

For the 30 prostate cancer patients, the automatically generated VMAT plans of the LRPM were clinically acceptable. The LRPM performed better on the high priorities (as we tuned it) and worse for lower priorities. High doses delivered to the rectum were reduced when compared to the VMAT plans of the 2pϵc method. The differences in mean doses of the rectum and anus were minimal but in favour of the 2pϵc method, and the differences for the tumour shells, bladder and hips (lower priorities) were also in favour of the 2pϵc method. The differences were found neither clinically nor statistically relevant. Concerning the computation time, we observed a speed-up factor of nearly 12 for the LRPM.

For the 2 head-and-neck cancer patients, the LRPM performed worse for the mean doses of the parotids glands (within a margin of 2 Gy), which are the highest prioritized organs at risk, but improved several of the lower priorities (maximum doses of the cord and brainstem and/or the mean doses of the larynx, swallowing muscles and esophagus). The treatment plans of the LRPM were found as good or better (for head-and-neck cancer patient II) as the treatment plans of the 2pϵc method. For the computation time, we observed a speed-up factor of 3-4. Recall that the 2 head-and-neck cancer patients suffered from a bilateral tumour and that the set of uniform sensitivity parameters performed poorly for unilateral cases. Also, the sample size of 2 is too small to draw a conclusion on the quality of the fixed sensitivity parameters.

8.3 Further research

The possibilities of the LRPM have not been tested extensively, but the results obtained so far are promising. The recommendations for further research mainly concern the configuration of the LRPM.

- Sensitivity parameters of the LRPM.
  In this study, the sensitivity parameters in the LRPM were chosen by a trial-and-error process. For a fixed case, several sensitivity parameters were tested. The most reasonable set of parameters were picked and tested on another case, the parameters were adapted until we were satisfied with both results. The associated parameters were then tested on another case and so on.

  This trail-and-error process is time intensive, for the prostate cancer patients 12 parameters needed to be tuned and 21 for the head-and-neck cancer patients. Moreover, the final choice of parameters is not optimal. We are looking for an automated method to settle the sensitivity parameters. One idea is to generate a lot of treatment plans (for a specific patient group) with the 2pϵc method and use this data to deterministically set the sensitivity parameters.

- Subdivision of patient groups.
  For the head-and-neck cancer patients, a uniform set of sensitivity parameters was used. Both patients suffered from a bilateral (two-sided) tumour. The same set of sensitivity parameters was tested on unilateral (one-sided) cases and compared to the 2pϵc method. The results were poor, which led to the idea of dividing the head-and-neck cancer patients into subgroups (based on tumour anatomy). For each subgroup, we aim for a uniform set of sensitivity parameters.

- Algorithm for the reference list.
  Algorithm 6.1 automatically generates the reference list for a fixed wish-list. However, the algorithm may not be advanced enough. For instance, the reference list does not incorporate upper bounds for the criteria. Introducing upper bounds leads to more reference points which increases the complexity of the minimization problem associated with the LRPM. Whether such an extended reference list is an issue for the solver, needs to be tested.

- Solvers for a single criterion optimization model.
  Whether we apply the 2pϵc method, the LRPM or any other multicriteria method to generate treatment plans, they all need to solve single criterion minimization problem(s). Speeding up the solver for these problems reduces the computation time. Although the current solver (Breedveld, 2013, chap. 11.8) is optimized for radiation therapy, research on alternative solvers is done. This research may also be synergistic with research on the algorithm for the reference list. Solvers that can cope well with the complexity of the single criterion minimization model of the LRPM, may allow larger (more advanced) reference lists.

Bibliography

M. Alber and R. Reemtsen. Intensity modulated radiotherapy treatment planning by use of a barrier-penalty multiplier method. *Optimization Methods and Software*, 22(3):391–411, 2007.

M.A. Armstrong. *Basic Topology*. Springer, 1983.

J. Borwein. On the existence of Pareto efficient points. *Mathematics of Operations research*, 8: 64–73, 1983.

S. Boyd and L. Vandenberghe. *Convex Optimization*. Cambridge University Press, 2004.

S. Breedveld. *Towards Automated Treatment Planning in Radiotherapy*. PhD thesis, Erasmus University Rotterdam, 2013.

S. Breedveld, P. Storchi, M. Keijzer, A. Heemink, and B. Heijmen. A novel approach to multi-criteria inverse planning for IMRT. *Physics in medicine and biology*, 52:6339–6353, 2007.

S. Breedveld, P. Storchi, and B. Heijmen. The equivalence of multi-criteria methods for radiotherapy plan optimization. *Physics in medicine and biology*, 54:7199–7209, 2009.

S. Breedveld, P. Storchi, P. Voet, and B. Heijmen. iCycle: integrated, multi-criterial beam angle and profile optimization for generation of coplanar and non-coplanar IMRT plans. *Medical Physics*, 39:951–963, 2012.

V. Chankong and Y. Haimes. *Multiobjective Decision Making: Theory and Methodology*. Elsevier Science, New York, 1983.

H. Corley. An existence result for maximizations with respect to cones. *Journal of Optimization Theory and Applications*, 31:277–281, 1980.

M. Ehrgott. *Multicriteria Optimization*. Springer, second edition, 2005.

J. Granat and M. Makowski. Interactive specification and analysis of aspiration-based preferences. *European journal of Operational Research*, 122(2):469–485, 2000.

R. Hartley. On cone-efficiency, cone-convexity and cone-compactness. *SIAM Journal on Applied Mathematics*, 34:211–222, 1978.

B. Heijmen, R. van Haveren, P. Voet, and S. Breedveld. A fast lexicographic optimizer for fully automated multi-objective plan generation, 2014. ESTRO (Radiotherapy Oncology 111 S165-S166).

J. Hiriart-Uruty and C. Lemaréchal. *Convex Analysis and Minimization Algorithms I*. Springer-Verlag, Berlin, 1993.

K. Mietinnen. *Nonlinear Multiobjective Optimization*, volume 12 of *International Series in Operations Research and Management Science*. Kluwer Academic Publishers, Dordrecht, 1999.

W. Ogryczak and B. Kozłowski. Reference point method with importance weighted ordered partial achievements. *TOP*, 19(2):380–401, 2009.

R. Rockafellar. *Convex Analysis*. Princeton University Press, 1970.

W. Rudin. *Principles of Mathematical Analysis*. McGraw-Hill, third edition, 1976.

Y. Sawaragi, H. Nakayama, and T. Tanino. *Theory of Multiobjective Optimization*. Academic Press, Orlando, 1985.

P. Storchi and E. Woudstra. Calculation of the absorbed dose distribution due to irregularly shaped photon beams using pencil beam kernels derived from basic beam data. *Physics in Medicine and Biology*, 41(4):637–656, 1996.

P. Voet, M. Dirkx, S. Breedveld, D. Fransen, P. Levendag, and B. Heijmen. Toward fully automated multicriterial plan generation: a prospective study. *International Journal of Radiation Oncology Biology Physics*, 85(3):866–872, 2013.

P. Voet, M. Dirkx, S. Breedveld, A. Al-Mamgani, L. Incrocci, and B. Heijmen. Fully automated volumetric arc therapy plan generation for prostate cancer patients. *International Journal of Radiation Oncology Biology Physics*, 88(5):1175–1179, 2014.

A.R. Warburton. Quasiconcave vector maximization: Connectedness of the sets of Pareto-optimal and weak Pareto-optimal alternatives. *Journal of Optimization Theory and Applications*, 40:537–557, 1983.

A. Wierzbicki. On the completeness and constructiveness of parametric characterizations of efficient solutions. *OR spectrum*, 8:73–87, 1986.

S. Wright. *Primal-Dual Interior-Point Methods*. SIAM, 1997.