Multi-objective Optimization for Supporting Radiation Therapy Treatment Planning

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Overview

Overview

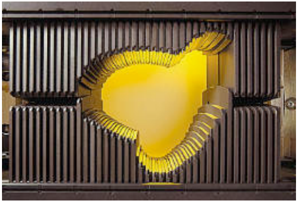
Radiotherapy

George sang along to the tune, wondering what the big deal was about Radiotherapy

Radiotherapy

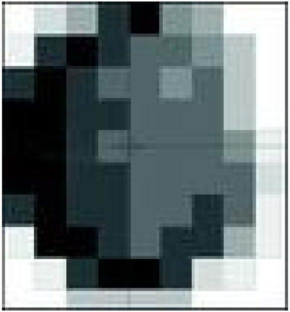
(Intensity Modulated Radiotherapy) IMRT represents an advance in the means that radiation is delivered to the target, and it is believed that IMRT offers an improvement over conventional and conformal radiation in its ability to provide higher dose irradiation of tumor mass, while exposing the surrounding normal tissue to less radiation.

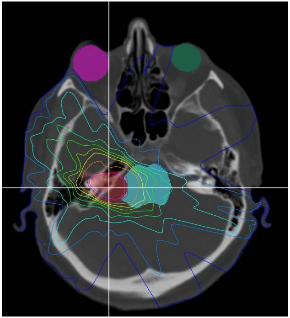
http://www.cancernews.com/data/Article/259.asp



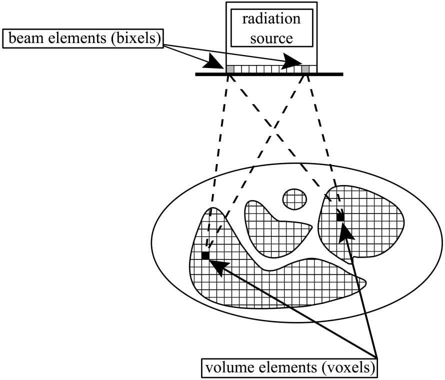
Radiotherapy Treatment Planning

For each beam directions find a fluence map such that the resulting dose distribution achieves the treatment goals of tumour control and normal tissue protection





Mathematical Model



a_{ij} = dose delivered to voxel i by unit intensity of bixel j

x_j = intensity of bixel j

d_i = dose delivered to voxel i

A Multi-objective Linear Programming Model

$$\begin{array}{llclcl}
\min & (\alpha,\beta,\gamma) & & & & \\
\text{s.t.} & TLB - \alpha e & \leqq & A_{\mathcal{T}} x & \leqq & TUB \\
& A_{\mathcal{C}} x & \leqq & CUB + \beta e & & \\
& A_{\mathcal{N}} x & \leqq & NUB + \gamma e & & \\
& 0 & \leqq & \alpha & \leqq & \alpha UB \\
& -CUB & \leqq & \beta & \leqq & \beta UB \\
& 0 & \leqq & \gamma & \leqq & \gamma UB \\
& 0 & \leqq & x. & &
\end{array}$$

- αUB,βUB, γUB restrict solutions to clinically relevant values
- MOLP is always feasible and bounded
- Multi-objcetive version of elastic LP model of (Holder, 2003)

Overview

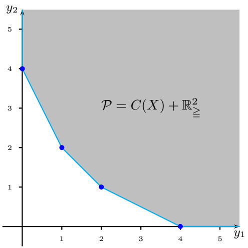
Multi-objective Linear Programming

$$\min\{Cx : Ax \geqq b, x \in \mathbb{R}^n\} \tag{1}$$

- $C \in \mathbb{R}^{p\times n}$, $A \in \mathbb{R}^{m\times n}$, $b \in \mathbb{R}^m$
- $X = \{x \in \mathbb{R}^n : Ax \geqq b\}$
- $Y = \{Cx \in \mathbb{R}^p : x \in X\}, \mathcal{P} = Y + \mathbb{R}^p_{\geqq}$
- $\hat{x} \in X$ is (weakly) efficient if there is no $x \in X$ with $Cx \leq C\hat{x}$ $(Cx < C\hat{x})$
- If $\hat{x}$ is (weakly) efficient then $C\hat{x}$ is (weakly) non-dominated
- X_{wE} set of weakly efficient solutions, Y_{wN} set of non-dominated points
- $\hat{x} \in X$ is (weakly) ε-efficient if there is no $x \in X$ with $Cx \leq (<) C\hat{x} - \varepsilon$.
- $C\hat{x}$ is (weakly) ε-nondominated

An MOLP Example

$$C = \begin{pmatrix} 1 & 0 \\ 0 & 1 \end{pmatrix}, \; A = \begin{pmatrix} 2 & 1 \\ 1 & 1 \\ 1 & 2 \\ 1 & 0 \\ 0 & 1 \end{pmatrix}, \; b = \begin{pmatrix} 4 \\ 3 \\ 4 \\ 0 \\ 0 \end{pmatrix}.$$



Solution Methods

- Simplex methods: Exponential number of efficient extreme points
- Interior point methods: Find single solution or efficient facet
- Objective space methods: Smaller dimension

Objective Space Algorithms

- Benson (1998), Ehrgott *et al.* (2012): Primal exact algorithm to compute $\mathcal{P}_{wN}$
- Shao and Ehrgott (2008a): Primal approximation algorithm to compute set of weakly ε-nondominated points
- (Ehrgott *et al.*, 2012): Dual exact algorithm to compute $\mathcal{P}_{wN}$
- (Shao and Ehrgott, 2008b): Dual approximation algorithm to compute set of weakly ε-nondominated points

Primal Exact Algorithm

$$P_2(y) \quad \min\{z : Ax \geqq b, Cx - ez \leqq y\}$$

$$D_2(y) \quad \max\{b^T u - y^T w : A^T u - C^T w = 0, e^T w = 1, u, w \geqq 0\}$$

Algorithm

Init: *Compute interior point* $\hat{p} \in \mathcal{P}$
Construct p-dimensional simplex $\mathcal{S}^0 := y^I + \mathbb{R}^p_{\geqq} \supset \mathcal{P}$

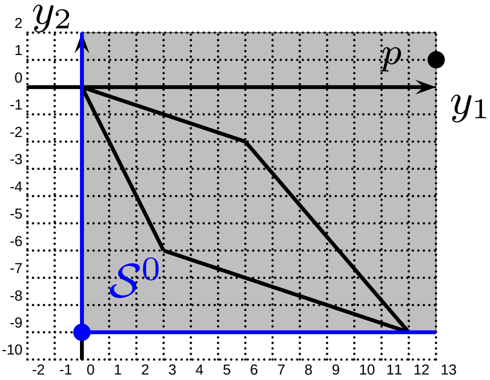
It k**1:** *If* $vert(\mathcal{S}^{k-1}) \subset \mathcal{P}$ *STOP:* $\mathcal{P} = \mathcal{S}^{k-1}$
Otherwise choose $s^k \in vert(\mathcal{S}^{k-1}) \setminus \mathcal{P}$

It k**2:** *Find* $0 < \alpha_k < 1$ *with* $y^k := \alpha_k s^k + (1 - \alpha_k)\hat{p} \in bd\ \mathcal{P}$

It k**3:** *Compute* (u^{k^T}, w^{k^T}) *optimal solution to* $D_2(y^k)$
Set $\mathcal{S}^k = \mathcal{S}^{k-1} \cap \{y \in \mathbb{R}^p : w^{k^T} y \geqq b^T u^k\}$

An Outer Approximation Approach

- Find best values of all objectives
- Step 1: Connect extreme point with interior point, find intersection, and find supporting hyperplane
- Update corner points and repeat until no corner points outside feasible set left



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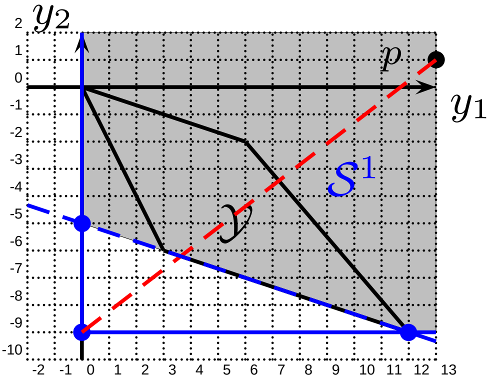

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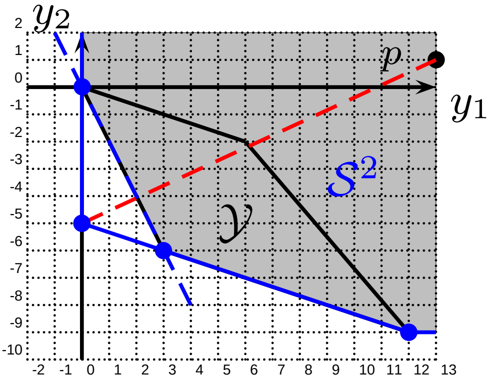


Primal Approximation Algorithm

- If $d(s^k, y^k) < \epsilon$ do not construct hyperplane
- Keep $s^k \in \mathcal{O}$ and $y^k \in \mathcal{I}$ for outer and inner approximation
- $V_o(\mathcal{S}^{k-1}) = \text{vert}(S^{k-1})$, $\mathcal{V}_i(\mathcal{S}^{k-1}) = (\text{vert}(\mathcal{S}^{k-1}) \setminus \mathcal{O}) \cup \mathcal{I}$
- $\mathcal{P}^i = \text{conv}(\mathcal{V}_i(\mathcal{S}^{k-1}))$, $\mathcal{P}^o = \text{conv}(\mathcal{V}_o(\mathcal{S}^K))$

Theorem

Let $\varepsilon = \epsilon e$, where $e = (1, \dots, 1) \in \mathbb{R}^p$. Then $\mathcal{P}^i_{wN}$ is a set of weakly ε-nondominated points of $\mathcal{P}$.

The Geometric Dual MOLP Heyde and Löhne (2008)

- Primal MOLP:

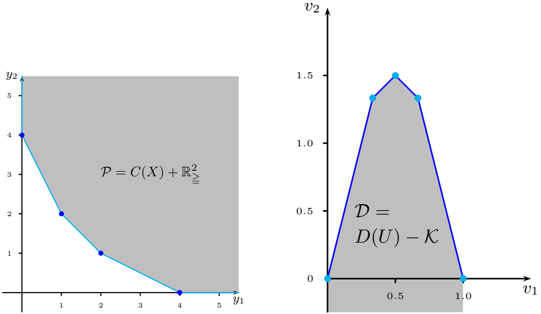
$$\min\{Cx : x \in \mathbb{R}^n, Ax \geqq b\}$$

- $\mathcal{K} := \mathbb{R}_{\geqq} e^p = \{y \in \mathbb{R}^p : y_1 = \cdots = y_{p-1} = 0, y_p \geqq 0\}$
- Dual MOLP:

$$\max{}_{\mathcal{K}}\{D(u,\lambda) : (u,\lambda) \in \mathbb{R}^m \times \mathbb{R}^p, (u,\lambda) \geqq 0, A^T u = C^T \lambda, e^T \lambda = 1\}$$

$$D(u,\lambda) := (\lambda_1, \ldots, \lambda_{p-1}, b^T u)^T = \begin{pmatrix} 0 & I_{p-1} & 0 \\ b^T & 0 & 0 \end{pmatrix} \begin{pmatrix} u \\ \lambda \end{pmatrix}$$

- $\mathcal{D} := D(U) - \mathcal{K}$



Let $(u, \lambda) \in U$ and $x \in X$ be feasible solutions to the dual and primal MOLP:

$$b^T u = \lambda^T Cx$$

if and only if Cx is a weakly nondominated point of $\mathcal{P}$ and $(\lambda_1, \dots, \lambda_{p-1}, b^T u)$ is a $\mathcal{K}$-nondominated point of $\mathcal{D}$.

$$\varphi(y, v) := \sum_{i=1}^{p-1} y_i v_i + y_p \left(1 - \sum_{i=1}^{p-1} v_i\right) - v_p$$

Theorem (Heyde and Löhne (2008))

There is an inclusion reversing one-to-one map Ψ between the set of all proper $\mathcal{K}$-nondominated faces of $\mathcal{D}$ and the set of all proper weakly nondominated faces of $\mathcal{P}$.
Moreover, for every proper $\mathcal{K}$-maximal face $\mathcal{F}^*$ of $\mathcal{D}$ and its associated proper $\mathcal{K}$-nondominated face $\Psi(\mathcal{F}^*)$ of $\mathcal{P}$ it holds

$$\dim \mathcal{F}^* + \dim \Psi(\mathcal{F}^*) = p - 1$$

Dual Exact Algorithm

$$P_1(v) \qquad \min\left\{\lambda(v)^T Cx : x \in \mathbb{R}^n, Ax \geqq b\right\}$$

$$D_1(v) \quad \max\left\{b^T u : u \in \mathbb{R}^m, u \geqq 0, A^T u = C^T \lambda(v)\right\}$$

$$\lambda(v) = (v_1, \ldots, v_{p-1}, 1 - \textstyle\sum_{k=1}^{p-1} v_i)$$

Algorithm

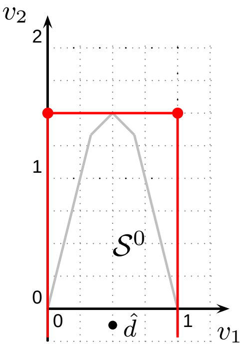
Init: *Compute* $\hat{d} \in$ *int* $\mathcal{D}$ *find optimal solution* x^0 *of* $P_1(\hat{d})$
Set $\mathcal{S}^0 := \{v \in \mathbb{R}^p : \lambda(v) \geqq 0, \varphi(Cx^0, v) \geqq 0\}$*;* $k := 1$

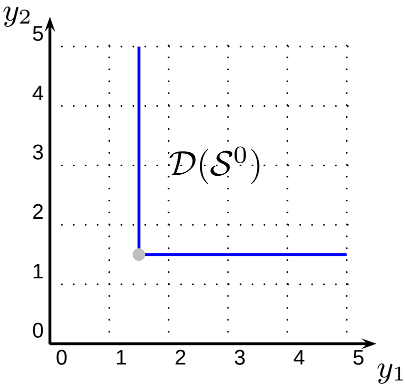
It $k1$ **:** *If vert*$(\mathcal{S}^{k-1}) \subset \mathcal{D}$ *STOP:* $\mathcal{S}^{k-1} = \mathcal{D}$
Otherwise choose $s^k \in$ *vert*$(\mathcal{S}^{k-1}) \setminus \mathcal{D}$

It $k2$ **:** *Find* α^k *with* $v^k := \alpha^k s^k + (1 - \alpha^k)\hat{d} \in$ *bd* $\mathcal{D}$

It $k3$ **:** *Compute optimal solution* x^k *of* $P_1(v^k)$
Set $\mathcal{S}^k := \mathcal{S}^{k-1} \cap \{v \in \mathbb{R}^p : \varphi(Cx^k, v) \geqq 0\}$

An Interior Approximation Approach





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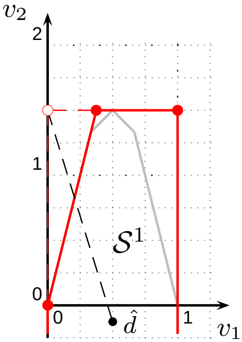

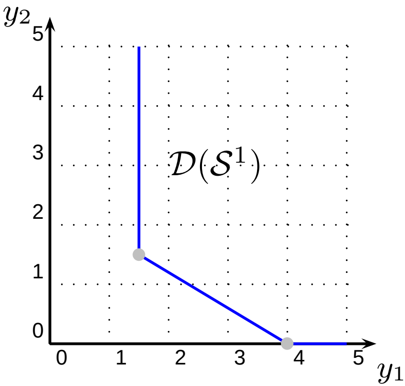

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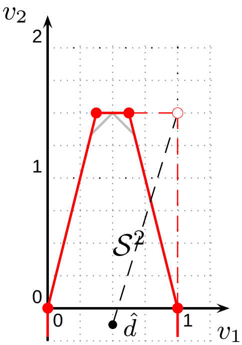

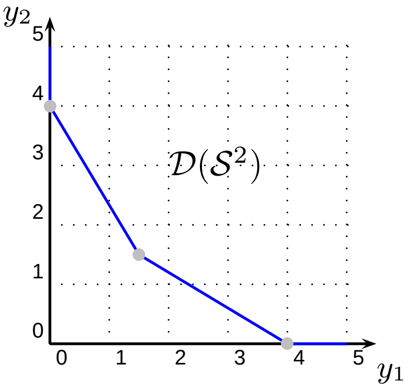

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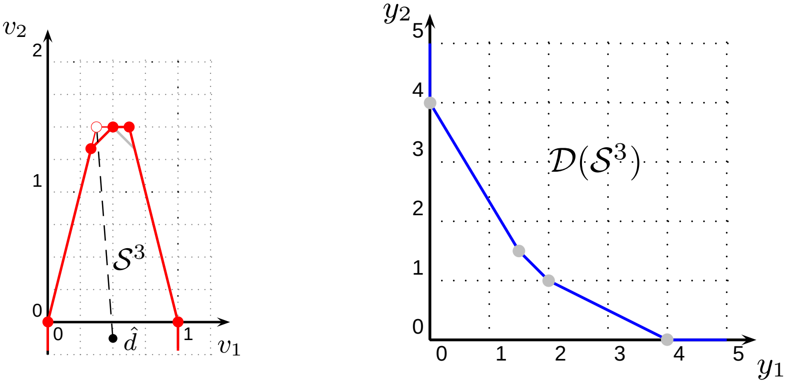

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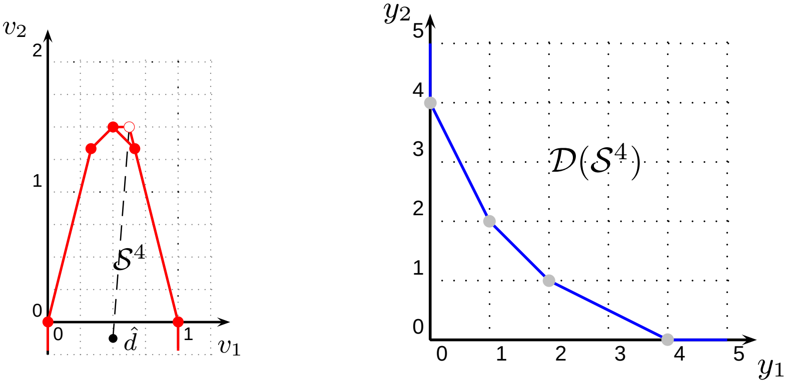


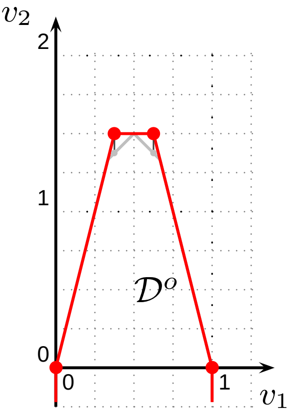
Dual Approximation Algorithm

- If $\text{vert}(\mathcal{S}^k) \subset \mathcal{D} + \epsilon e^p$ do not construct hyperplane
- If $v_p - f \leqq \epsilon$ then $v \in \mathcal{D} + \epsilon e^p$ where f is optimum of $D_2(v)$
- $\mathcal{D}^o := \mathcal{S}^{k-1} \supset \mathcal{D}$ is outer approximation of $\mathcal{D}$
- $$\mathcal{P}^i := \mathcal{D}(\mathcal{D}^o) \subset \mathcal{D}(\mathcal{D}) = \mathcal{P}$$
  is inner approximation of $\mathcal{P}$

Theorem

Let $\varepsilon = \epsilon e$, then $\mathcal{P}^i_{wN}$ is a set of weakly ε-nondominated points of $\mathcal{P}$.

- $\epsilon = 3/20$
- Two cuts as before
- $d(v^1, bd^1) = 1/8$, $d(v^2, bd^2) = 1/8$
- $\mathcal{D}^o = \mathcal{S}^2$
- $\mathcal{P}^i = \mathcal{D}(\mathcal{D}^o)$



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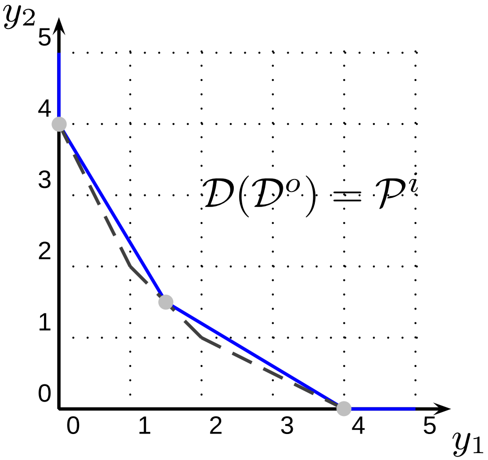
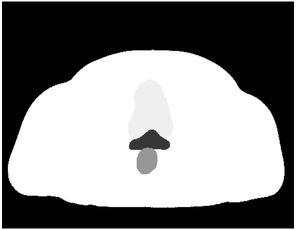
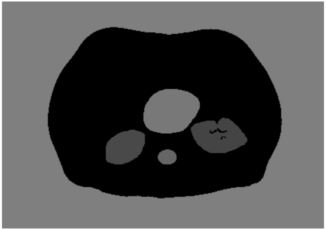


Overview

The Test Cases


Acoustic Neuroma

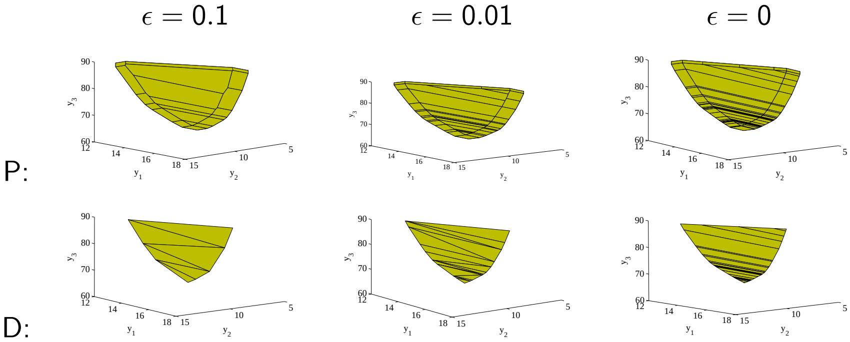

Prostate

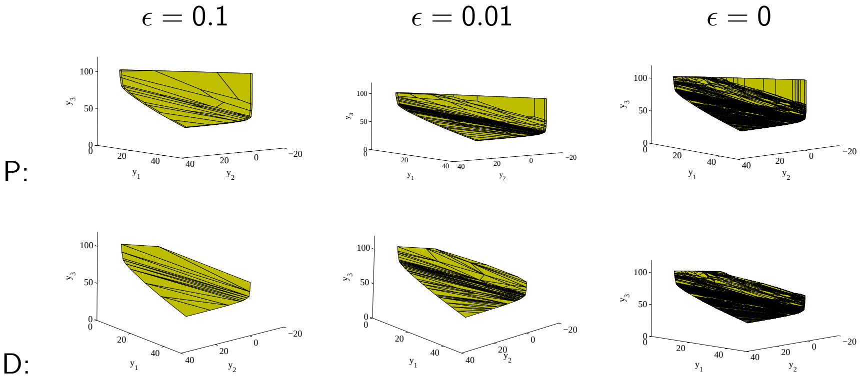

Pancreatic Lesion

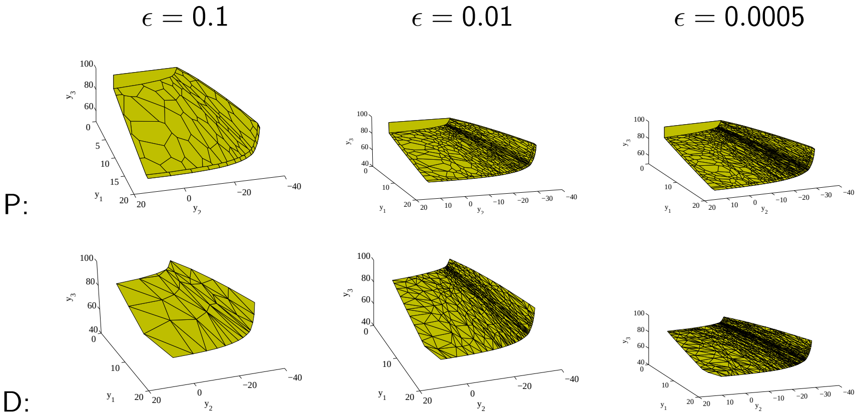
- Dose calculation inexact
- Inaccuracies during delivery
- Planning to small fraction of a Gy acceptable

Case	AN	P	PL
Tumour voxels	9	22	67
Critical organ voxels	47	89	91
Normal tissue voxels	999	1182	986
Bixels	594	821	1140
TUB	87.55	90.64	90.64
TLB	82.45	85.36	85.36
CUB	60/45	60/45	60/45
NUB	0.00	0.00	0.00
αUB	16.49	42.68	17.07
βUB	12.00	30.00	12.00
γUB	87.55	100.64	90.64

	ϵ	Solving the dual			Solving the primal		
		Time	Vert.	Cuts	Time	Vert.	Cuts
AC	0.1	1.484	17	8	5.938	27	21
	0.01	3.078	33	18	8.703	47	44
	0	8.864	85	55	13.984	55	85
PR	0.1	4.422	39	19	14.781	56	42
	0.01	18.454	157	78	64.954	296	184
	0	792.390	3280	3165	995.050	3165	3280
PL	0.1	58.263	85	44	164.360	152	90
	0.01	401.934	582	298	1184.950	1097	586
	0.005	734.784	1058	539	2147.530	1989	1041


$\epsilon = 0.1$
$\epsilon = 0.01$
$\epsilon = 0$
P:
D:
y_1
y_2
y_3


$\epsilon = 0.1$
$\epsilon = 0.01$
$\epsilon = 0$
P:
D:
y_1
y_2
y_3


$\epsilon = 0.1$
$\epsilon = 0.01$
$\epsilon = 0.0005$
P:
D:
y1
y2
y3

Overview

Finite Representation

Definition

A finite representation of Y_N is a subset R of Y_N such that $|R| < \infty$.

Criteria for quality of representation (Sayin, 2000)

1. Cardinality – contains reasonable number of points
2. Uniformity – does not contain points that are very close to each other
   Uniformity level $\delta := \min_{r^1, r^2 \in R} d(r^1, r^2)$
3. Coverage – contains point close to each nondominated point
   Coverage error $\varepsilon := \max_{y \in Y_N} \min_{r \in R} d(y, r)$

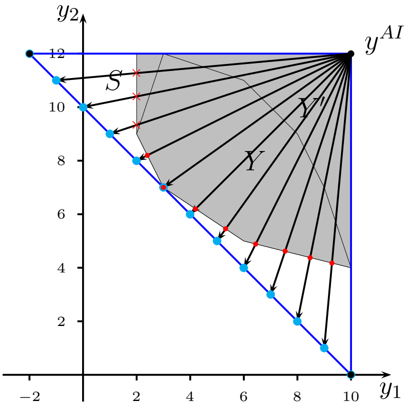
Finite Representation

Definition

Let R be a representation of Y_N, d a metric and $\varepsilon > 0$ and $\delta > 0$ be real numbers.

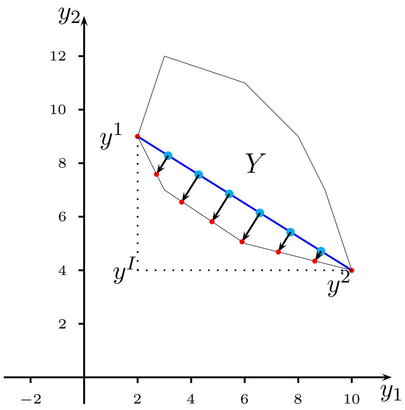
- R is called a d_ε-representation of Y_N if for any $y \in Y_N$, there exists $r \in R$ such that $d(y, r) \leqq \varepsilon$.
- R is called a δ-uniform d_ε-representation if $\min_{r^1, r^2 \in R, r^1 \neq r^2}\{d(r^1, r^2)\} \geq \delta$.

Existing Methods



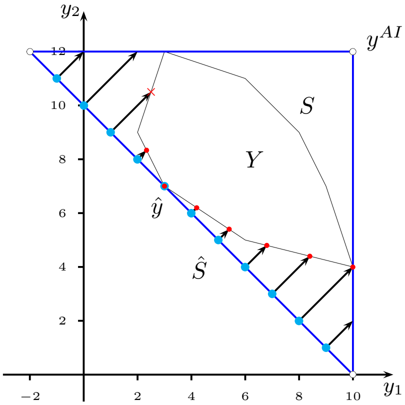
Global shooting method
(Benson and Sayin, 1997)
Good coverage
Uniformity can be bad

Existing Methods



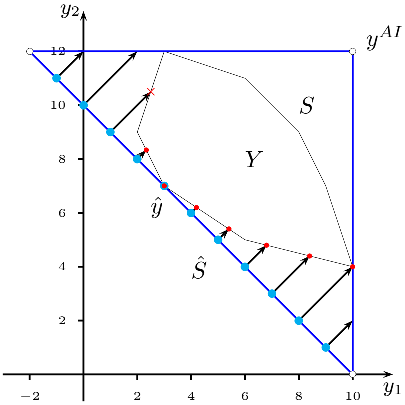
Normal boundary intersection (NBI) method
(Das and Dennis, 1998)
Good uniformity
Coverage may be bad

The Revised Boundary Intersection Method



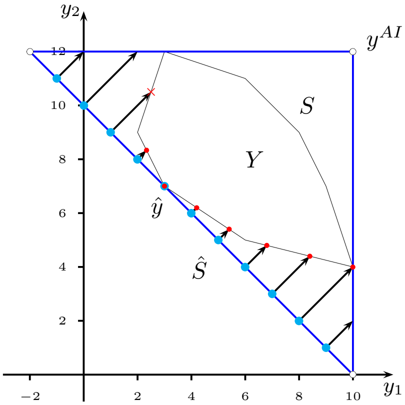
Input: MOLP data A, b, C and $ds > 0$.

The Revised Boundary Intersection Method



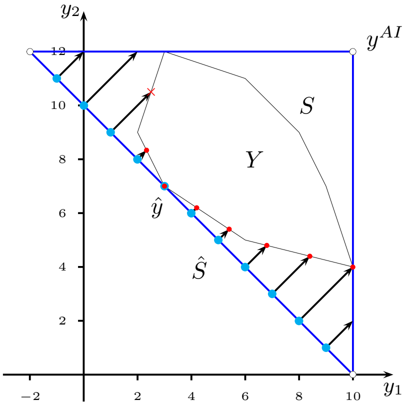
Find y^{AI} defined by $y_k^{AI} = \max\{y_k : y \in Y\}$, $k = 1, \ldots, p$.

The Revised Boundary Intersection Method



Find a non-dominated point $\hat{y}$ by solving the LP $\phi := \min\{e^T y : y \in Y\}$.

The Revised Boundary Intersection Method

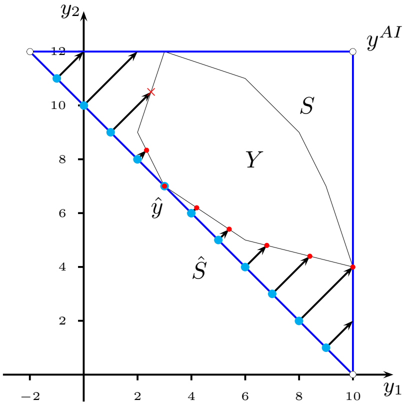


Compute $p+1$ points $v^k, k = 0, \ldots, p$ in $\mathbb{R}^p$

$$v_l^k = \begin{cases} y_l^{AI}, & l \neq k, \\ \phi + \hat{y}_k - e^T v^0 & l = k. \end{cases}$$

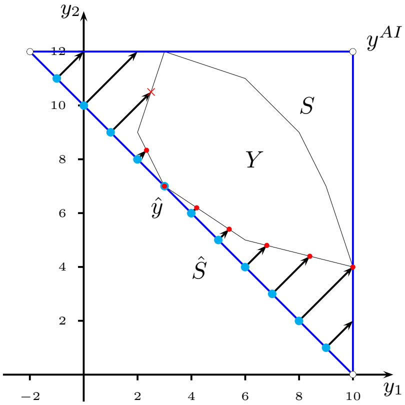
The convex hull S of $\{v^0, \ldots, v^p\}$ is a simplex containing Y.
The convex hull $\hat{S}$ of $\{v^1, \ldots, v^p\}$ is a hyperplane with normal e supporting Y in $\hat{y}$.

The Revised Boundary Intersection Method



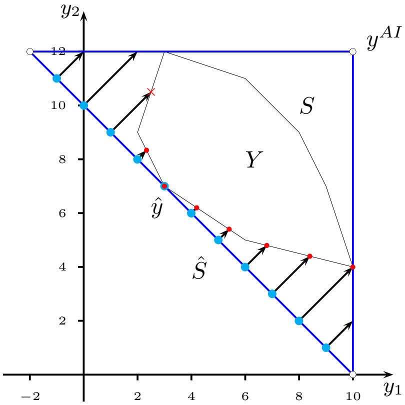
Compute equally spaced reference points q^i with distance ds on $\hat{S}$.

The Revised Boundary Intersection Method



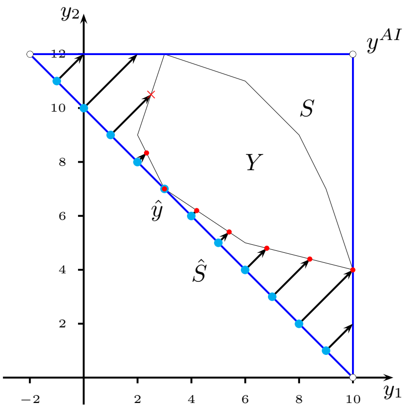
For each reference point q solve the LP $\min\{t : q + te \in Y, t \geq 0\}$.
If this LP is infeasible, the ray $q + te$ does not intersect Y, otherwise for the optimal value $\hat{t}$, $q = \hat{t}y \in Y$.
The LP cannot be unbounded.

The Revised Boundary Intersection Method



For each weakly non-dominated point $\hat{y}$ found in the previous step solve the LP $\min\{e^T y : y \in Y, y \leqq \hat{y}\}$.
It holds that $\hat{y}$ is non-dominated if and only if it is an optimal solution of this LP.

The Revised Boundary Intersection Method



Output: Representation R consisting of the non-dominated points confirmed in the last step.

Revised Normal Boundary Intersection

Theorem

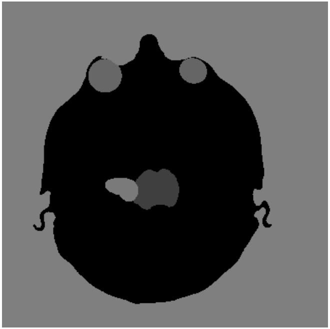
Let R be the representation of Y_N obtained with the RNBI method and let q^1, q^2 be two reference points with $d(q^1, q^2) = ds$ that yield non-dominated representative points r^1, r^2. Then $ds \leqq d(r^1, r^2) \leqq \sqrt{p}ds$. Hence R is a ds-uniform representation of Y_N.

Theorem

Let R be the representation of Y_N obtained with the RNBI method and assume that the width $w(S^j) \geqq ds$ for the projection S^j of all maximal faces Y^j of Y_N on $\hat{S}$. Then R is a ds-uniform $d_{\sqrt{p}ds}$-representation of Y_N.

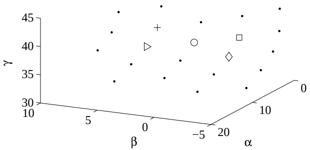
Overview

Acoustic Neuroma



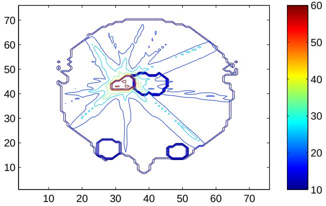
- 3 CT images, 3mm voxel size
- 78 tumour voxels, 472 critical organ voxels, 6778 normal tissue voxels, 597 bixels
- TLB = 57.58, TUB = 61.14, CUB(brain stem) = 50, CUB(eyes) =5 Gy, NUB = 0
- MOLP size $m = 7.410, n = 600, p = 3$

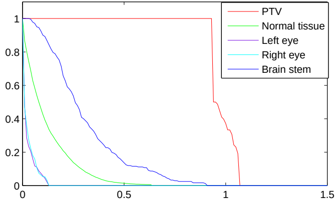
Acoustic Neuroma



- $ds = 3.47$ (153 reference points)
- 22 nondominated points (140 seconds of CPU time)
- Points marked are referred to in the simulated planning session

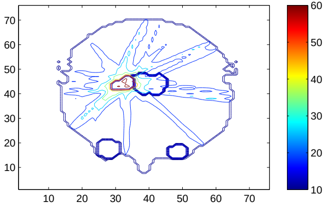
Finding a Suitable Plan

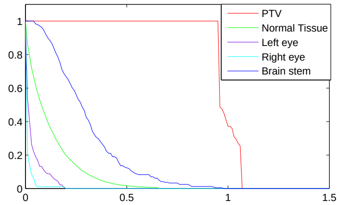




Plan 1, objectives as equal as possible (3.882, 2.366, 36.354)

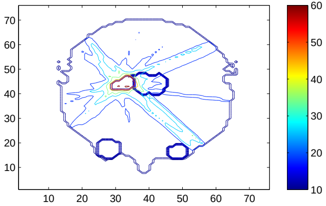
Finding a Suitable Plan

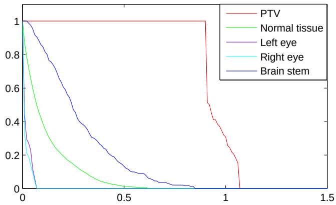




Plan 2, objective values (2.663, 6.048, 37.585) depicted by +

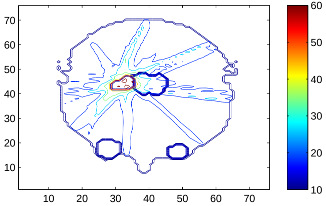
Finding a Suitable Plan

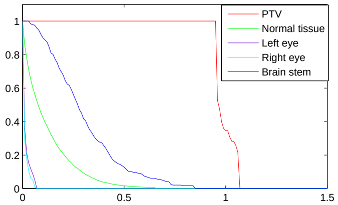




Plan 3, objective values (5.231, -1.185, 35.253) depicted by ◇

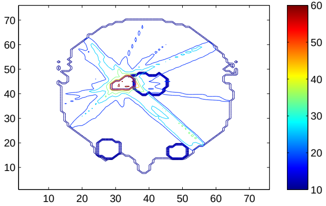
Finding a Suitable Plan

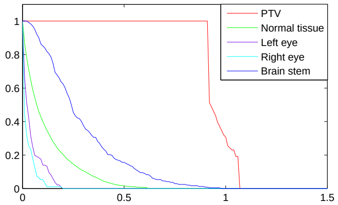




Plan 4, objective values (2.770, -1.196, 37.693) depicted by ⊡

Finding a Suitable Plan





Plan 5, objective values (5.148, 6.083, 35.170) depicted by ▷

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