New Mathematical Algorithms for Intensity Modulated Proton and Ion Therapy

LOMA LINDA UNIVERSITY HEALTH

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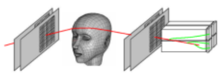

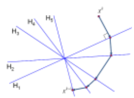

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  - ANDANTE Project (track structure detector, treatment planning)

Outline

- Novel Algorithmic Approaches to solving the IMPT problem
  - Feasibility-seeking projection methods
  - Superiorization vs. optimization
  - Additional dose-volume constraints

Novel Algorithmic Approaches

PROJECTION METHODS

Forward Problem Solver

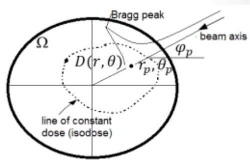
- Traditional proton treatment planning systems were 'forward problem solvers', that calculated the proton dose distribution based on the known physical characteristics of proton pencil beams in water
- The dose profiles were scaled according to the tissue properties (relative stopping power)
- Even these forward solvers had an inverse components: the energy and fluence of individual pencil beams had to be intensity-modulated to obtain a flat SOBP profile covering the GTV or CTV plus margin
- The 'forward-calculated' plan was then reviewed by the planner and physician and modified as needed – often a time-consuming process

From Forward to Inverse Treatment Planning in Proton Therapy

- With increasing use of actively scanned pencil beams replacing passively spread and modulated proton beams, inverse planning of IMPT is now at the forefront of interest
- IMPT plans can be generated in a similar fashion as IMRT plans, however the computational demand is much higher due to the larger degrees of freedom

Forward Problem - Description

- Let $D(r,\theta)$be real-valued, non-zero function of polar coordinates, representing the dose in the central beam axis plane, defined on a known patient cross-section Ω
- Let a proton pencil beam be defined by the real-valued function $\rho(r_p,\theta_p,\varphi_p)$, where r_p,θ_p is the location of the Bragg peak on the beam axis, $\varphi_p$is the angle of the beam axis with the 0-deg axis of the coordinate system, and ρ is the intensity of the beam



Forward Problem - Mathematical Definition

- Mathematical definition of the forward problem:

  Given a radiation intensity function of proton pencil beams $\rho_p(r_p,\theta_p,\varphi_p)$, $0 \le r_p \le r_{max}$, $0 \le \theta_p, \varphi_p \le 2\pi$, find the dose function $D(r,\theta)$ for all $(r,\theta) \in \Omega$ from the formula

  $$D(r,\theta) = \Delta[\rho_p(r_p,\theta_p,\varphi_p)](r,\theta)$$

  where Δ is the dose operator that relates the dose function to the radiation intensity function
- The dose operator Δ is represented by the treatment planning algorithm

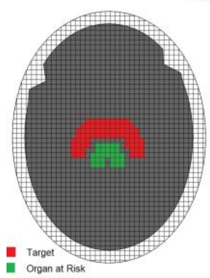
Inverse Problem – Mathematical Definition

- Let $D(r,\theta)$ be the dose function in a known cross section Ω of a patient prescribed by a physician (taking into account the target dose and maximum allowable doses to organs at risk), find a radiation intensity function $\rho_p(r_p,\theta_p,\varphi_p)$ such that

  $$\rho_p(r_p,\theta_p,\varphi_p) = \Delta^{-1}[D(r,\theta)]$$

Inverse Problem: Discrete Model Formulation

- The patient cross section is divided into a discrete grid of dose calculation points, and from this we chose the *J* pairs $\{(r_j, \theta_j) | j = 1,2, \cdots J\}$, for which we want to calculate dose
- Further, we define a discrete grid of beam aiming points within the target and a set of beam directions, from which we pick the *I* pencil beams, given by the triplets $\{(r_i, \theta_i, \varphi_i) | i = 1,2, \cdots I\}$



Discrete Inverse Problem: Definition

- Let a_{ij} be the dose delivered by the *i*-th pencil beam of unit intensity (or proton fluence) to the *j*-th dose grid point,
- let x_i be the actual intensity of the *i*-th pencil beam, i.e., the solution we are seeking,
- let b_j be the prescribed dose to the *j*-th dose grid point,
- the fully discretized inverse problem of proton beam therapy then becomes to find an proton pencil beam vector x^* that solves the linear problem

$$Ax^* = b,\ x \geq 0 \qquad (1)$$

- Where *A* is the matrix comprised of doses of all unit intensity pencil beams to the *J* dose grid points, and x^* and b are *I*-dimensional column vectors.

Approaches to Solving the Inverse Problem: Feasibility

- In practical IMRT (and IMPT), we do not demand equality in eq. (1), instead we allow the constraints to become inequalities with upper and lower dose bounds, $\overline{D}^j$ and $\underline{D}^j$, for each dose grid point
- A feasible solution of the inverse problem, if found, fulfills these constraints and will, therefore, be accepted by the physician
- It is important to note that dose inequality constraints are convex functions in hyper-dimensional dose vector space

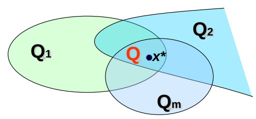
Convex Feasibility Problem

Find a point x^* in the intersection Q of m closed convex sets $Q_1, Q_2, \ldots, Q_m \subseteq R^n$.

We assume that Q_i is expressed as

$$Q_i = \{x \in R^n \mid f_i(x) \le 0\},$$

where $f_i : R^n \to R$ is a convex function for all $i = 1, 2, \ldots, m$.



Discrete Inverse CFP for IMPT - Definition

- Given a known cross section Ω of a patient with J discrete dose grid points, $j = 1,2,\cdots J$,
- given two dose vectors, $\overline{D} = (\overline{D}_j)$ and $\underline{D} = (\underline{D}_j)$, representing upper and lower dose limits of each dose grid point
- find a proton pencil beam intensity vector x such that

$$\underline{D}_j \le \sum_{i=1}^{N} a_{ij} x_i \le \overline{D}_j, j = 1,2,\cdots J$$
$$0 \le x_i \le x_{\max}, i = 1,2,\cdots I$$

Discrete Inverse CFP: Groups of Dose-Inequality Constraints

$$\begin{cases} \langle a^j, x\rangle \le b_l, & \texttt{for all} \quad j \in B_l,\ l = 1,2,\ldots,L, \\ t_q \le \langle a^j, x\rangle, & \texttt{for all} \quad j \in T_q,\ q = 1,2,\ldots,Q, \\ \langle a^j, x\rangle \le c, & \texttt{for all} \quad j \in C, \\ x_i \ge 0, & \texttt{for all} \quad i = 1,2,\ldots,I. \end{cases}$$

Dose constraints for target voxels

Dose constraints for OAR voxels

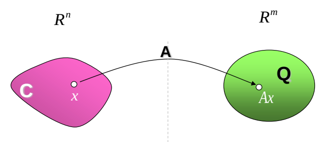
Dose constraints for voxels in 'complement'

Intensity constraints for pencil beams (non-negativity)

The 'Split Feasibility Problem' (SFP)

Let C and Q be nonempty closed convex sets in the Euclidean spaces R^N and R^M, respectively, and let A be a m x n real matrix.

The two sets *split feasibility problem* (SFP) is to find $x \in C$, such that $Ax \in Q$, if such an x exists.



Censor and Elfving 1994, Byrne 2002

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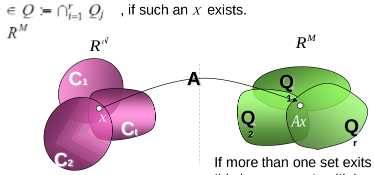
The 'Multiple-Sets Split Feasibility Problem' (MS SFP)

Let $C_{1,2...}$ and $Q_{1,2...}$ be nonempty closed convex sets in the Euclidean spaces R^N and R^M, respectively, and let A be a m x n real matrix.

The multiple-set *split feasibility problem* (SFP) is to find $x \in C := \cap_{i=1}^{t} C_i$, such that $Ax \in Q := \cap_{j=1}^{r} Q_j$, if such an x exists.



If more than one set exits in C and Q, this becomes a 'multiple-sets split feasibility problem' (MS SFP)

Censor and Elfving 1994, Byrne 2002

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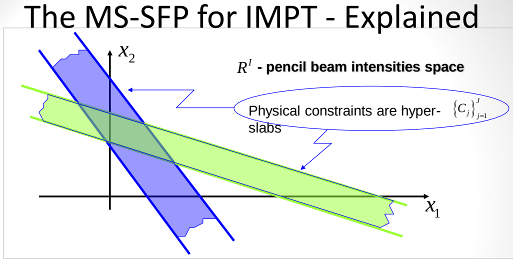
The MS-SFP for IMPT - Explained

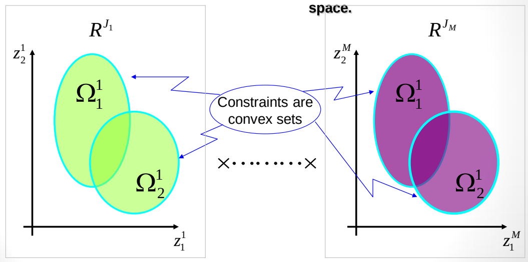


$b = Ax$

18 Censor, Elfving, Kopf and Bortfeld 2005, Censor, Bortfeld, Martin and Trofimov 2006

$$b = Ax$$

$R^{J} = R^{J_1} \times R^{J_2} \times \cdots \times R^{J_M}$ - **doses in voxels space.**



19 Censor, Elfving, Kopf and Bortfeld 2005, Censor, Bortfeld, Martin and Trofimov 2006

How to solve this? – Projection Methods

- Projection methods are iterative algorithms that reach a goal associated with a family of (convex) sets by performing individual ‘projections’ onto these (convex) sets
- Projection algorithms operate on multi-dimensional vectors and can be of different kind (e.g., Bregman, entropy, orthogonal etc.)
- They can be used to solve CFPs and are able to handle huge-size linear problems $Ax = b$, particularly when sparse.

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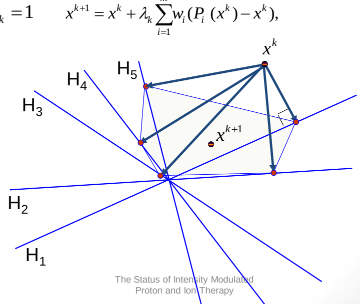
Example: Simultaneous Projections

All the sets are hyperplanes…

$$\lambda_k = 1 \qquad x^{k+1} = x^k + \lambda_k \sum_{i=1}^{m} w_i (P_i(x^k) - x^k),$$



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Example: Sequential Projections

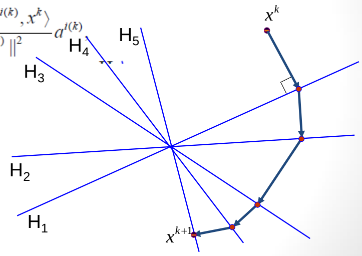
Sequential Successive Projections (POCS, ART, Kaczmarz, Row-Action)

$$x^{k+1} = x^k + \lambda_k (P_{C_{i(k)}}(x^k) - x^k),\ \lambda_k = 1$$

$$\langle a^i, x\rangle - b_i = 0,\quad i = 1,2,\ldots,m,$$

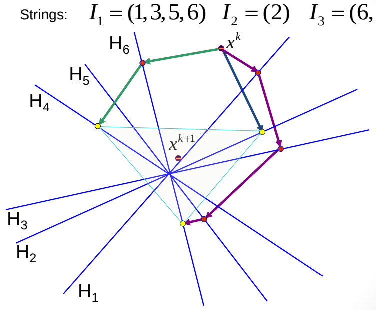
$$x^{k+1} = x^k + \lambda_k \frac{b_{i(k)} - \langle a^{i(k)}, x^k\rangle}{\| a^{i(k)} \|^2} a^{i(k)}$$

One projection at a time; makes ART very slow



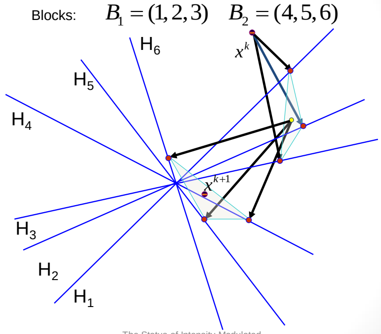
Parallelizable: String Averaging Projections (SAP)

Strings: $I_1 = (1,3,5,6)$ $I_2 = (2)$ $I_3 = (6,4)$



Parallelizable: Block Iterative Projections (BIP)

Blocks: $B_1 = (1,2,3)$ $B_2 = (4,5,6)$



IMPT & Projection Methods – Take Home Points

- Feasibility-seeking could be conceptually "simpler" than seeking a minimizer which finds a specific point in solution space whereas feasibility is contended with "any" point in the intersection.
- Projection methods are computationally effective and easy to program
- ART, being sequential in nature, may be too slow, but modern projection methods, like BIP and SAP, allow parallelization on dedicated hardware, GPGPUs
- In IMPT, the linear systems are by orders of magnitude larger than those in IMRT because of the stacking of pencil beams with different energies along each central axis

Novel Algorithmic Approaches

SUPERIORIZATION

What is Superiorization and how is it used with CFP-solving Projection Methods?

- Superiorization methodology (SM) is a recent development (since ~2007) that is based on perturbation resilience of some projection operators
- SM drives a cost (or objective) function ϕ along its negative gradient to smaller values by performing small perturbations of the solution vector repeatedly during feasibility seeking
- SM is intermediate between pure feasibility seeking and optimization

Bounded Perturbations Resilience

- Let Ψ be a nonempty subset of Ω in R^J. An algorithmic operator $\mathcal{A}$: Ω → Ω is said to be bounded perturbations resilient with respect to Ψ if the following is true:

if

any sequence $\{x^k\}_{k=0}^{\infty}$ generated by $x^{k+1} = \mathcal{A}(x^k)$ for all k ≥ 0 converges to a point in Ψ for all x^0 ∈ Ω,

then

any sequence $\{y^k\}_{k=0}^{\infty}$ in R^J that is generated by $\mathcal{A}(y^k + \beta_k v^k)$ for all k ≥ 0 also converges to a point in Ψ for all y^0 ∈ Ω provided that, for all k ≥ 0, $\beta_k v^k$ are bounded perturbations, meaning that $\beta_k \geq 0$ for all k ≥ 0 such that $\sum_{k=0}^{\infty} \beta_k < \infty$ and such that the sequence is bounded

Superiorization Algorithm

★ Take a $\mathcal{A}$ that solves the feasibility problem $T = \{C_i\}_{i=1}^{I}$(originally **SAP)**

★ Perform perturbations via $x^{k+1} = \mathcal{A}\left(x^k + \beta_k v^k\right)$

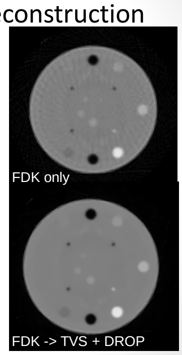
★ with $\beta_k \geq 0$, $\sum_{k=0}^{\infty} \beta_k < \infty$, and

$$v^k := \begin{cases} -s^k / \parallel s^k \parallel, & \text{if } s^k \neq 0, \\ 0, & \text{if } s^k = 0, \end{cases}$$

where $s^k \in \partial\phi(x^k)$.

Superiorization of Total Variation works well for Proton CT Reconstruction

- Proton CT with individual proton histories requires solving a(n even) large(r) linear system as well
- As shown, TV superiorization + DROP cancels artifacts inherent in FDK proton CT reconstruction



IMPT & Superiorization – Take Home Points

- Superiorization of a feasibility-seeking algorithm has shown promising results in image reconstruction in recent year (see Penfold et al Med Phys. 2010, Censor et al J Optim App Theor, 2014)
- Superiorization, not seeking for a single minimum, is computationally more efficient than optimizations, and may lead to a more robust result
- Superiorization applied in IMPT has yet to be investigated; TV superiorization in dose space is an interesting end point as it may minimize hot and cold spots

Novel Algorithmic Approaches

ADDITIONAL DOSE-VOLUME CONSTRAINTS

Dose-Volume Constraints (DVCs) in Practice

- The competing goals of maximizing PTV dose and minimizing OAR doses, may lead to an empty solution set (in both IMRT & IMPT), i.e., the solution presented is not feasible
- Additional DVCs are usually implemented (see example below) to allow limited constraint violations
- Without properly incorporating such DVCs into the solution algorithm itself it is not possible to guarantee that a satisfactory solution will be found
- Past work to solve this has been theoretically and algorithmically unsatisfactory

RTOG 0822

6.4.3.4 PTV planning dose-volume constraints:
- ≥ 98% of the PTV receives ≥ 93% of the prescribed dose
- ≤ 10% of the PTV receives ≥ 105% of the prescribed dose
- ≤ 5% of the PTV receives ≥ 110% of the prescribed dose
- None of the PTV is to receive ≥ 115% of the prescribed dose

6.5 Critical Structures (IMRT Planning Constraints)

6.5.1 Small bowel:
- No more than 180 cc above 35 Gy
- No more than 100 cc above 40 Gy
- No more than 65 cc above 45 Gy
- No small bowel volume should receive 50 Gy

6.5.2 Femoral heads:
- No more than 40% volume above 40 Gy

DVC –Supporting Feasibility Algorithm

- We have developed an approach to incorporate DVCs into the CFP by ...
  - Formulating the CFP + DVC mathematically (Problem 1)
  - Formulating an alternative mathematical problem (Problem 2) that can be solved by an iterative projection method
  - Proving that Theorem that solving Problem 2 will also solve Problem 1

DVC-Supporting Feasibility Algorithm

Problem 1 The dose-volume constraints (DVCs) feasibility problem *is as follows. Given a finite index set B (that contains all voxel indices of the voxels that belong to a structure $\mathcal{B}$), the vectors $\{a^j\}_{j\in B}$, upper bounds on doses to voxels that are real positive numbers u_j for all $j \in B$, and two real numbers $0 \le \alpha \le 1$ and $0 < \beta < 1$, find a vector x^* that solves the system*

$$\left\langle a^j, x \right\rangle \le u_j \text{ for all } j \in B \tag{1}$$

subject to the additional constraint that:

in up to α% of the inequalities the right-hand sides u_j may be potentially violated by up to β%.

DVC-Supporting Feasibility Algorithm

Problem 2 *Given a finite index set B, vectors $\{a^j\}_{j\in B}$, real positive numbers u_j for all $j \in B$, and two real numbers $0 \le \alpha \le 1$ and $0 < \beta < 1$, find a vector x^* that solves the system*

$$\begin{cases} \text{(i) } \left\langle a^j, x \right\rangle \le (1+\beta)u_j, & \text{for all } j \in B, \\ \text{(ii) } h(x) \le \alpha\beta|B|, & \end{cases} \tag{2}$$

where the real-valued function $h : R^I \to R$, (R^I stands for the I-dimensional Euclidean vector space) is a specific explicitly defined function of the vector variable x and parameters a^j, u_j, and β, which is convex in x and its subgradients or gradients are easily calculated.

DVC-Supporting Feasibility Algorithm

Theorem 3 *Given are a finite index set B, vectors $\{a^j\}_{j\in B}$, real positive numbers u_j for all $j \in B$, and two real numbers $0 \leq \alpha \leq 1$ and $0 < \beta < 1$. If x^* is a solution of Problem 2 then it solves Problem 1. By this we mean that when x^* will be substituted into the inequalities (1) there will be no more than α% of the inequalities in (1) that will violate the inequalities of (1) by yielding $\left\langle a^j, x^* \right\rangle > u_j$ with $\left\langle a^j, x^* \right\rangle \leq (1+\beta)u_j$ while all other inequalities will obey $\left\langle a^j, x^* \right\rangle \leq u_j$.*

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Conclusion

- IMPT, like IMPRT, problems have been traditionally approached with linear solvers under minimization constraints of cost functions
- New algorithmic structures based on projection methods +/- superiorization that have shown good performance in other applications (e.g., image reconstruction) may also prove useful for IMPT
- Incorporation of additional dose-volume constraints into feasibility seeking algorithms should be investigated

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Danke Schön

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Pronounced: "Toda Raba"

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