Chapter 5

Application of Graph Theory and Linear Programming for Intensity Modulated Radiation Therapy (IMRT) Cancer Treatment

This chapter addresses the problem formulation for optimal aperture formation of MLC. The problem implementation and analysis of result generated from Bellman-Ford algorithm is done. The linear programming formulation for longest route problem is discussed and a critical path method formulation to generate maximal aperture geometry is formed and solved by primal-dual interior point algorithm. The results generated from both the algorithms are compared to confirm the accuracy of maximal aperture geometry for Multi-Leaf Collimator (MLC). Finally the conclusion and future work are discussed.

5.1 PROBLEM FORMULATION

In external beam dose deposition with photon beams the main parameters are depth of the treatment Z, Source to Skin Distance (SSD), field size A, Source to Axis Distance (SAD), photon energy beams, number of beams used in dose delivery to the patient, treatment time for teletherapy machines and number of Monitor Units (MUs) for LINACS.

The Figure 5.1 shows the radiation source incident on the target volume of the patient along with the parameters. Generally for fixed SSD technique the monitor unit (MUs) is as in equation 5.1.

\[ MU = \frac{cGy(SSD)}{CF \times (OF \times PDD \times WF)} \]  

(5.1)

Where, (i) CF is the Calibration Factor  
(ii) PPD is Percentage Dose Depth  
(iii) WF is the Wedge Factor
The MLC fitted at the end of the gantry has list of mechanical constraints as follows:

(i) Formation of horseshoe shape in single aperture is infeasible.

(ii) Movement of leafs of left and right side operate with lower bound in millimeter precision. With these general restrictions the MLC is modelled as a square opening with equidistant grids forming an m*n matrix. For instance with 5 leaf on both sides and 10 equidistant points lead to 5*10 matrix. The problem formulation is modelled into a dataflow diagram as shown in Figure 5.2.
5.2 PROBLEM IMPLEMENTATION

The 6*10 matrix is considered as fluence-matrix input is shown in Table 5.1.

Table 5.1 Input Fluence -Matrix

<table>
<thead>
<tr>
<th></th>
<th>0</th>
<th>0</th>
<th>-0.1</th>
<th>-0.5</th>
<th>-0.6</th>
<th>1.3</th>
<th>1.4</th>
<th>0.3</th>
<th>-0.8</th>
<th>0</th>
</tr>
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<tr>
<td>-0.5</td>
<td>0.3</td>
<td>-1.3</td>
<td>-2.4</td>
<td>3.2</td>
<td>1.2</td>
<td>-1.3</td>
<td>-0.6</td>
<td>0.5</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>0.6</td>
<td>0.8</td>
<td>-1.3</td>
<td>-2.5</td>
<td>0.1</td>
<td>1.1</td>
<td>-1.3</td>
<td>-1.3</td>
<td>-1.2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>1.5</td>
<td>1.3</td>
<td>-0.1</td>
<td>-0.6</td>
<td>-1.7</td>
<td>-1.5</td>
<td>-2.6</td>
<td>1.5</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>0</td>
<td>-1.4</td>
<td>-2.6</td>
<td>1.3</td>
<td>0.4</td>
<td>1.7</td>
<td>-0.6</td>
<td>-0.2</td>
<td>-0.1</td>
<td>-0.7</td>
<td></td>
</tr>
<tr>
<td>-0.7</td>
<td>-1.4</td>
<td>-1.7</td>
<td>0.7</td>
<td>0.5</td>
<td>0.6</td>
<td>-0.3</td>
<td>-1.2</td>
<td>-1.4</td>
<td>-1.2</td>
<td></td>
</tr>
</tbody>
</table>

Figure 5.2 Data Flow for Problem Formulation
To generate weighted directed graph from the matrix, the list of rules are enumerated below.

(i) Group and sum the pattern of negative elements in each row to form node.

(ii) The calculated sum becomes weight between nodes.

(iii) Any two nodes are connected if pattern of negative elements of any two adjacent rows are interconnected.

Figure 5.3 Directed Weighted Graph Generated

With weighted directed graph is framed as shown in Figure 5.3. The Bellman-Ford method is applied to trace the least path. The pseudo code of the algorithm is as follows.

Initialize \( dx = 0 \) and \( dy = \infty \) for all \( y \neq x \)

For \( i = 1 \ldots n-1 \):

For each edge \( x \rightarrow y \) of cost \( c \):

\[ dx = \min(dx + c) \]

For each edge \( x \rightarrow y \) of cost \( c \):

\[ \text{If} \ dx > dy + c \]

Negative cycle graph persist
The calculated shortest path corresponds to optimal feasible aperture of MLC that covers larger area of tumour geometry. The various possible traversals are shown in the Table 5.2 with optimal winning path being A, B, E, G, I, J, L. The optimal traversed shortest distance is -23.

**Table 5.2 Various Possible Path Traversals from Start Node**

<table>
<thead>
<tr>
<th>Starting Node</th>
<th>Ending Node</th>
<th>Distance Travelled</th>
<th>Winning Path</th>
<th>Predecessor Nodes</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>A</td>
<td>0</td>
<td>A</td>
<td>N/A</td>
</tr>
<tr>
<td>A</td>
<td>B</td>
<td>-1.2</td>
<td>A,B</td>
<td>A</td>
</tr>
<tr>
<td>A</td>
<td>C</td>
<td>-0.8</td>
<td>A,C</td>
<td>A</td>
</tr>
<tr>
<td>A</td>
<td>D</td>
<td>-0.5</td>
<td>A,D</td>
<td>A</td>
</tr>
<tr>
<td>A</td>
<td>E</td>
<td>-4.9</td>
<td>A,B,E</td>
<td>B</td>
</tr>
<tr>
<td>A</td>
<td>F</td>
<td>-1.9</td>
<td>A,F</td>
<td>A</td>
</tr>
<tr>
<td>A</td>
<td>G</td>
<td>-8.7</td>
<td>A,B,E,G</td>
<td>E</td>
</tr>
<tr>
<td>A</td>
<td>H</td>
<td>-5.7</td>
<td>A,F,H</td>
<td>F</td>
</tr>
<tr>
<td>A</td>
<td>I</td>
<td>-15.2</td>
<td>A,B,E,G,I</td>
<td>G</td>
</tr>
<tr>
<td>A</td>
<td>J</td>
<td>-19.20</td>
<td>A,B,E,G,I,J</td>
<td>I</td>
</tr>
<tr>
<td>A</td>
<td>K</td>
<td>-16.80</td>
<td>A,B,E,G,I,K</td>
<td>I</td>
</tr>
<tr>
<td>A</td>
<td>L</td>
<td>-23</td>
<td>A,B,E,G,I,J,L</td>
<td>J</td>
</tr>
<tr>
<td>A</td>
<td>M</td>
<td>-20.90</td>
<td>A,B,E,G,I,K,M</td>
<td>K</td>
</tr>
</tbody>
</table>

**5.3 CRITICAL PATH METHOD**

To check the optimal distance traversed value obtained from Bellman-Ford shortest path algorithm, the critical path method opposite to shortest path is modelled. Therefore the objective is to find the longest traversed distance from the start node to the terminate node.
Let \( x_{ij} \) = Amount flow between any two nodes.

\( D_{ij} \) = Weight between any two nodes.

The objective function is

Maximize

\[
Z = \sum_{i,j} D_{ij} x_{ij}
\]  

(5.2)

Subject to the constraints:

Conversation of flow:

**Total input flow = Total output flow**

Now the fluence matrix shown in Table 5.1 is used to draw network diagram with nodes and edges and then formulated as a linear programming problem.

![Network with Critical Path Calculations](image)

**Figure 5.4** Network with Critical Path Calculations.
5.3.1 THE INTERIOR POINT ALGORITHM FOR LINEAR PROGRAMMING

The standard form of linear programming is as in equation 5.3.

Let \( A \in \mathbb{R}^{m \times n} \), \( a \in \mathbb{R}^m \), \( B \in \mathbb{R}^{p \times n} \), \( b \in \mathbb{R}^p \).

\[
C^T x \rightarrow \min \tag{5.3}
\]

s.t.
\[
Ax \leq a \\
Bx = b \\
lb \leq x \leq ub
\]

Now set \( \bar{x} = x - lb \), then equation 5.3 is modified as in equation 5.4.

\[
C^T \bar{x} - C^T lb \rightarrow \min \tag{5.4}
\]

s.t.
\[
A\bar{x} \leq a - A(lb) \\
B\bar{x} = b - B(lb) \\
0 \leq \bar{x} \leq ub - lb
\]

Next by adding slack variables \( y \in \mathbb{R}^p \) and \( s \in \mathbb{R}^n \), the equation 5.4 is transformed as in equation 5.5.

\[
C^T \bar{x} - C^T lb \rightarrow \min \tag{5.5}
\]

s.t.
\[
A\bar{x} + y = a - A(lb) \\
B\bar{x} = b - B(lb) \\
\bar{x} + s = ub - lb \\
\bar{x} \geq 0, y \geq 0, s \geq 0
\]

Now enclosing constraints of equation 5.5 in single matrix gives equation 5.6.

\[
C^T \bar{x} - C^T lb \rightarrow \min \tag{5.6}
\]
Since the constant in the objective function of equation 5.6 is negligible, it is eliminated and also split into two forms namely the Primal Problem (PP) as in equation 5.7.

$$\min C^T x \rightarrow \min$$  \hspace{1cm} (5.7)

\[ \begin{align*}
\text{s.t.} & \quad A x + O_{m,n} \begin{pmatrix} x \\ y \\ s \end{pmatrix} = a - A(lb) \\
& \quad b - B(lb) \\
& \quad ub - lb \\
& \quad \bar{x} \geq 0, y \geq 0, s \geq 0
\end{align*} \]

Associated with the PP is the Dual Problem (DP), which is of the form as in equation 5.8.

$$\max b^T x \rightarrow \max$$  \hspace{1cm} (5.8)

\[ \begin{align*}
\text{s.t.} & \quad A w \leq c \\
& \quad w \in \mathbb{R}^n
\end{align*} \]

By applying slack variable $s \in \mathbb{R}^n$ in equation 5.8, the Dual Problem (DP) is as in equation 5.9.

$$\max b^T x \rightarrow \max$$  \hspace{1cm} (5.9)

\[ \begin{align*}
\text{s.t.} & \quad A^T w + s = c \\
& \quad w \in \mathbb{R}^n \\
& \quad x \geq 0 \\
& \quad s \geq 0
\end{align*} \]

These two problems equation 5.7 & 5.9 namely the PP and DP are known as Primal-Dual pairs.
5.3.2 OPTIMALITY CONDITION

The vector \( \begin{pmatrix} x^* \ w^* \ s^* \end{pmatrix} \) is the solution of Primal-Dual pair only when it satisfies the Karush-Kuhn-Tucker (KKT) optimality conditions. The KKT conditions are as in equation 5.10.

\[
F(x, w, s) = \begin{bmatrix} A^T w + s - c \\ Ax - a \\ XSe \end{bmatrix} = 0
\] (5.10)

\[
(x \ s) \geq 0
\]

Here

\[
X = diag(x_1, x_2, \ldots, x_n)
\]

\[
S = diag(s_1, s_2, \ldots, s_n) \in \mathbb{R}^{n \times n}
\]

\[
e = (1, 1, \ldots, 1)^T \in \mathbb{R}^n
\]

The Primal-Dual interior point method generates iteration \( \begin{pmatrix} x^k \ w^k \ s^k \end{pmatrix} \) such that the KKT conditions are satisfied.

5.3.3 CENTRAL PATH

Consider \( \tau > 0 \) be a parameter. The central path is a curve \( C \) with set of point \( (x(\tau), w(\tau), s(\tau)) \in C \) and satisfy the equation 5.11.

\[
F\left( x(\tau), w(\tau), s(\tau) \right) = \begin{bmatrix} 0 \\ 0 \\ \tau e \end{bmatrix}, (x(\tau), s(\tau)) > 0
\] (5.11)

Obviously, as \( \tau \) approaches zero, the equation 5.11 goes close to the equation 5.7 & 5.9. Therefore the Primal-Dual algorithm theoretically solves equation 5.12 to find a search direction \( (\Delta x(\tau), \Delta w(\tau), \Delta s(\tau)) \).
\[
J(x(\tau), w(\tau), s(\tau)) \begin{bmatrix}
\Delta x(\tau) \\
\Delta w(\tau) \\
\Delta s(\tau)
\end{bmatrix} = \begin{bmatrix}
0 \\
0 \\
-XSe + \tau e
\end{bmatrix}, (x(\tau), s(\tau)) > 0 \quad (5.12)
\]

Where \( J(x(\tau), w(\tau), s(\tau)) \) is the Jacobian of \( F(x(\tau), w(\tau), s(\tau)) \). By applying the equation 5.12 the new iterate is generated as in equation 5.13.

\[
(x^+(\tau), w^+(\tau), s^+(\tau)) = (x(\tau), w(\tau), s(\tau)) + \alpha (\Delta x(\tau), \Delta w(\tau), \Delta s(\tau)) \quad (5.13)
\]

Where \( \alpha \) is a step length, such that \( \alpha \in [0,1] \), generated such that \( (x^+(\tau), w^+(\tau), s^+(\tau)) \in C \).

For practical method \( \tau = \sigma \mu \).

Where \( \sigma \in [0,1] \) is a constant and \( \mu = \frac{x^T s}{n} \). The numerator is the duality gap between the Primal-Dual pairs. Then \( \mu \) is the measure of average duality gap. In general \( \mu \geq 0 \) and \( \mu = 0 \) when \( x \) and \( s \) are primal dual optimal respectively. Thus the Newton step \( (\Delta x(\mu), \Delta w(\mu), \Delta s(\mu)) \) is determined by solving equation 5.14.

\[
\begin{bmatrix}
O_n & A^T & I_n \\
A & O_{\text{non}} & O_{\text{non}} \\
S & O_{\text{non}} & X
\end{bmatrix}
\begin{bmatrix}
\Delta x(\tau) \\
\Delta w(\tau) \\
\Delta s(\tau)
\end{bmatrix} = \begin{bmatrix}
0 \\
0 \\
-XSe + \sigma \mu e
\end{bmatrix} \quad (5.14)
\]

The Newton step is known as centering direction as it pushes iterates \((x^*(\mu), w^*(\mu), s^*(\mu))\) towards the central path \( C \) through which the method converges more rapidly. The parameter \( \sigma \) is the centering parameter.
5.3.4 PRIMAL-DUAL INTERIOR POINT ALGORITHM

Step 0: Start with initial values \((x^0, w^0, s^0)\) with \((x^{k+1}, s^{k+1}) > 0, k = 0\)

Step k: Choose \(\sigma_k \in [0,1]\), Set \(\mu_k = \frac{(x^k)^T s^k}{n}\) and solve equation 5.14

Set \((x^{k+1}, w^{k+1}, s^{k+1}) \leftarrow (x^k, w^k, s^k) + \alpha_k (\Delta x^k, \Delta w^k, \Delta s^k)\)

Assigning \(\alpha_k \in [0,1]\) such that \((x^{k+1}, s^{k+1}) > 0\).

If (CONVERGENCE) STOP

Else Set \(k \leftarrow k + 1\)

Go To Step \(k\)

Linear programming formulation based on Figure 5.4 is modeled as in equation 5.15.

Maximize

\[
Z = 1.2x_{12} + 1.9x_{13} + 0x_{23} + 3.7x_{24} \\
+ 3.8x_{35} + 3.8x_{45} + 6.5x_{56} + 4.6x_{67} \\
+ 1.6x_{68} + 3.8x_{79} + 4.1x_{89}
\]

Subject to constraints:

\[
\begin{align*}
x_{12} + x_{13} &= 1 \\
x_{12} - x_{23} - x_{24} &= 0 \\
x_{23} + x_{13} - x_{35} &= 0 \\
x_{24} - x_{45} &= 0 \\
x_{35} + x_{45} - x_{56} &= 0 \\
x_{56} - x_{68} - x_{67} &= 0 \\
x_{67} - x_{79} &= 0 \\
x_{68} - x_{89} &= 0 \\
x_{89} + x_{79} &= 1
\end{align*}
\]
Where,

\[ Z \text{ is the objective function and } x_{12}, x_{13}, x_{23}, x_{24}, x_{35}, x_{45}, x_{67}, x_{68}, x_{79}, x_{89}, \text{ are the variables.} \]

The formulated LLP is solved by MATLAB Linprog tool whose input/output arguments are shown in Figure 5.5. The optimal traversed longest distance computed for formulated LLP is 23. The various values of the variables satisfying the constraints are shown in Figure 5.6. When these values are assigned in objective function the optimal value is computed.

**Figure 5.5** Input Output Arguments for Linear Programming Formulation
Figure 5.6 Values of Variables to Compute Optimal Value

The optimal objective value is reached when the Duality Gap between the Primal-Dual pair approaches zero as shown in Figure 5.7.

Figure 5.7 Duality Gap Gradients for Convergence to Optimal Value
The optimal longest winning path being a, b, e, g, i, j, and l as shown by dotted arrows in Figure 5.4. The critical path calculations are also shown in Figure 5.7.

Thus from the considered 6*10 fluence-matrix the same optimal value and winning path is computed by both the methods discussed.

5.4 CONCLUSION

The need for mathematical optimization to deliver radiation to tumor geometry satisfying the mechanical constraint of MLC leafs is addressed. First the considered Fluence-Matrix is generated as a weighted directed graph and solved using Bellman-Ford algorithm to find optimal aperture such that large tumor region is covered in one fractional treatment. To verify the results arrived, the critical path method opposite to the shortest route is formulated as linear programming problem. The formulated LLP is solved by MATLAB Linprog tool. The results are in agreement with results generated from Bellman-Ford algorithm. The future scope of the paper is to formulate and analyze the role of mixed integer programming (MIP) to generate optimal sequence of segments or fractions to cover entire geometry of tumor region in minimal time.