Operations Research
and
Planning of Radiation Therapy

Horst W. Hamacher

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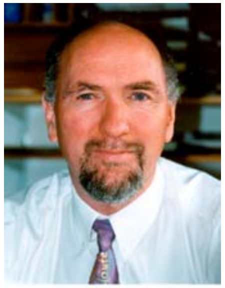

UNIVERSITÄT
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Alexander Scherrer

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Techno- und
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ITWM

Institut
Techno- und
Wirtschaftsmathematik

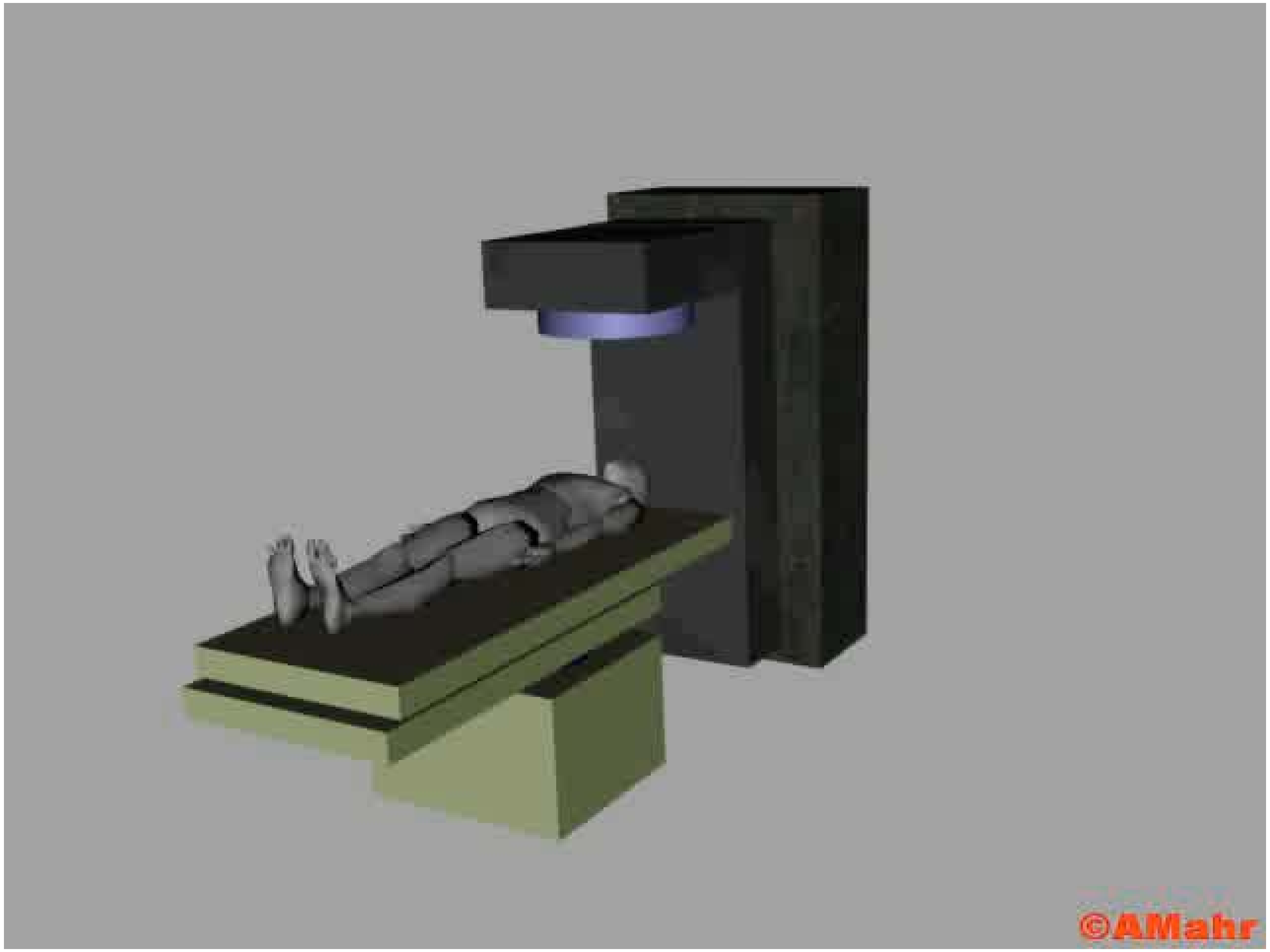
Reference to Radiation Therapy

Most pictures and films in this talk from:

Wolfgang Schlegel and Andreas Mahr:

3D Conformal Radiation Therapy:
A multimedia introduction to methods and techniques,
2001 (Springer Book and CD ROM)

Intensity Modulated Radiation Therapy (IMRT)



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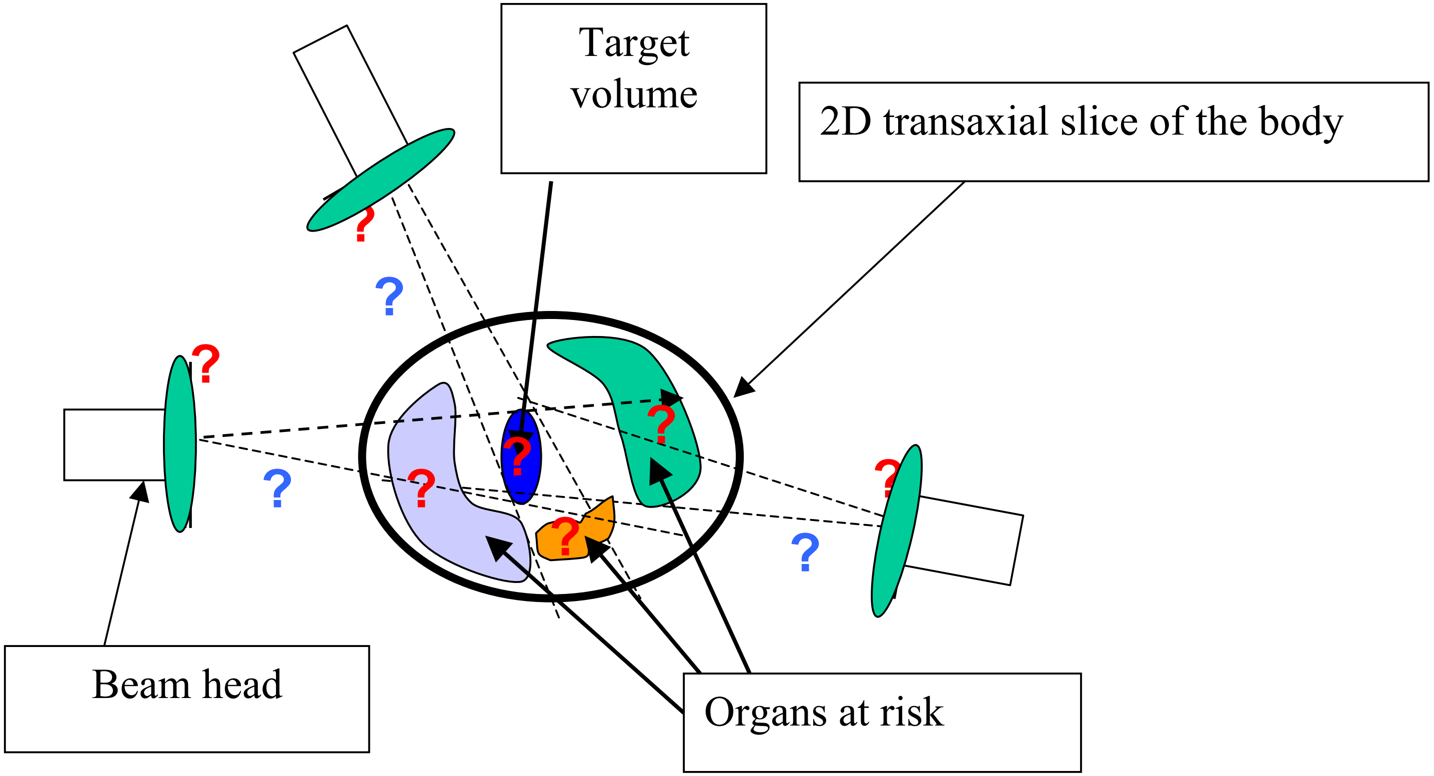


Geometry Problem: Where does the gantry stop?

Intensity Problem: How much radiation is sent off ?

Realization Problem: How is the radiation modulated?

Contents of this talk

Part I: Horst W. Hamacher

- Geometry Problem

- Intensity Problem:
  Multicriteria Approach - First Model

- Realization Problem:
  Sweep Technique and Linear Time Algorithm
  Technical Restrictions and Network Flow Solutions

Part II: Alexander Scherrer

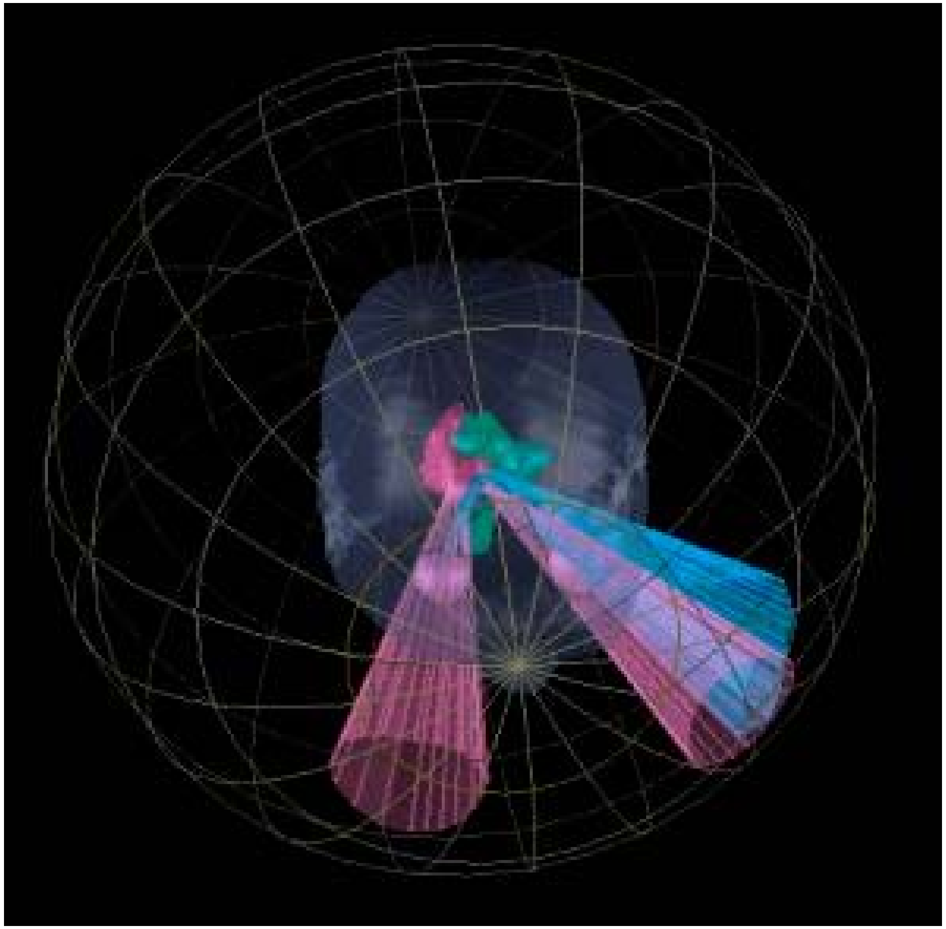
Algorithms and Numerics
Online Treatment Planning - A Decision Support Tool

Geometry Problem:
Where does the gantry stop

Ahmad S.A. Sultan, Diploma Thesis, Univ. of Kaiserslautern (2002)

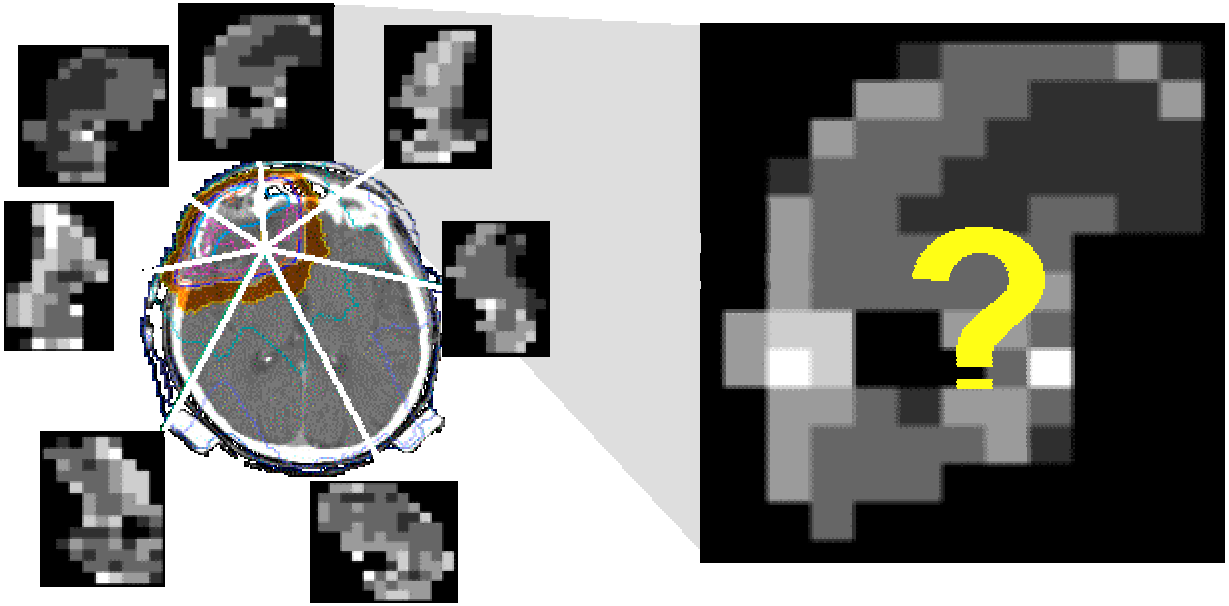
M. Ehrgott and R. Johnston, Optimisation of Irradiation Directions in IMRT Planning, OR Spectrum 2003
(Talk at this conference)

Mangalika Jayasundara, Spherical location problem
(Current Research)



Intensity Problem

Which intensity profiles gives the best conformal picture of tumor?



Intensity Problem

Conflicting criteria:

- high radiation in target volume (cancer cells should be killed)
- low radiation in organs at risk (organs should stay functional)

OR Solution Approach:

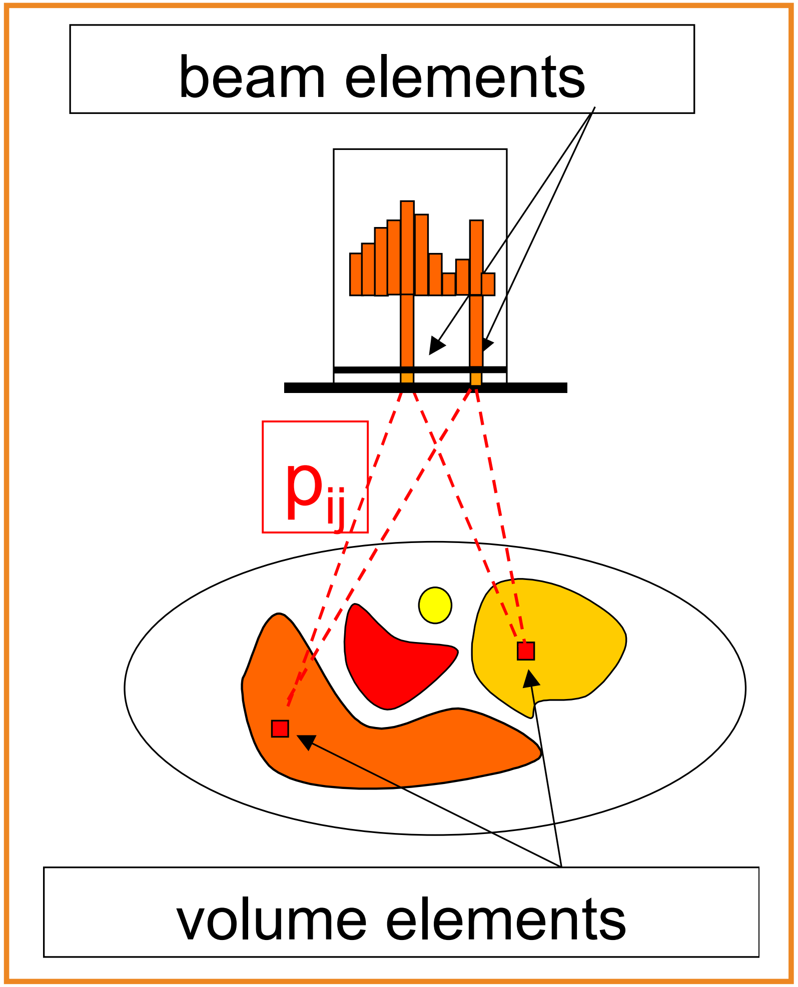
Compute set of 600 - 1,000 radiation plans which are Pareto solutions of multicriteria linear programs

(Hamacher, Küfer: Discrete Applied Mathematics, 2002
"Inverse Radiation Therapy Planning - A Multicriteria Approach")

Calculation of Dose Distribution

Discretize

- radiation beams into beam elements (bixels)
- body parts into volume elements (voxels)



Dose Volume Calculation

- P(i,j) = dose in voxel i irradiated from bixel j under unit intensity

- dose volume $D = P\,x$
  (x_j = radiation intensity in bixel j)

- partitioned into target volume ($k=1$)

  $D_1 = P_1\,x$

  and organs at risk ($k=2,\ldots,K$)

  $D_k = P_k\,x$

Ideal intensity profile - Simple Model

Given: Dose bounds $L_1 \geq 0$ and $U_k \geq 0$, $k = 2, \ldots, K$

Find: Intensity vector $x \geq 0$ satisfying the system of linear inequalities

$$D_1 = P_1 x \geq L_1 e \qquad \textit{(target condition)}$$

$$D_k = P_k x \leq U_k e, \quad k = 2, \ldots, K, \quad \textit{(risk conditions)}$$

System is in general inconsistent !

Such an x does in general not exist !

Penalize violation of constraints

minimize $\mu_1 F_1(x) + \ldots + \mu_K F_K(x)$ for given weights $\mu_1, \ldots, \mu_K > 0$

- Bortfeld, Schlegel, Brahme, Gustafsson ...

  $F_1(x) := \| L_1 e - P_1 x \|_2$

  $F_k(x) := \| (P_k x - U_k e)_+ \|_2 , \; k = 2, \ldots , K$

  Least square approach

- Holmes, Mackie, Burkard, ...

  $F_1(x) := \| (L_1 e - P_1 x)_+ \|_\infty$

  $F_k(x) := \| (P_k x - U_k e)_+ \|_\infty , \; k = 2, \ldots , K$

  Minimax approach

Disadvantage:
- time consuming
- unsatisfying results

Pareto intensity profile - Simple Model

minimize $(t_1, t_2, \dots , t_K)$

such that

$$P_1 x + t_1 L_1 e \geq L_1 e$$
$$P_k x - t_k U_k e \leq U_k e , \quad k = 2, \dots ,K$$

$$t = (t_1, t_2, \dots , t_K) \geq 0$$
$$x \geq 0$$

- Consistent system
- Too many Pareto solutions !

Pareto intensity profile - Advanced Model

Allow that part of risk organs are destroyed:

EUD = Equivalent Uniform Dose

Linear model

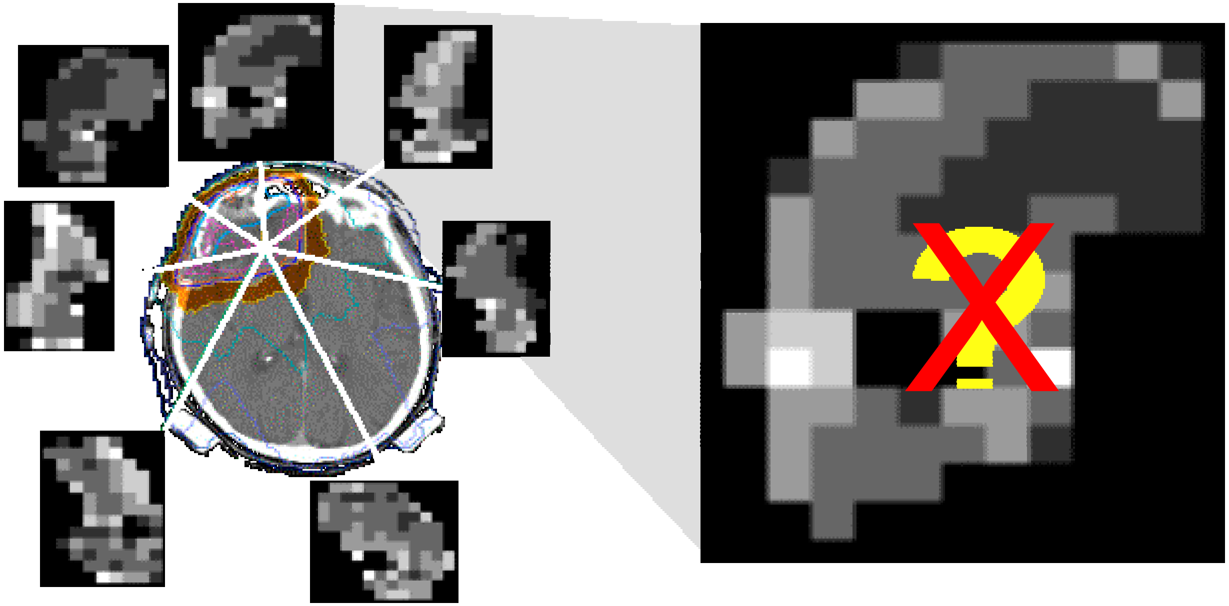
- $\mathrm{EUD}_{\mathrm{i}}(D_i) = (1-\alpha_{\mathrm{i}})\,\|D_i\|_{\mathrm{mean}} + \alpha_{\mathrm{i}}\,\|D_i\|_{\mathrm{max}}$ Thieke, Küfer, Bortfeld (2001)

$$\|D_i\|_1 \xleftrightarrow[\text{parallel organ} \qquad\qquad \text{serial organ}]{\qquad\qquad\qquad\qquad\qquad} \|D_i\|_\infty$$

More: Part II of this presentation !

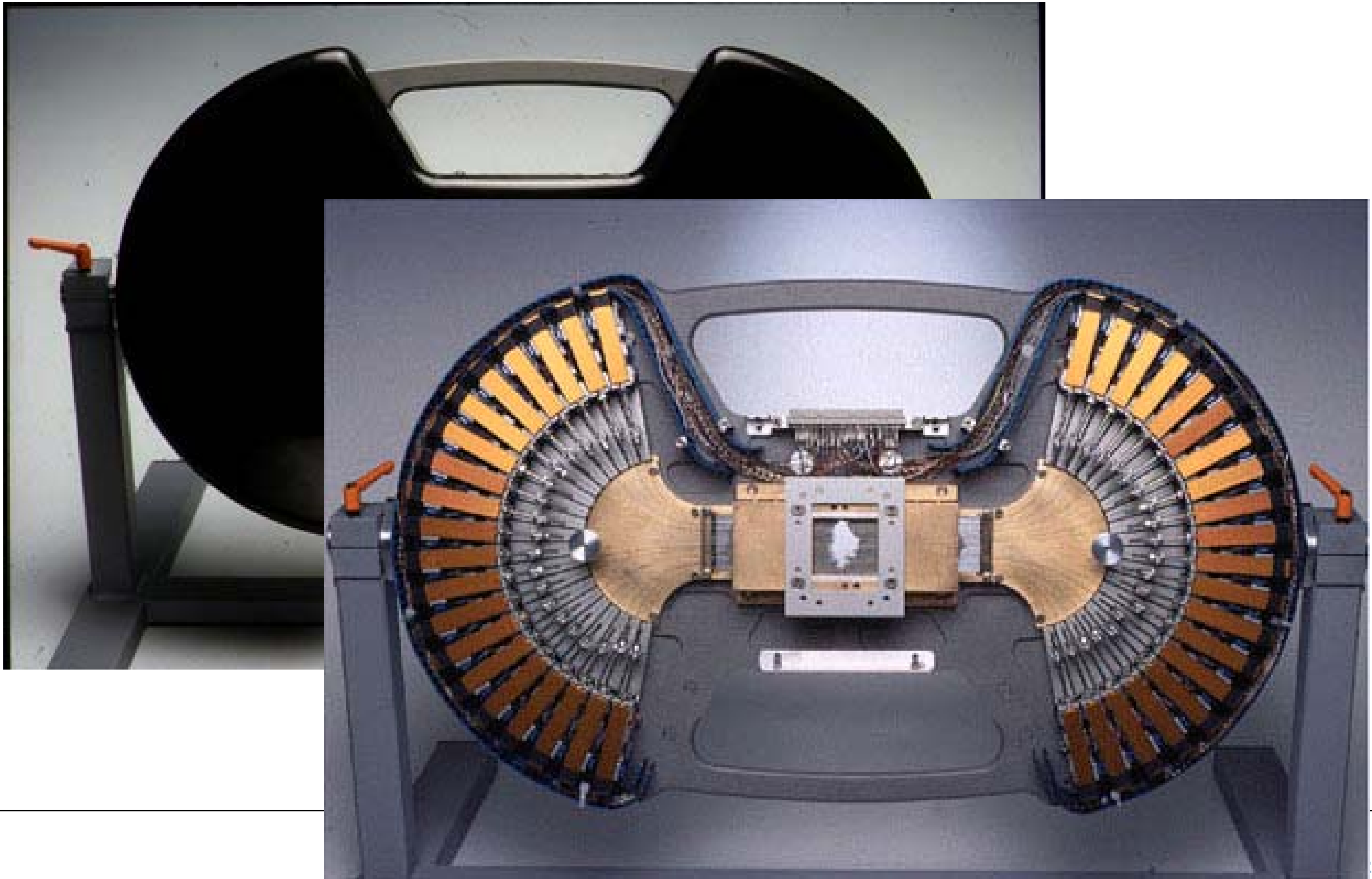
Realization Problem: Integer and Combinatorial Optimizaton

How are the intensity profiles generated?

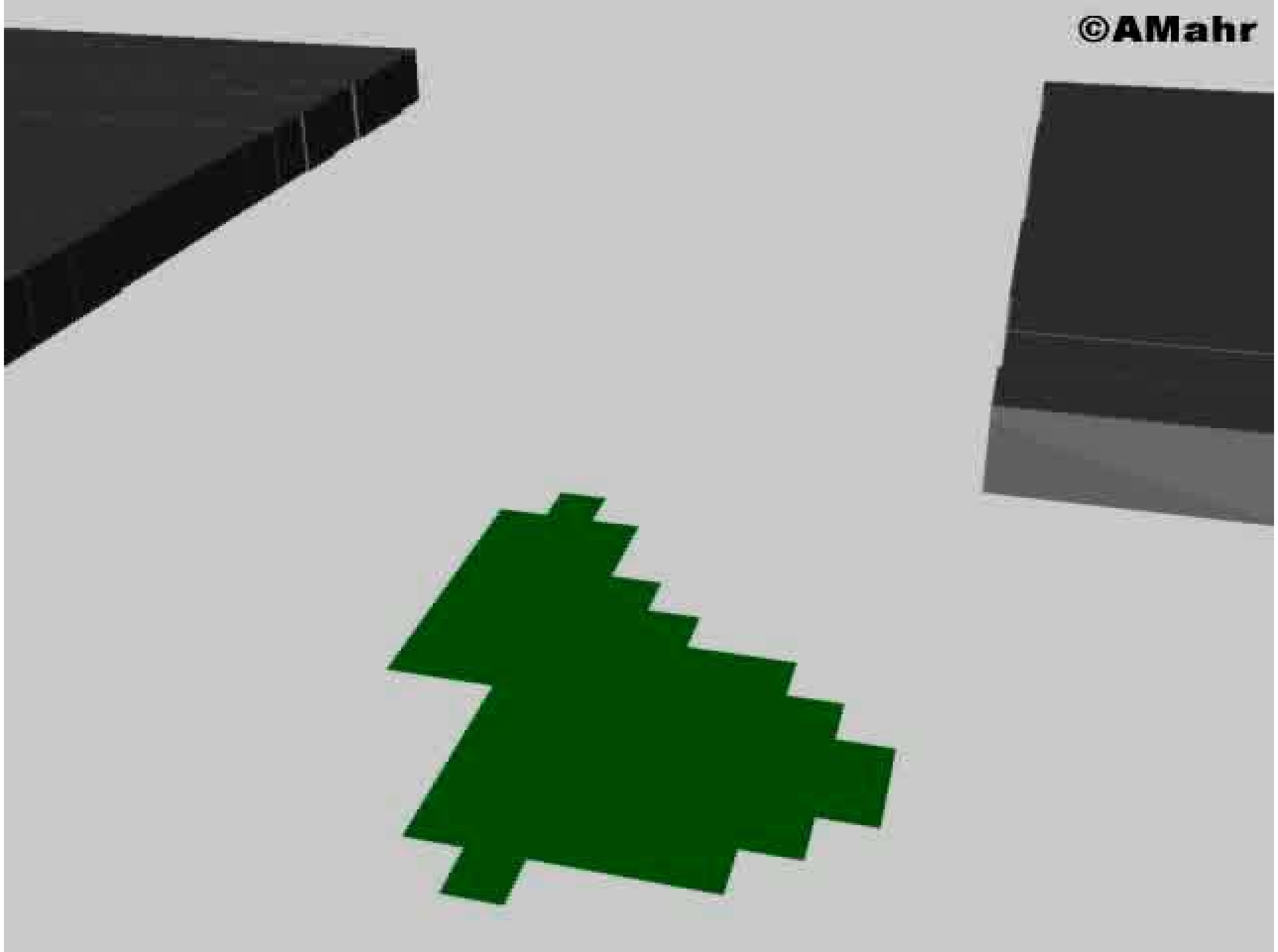


Modulate uniform radiation field using Multileaf Collimator (MLC)

Multileaf Collimators: Mechanics

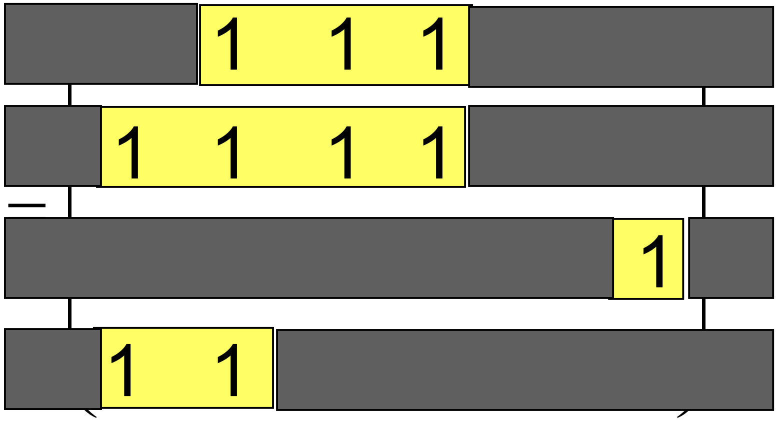


Multileaf Collimators in Action



(Strict) C1P Matrices

$Y = \left(y_{ij}\right) =$



mxn matrix

Various applications of C1P matrices: ...

- stops in public transportation
- radiation therapy ...

C1P-Decomposition of Integer Matrices

Given: Non-negative integer $m \times n$ matrix $I = (I_{ij})$

Find: „Good“ decomposition of I into C1P matrices

$$I = \sum_{t \in T} \alpha_t Y_t$$

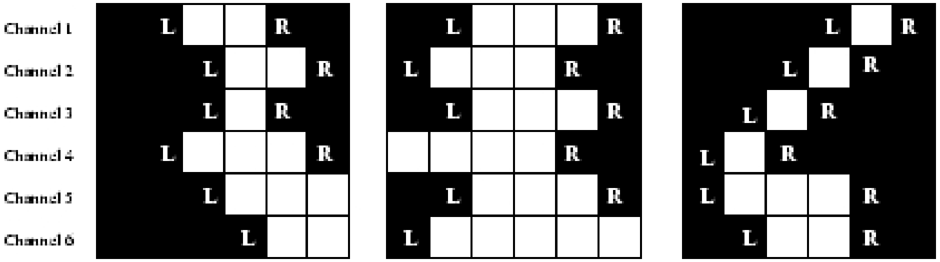
with $\alpha_t \geq 0$ for all t.

T ... index set of all C1P matrices

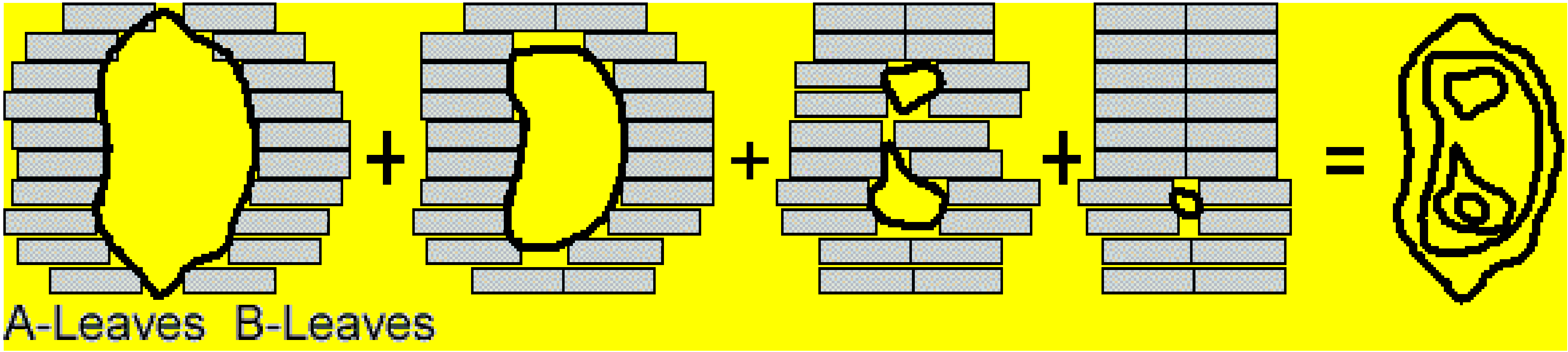
Sample Decomposition

$$I = \sum_{t \in T} \alpha_t Y_t$$

$$\begin{pmatrix} 0 & 0 & 2 & 2 & 2 & 0 \\ 0 & 1 & 1 & 3 & 1 & 0 \\ 0 & 0 & 2 & 2 & 1 & 0 \\ 1 & 2 & 2 & 2 & 1 & 0 \\ 0 & 1 & 2 & 3 & 2 & 1 \\ 0 & 1 & 2 & 2 & 2 & 2 \end{pmatrix} = \begin{pmatrix} 0 & 0 & 1 & 1 & 0 & 0 \\ 0 & 0 & 0 & 1 & 1 & 0 \\ 0 & 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 1 & 1 & 0 \\ 0 & 0 & 0 & 1 & 1 & 1 \\ 0 & 0 & 0 & 0 & 1 & 1 \end{pmatrix} + \begin{pmatrix} 0 & 0 & 1 & 1 & 1 & 0 \\ 0 & 1 & 1 & 1 & 0 & 0 \\ 0 & 0 & 1 & 1 & 1 & 0 \\ 1 & 1 & 1 & 1 & 0 & 0 \\ 0 & 0 & 1 & 1 & 1 & 0 \\ 0 & 1 & 1 & 1 & 1 & 1 \end{pmatrix} + \begin{pmatrix} 0 & 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 & 0 & 0 \\ 0 & 0 & 1 & 0 & 0 & 0 \\ 0 & 1 & 0 & 0 & 0 & 0 \\ 0 & 1 & 1 & 1 & 0 & 0 \\ 0 & 0 & 1 & 1 & 0 & 0 \end{pmatrix}$$



C1P-Decomposition in Cancer Therapy



Objective Function of C1P-Dec

$$\begin{pmatrix} 5 & 3 \\ 3 & 5 \end{pmatrix} = 5 * \begin{pmatrix} 1 & 0 \\ 0 & 0 \end{pmatrix} + 3 * \begin{pmatrix} 0 & 1 \\ 0 & 0 \end{pmatrix} + 3 * \begin{pmatrix} 0 & 0 \\ 1 & 0 \end{pmatrix} + 5 * \begin{pmatrix} 0 & 0 \\ 0 & 1 \end{pmatrix}$$

Beam-on time: 16
Set-Ups : 4

$$\begin{pmatrix} 5 & 3 \\ 3 & 5 \end{pmatrix} = 3 * \begin{pmatrix} 1 & 1 \\ 1 & 1 \end{pmatrix} + 2 * \begin{pmatrix} 1 & 0 \\ 0 & 1 \end{pmatrix}$$

Beam-on time: 5
Set-Ups: 2

Objective Function of C1P-Dec

minimize $\sum_{t \in T'} \alpha_t$ (decomposition time)

such that

$$\sum_{t \in T'} \alpha_t Y_t = I$$

$$\alpha_t \geq 0$$

$$Y_t \text{ C1-matrix}$$

$$T' \subseteq T$$

C1P-Dec is easy if T’=T

- C1P is separable into m independent row problems

- Each row problem is equivalent to min cost network flow problem (solvable in linear time: O(mn))

Ahuja, Hamacher 2003

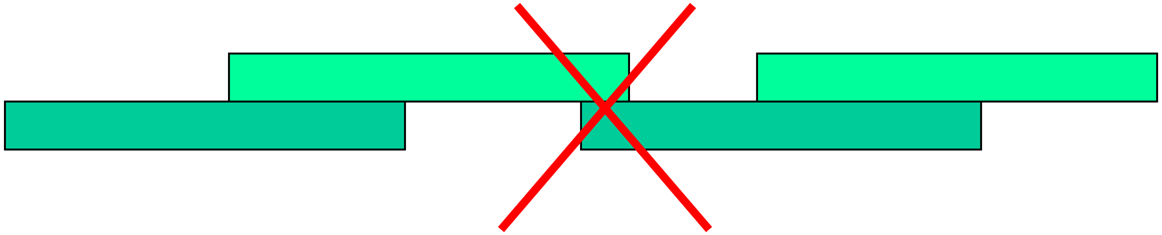
show transparencies

C1P-Dec is easy if T’=T

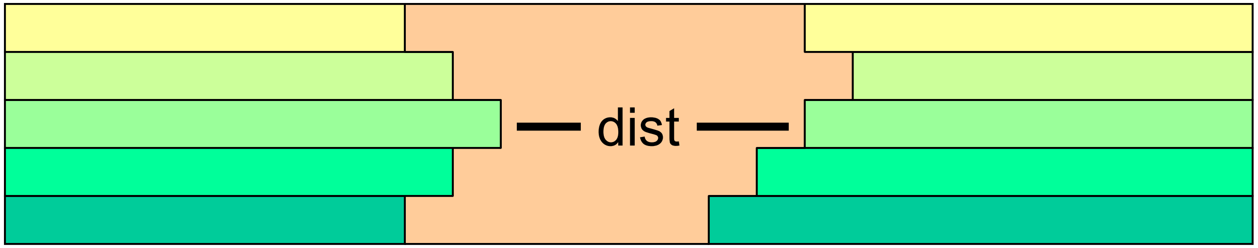
Bortfeld
and Boyer (1993):
Sweep algorithm

C1P-Dec with T’ ≠ T

- No collision (interleaf motion) between adjacent leaf pairs



- Minimal radiation width: dist $\geq \delta$



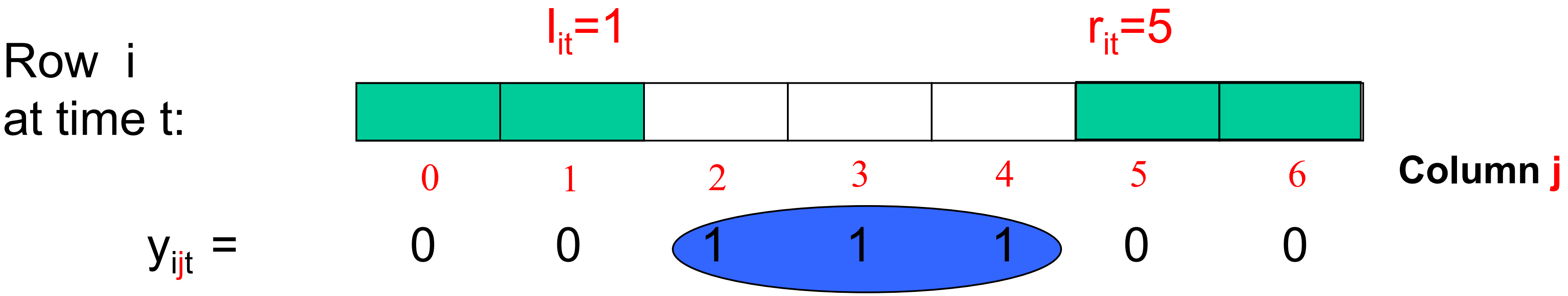
C1P-Dec with Technical Constraints

Boland, Hamacher, Lenzen, NETWORKS 2003
“Minimizing Beam-On Time in Cancer Radiation Treatment Using Multileaf Collimators”

Definition of Variables

$l_{it} \in \{0,\ldots,n\}$ position of left leaf in row i

$r_{it} \in \{1,\ldots,n+1\}$ position of right leaf in row i



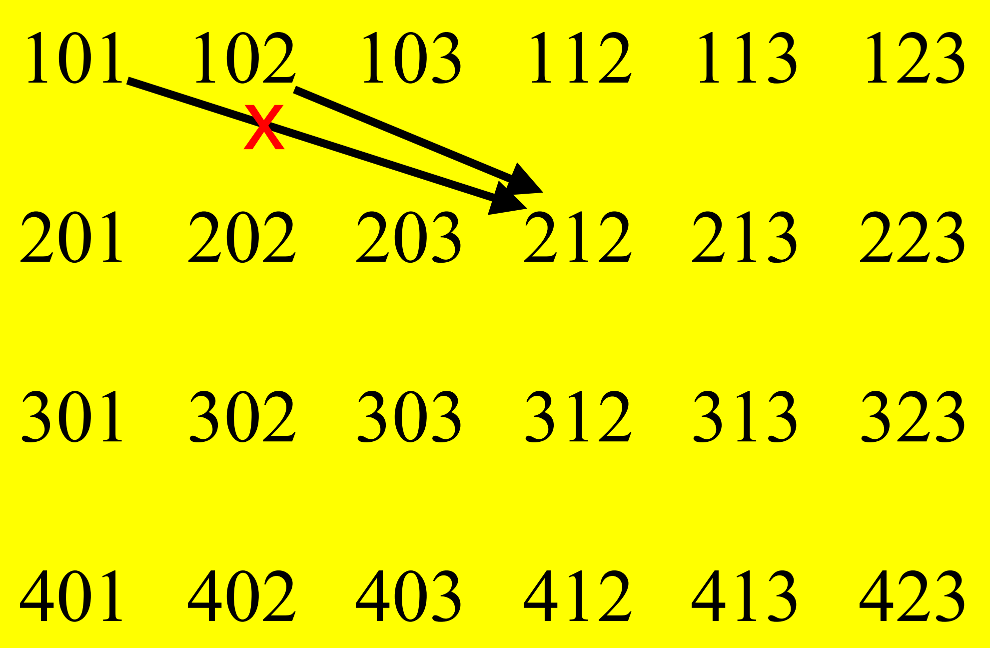
Constraints:

$r_{it} \geq l_{it}+\delta+1$ (radiation width)

$r_{i+1,t} \geq l_{it}+1$ and $r_{i-1,t} \geq l_{it}+1$ (interleaf motion)

$y_{ijt}= 1$ iff $l_{it} < j < r_{it}$ (radiation)

Path Representation of C1P



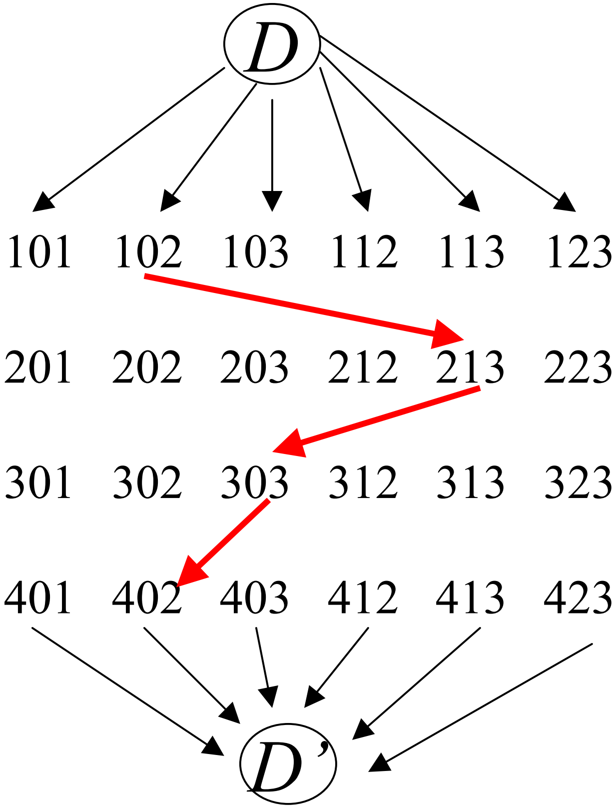
101	102	103	112	113	123
201	202	203	212	213	223
301	302	303	312	313	323
401	402	403	412	413	423

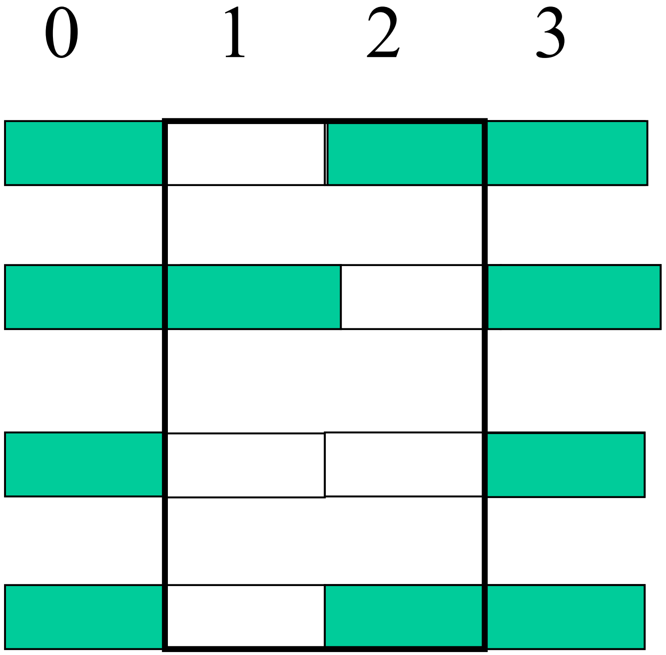
Graph $G = (V,E)$ with

- nodes $V = \{(k,l,r) : r \geq l+\delta+1,\ k = 1,\ldots m,\ l = 0,\ldots,n,\ r = 1,\ldots,n+1\}$
- edges E satisfying interleaf motion constraints

  $(k,l,r) \rightarrow (k+1,p,q)$ if $p \leq r-1$ and $q \geq l+1$
- plus super source and super sink

Source-sink paths correspond to feasible C1P matrices





$$= \begin{pmatrix} 1 & 0 \\ 0 & 1 \\ 1 & 1 \\ 1 & 0 \end{pmatrix}$$

C1P-matrix network (with $O(mn^2)$ nodes)

Optimal C1P Decomposition corresponds to minimal network flow problem

sending α_t units on path P_t

$\leftrightarrow$

use C1P matrix α_t times

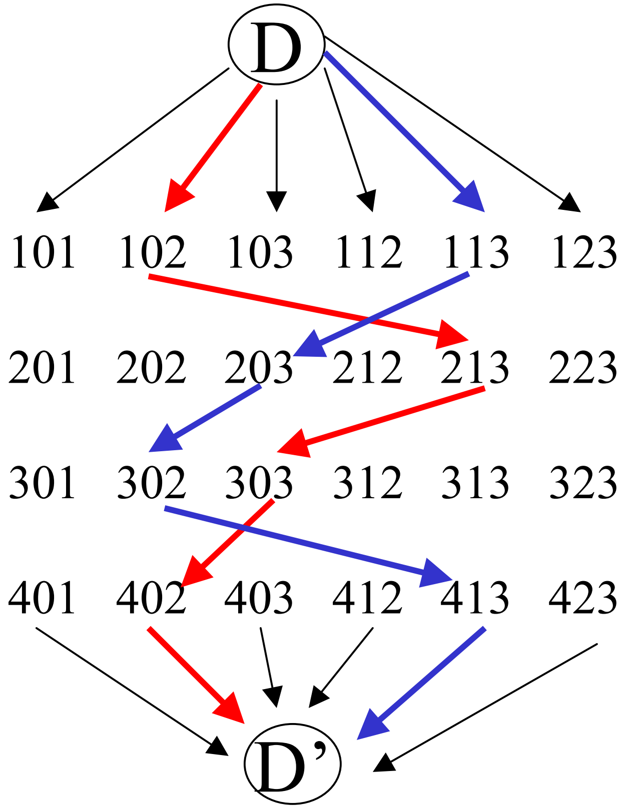
flow value

$\leftrightarrow$

decomposition time

minimal flow value = minimal decomposition time

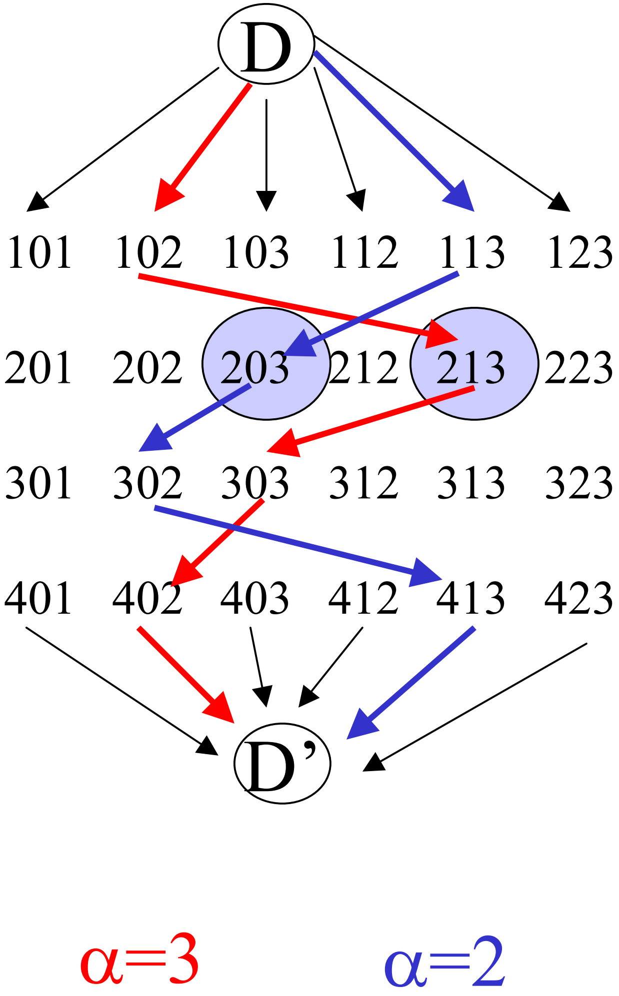
Example



$$\Leftrightarrow \qquad 3\begin{pmatrix}1&0\\0&1\\1&1\\1&0\end{pmatrix}+2\begin{pmatrix}0&1\\1&1\\1&0\\0&1\end{pmatrix}=\begin{pmatrix}3&2\\2&5\\5&3\\3&2\end{pmatrix}$$

$\alpha=3$ $\qquad$ $\alpha=2$

Which nodes contribute to I_{ij}?



Example: $I_{22}=5$

$i=2$

$j=2$

Constraint:

$$\sum_{l=0}^{j-1}\sum_{r=j+1}^{n+1}\sum_{e\in E\_(i,l,r)} x_e = I_{ij}$$

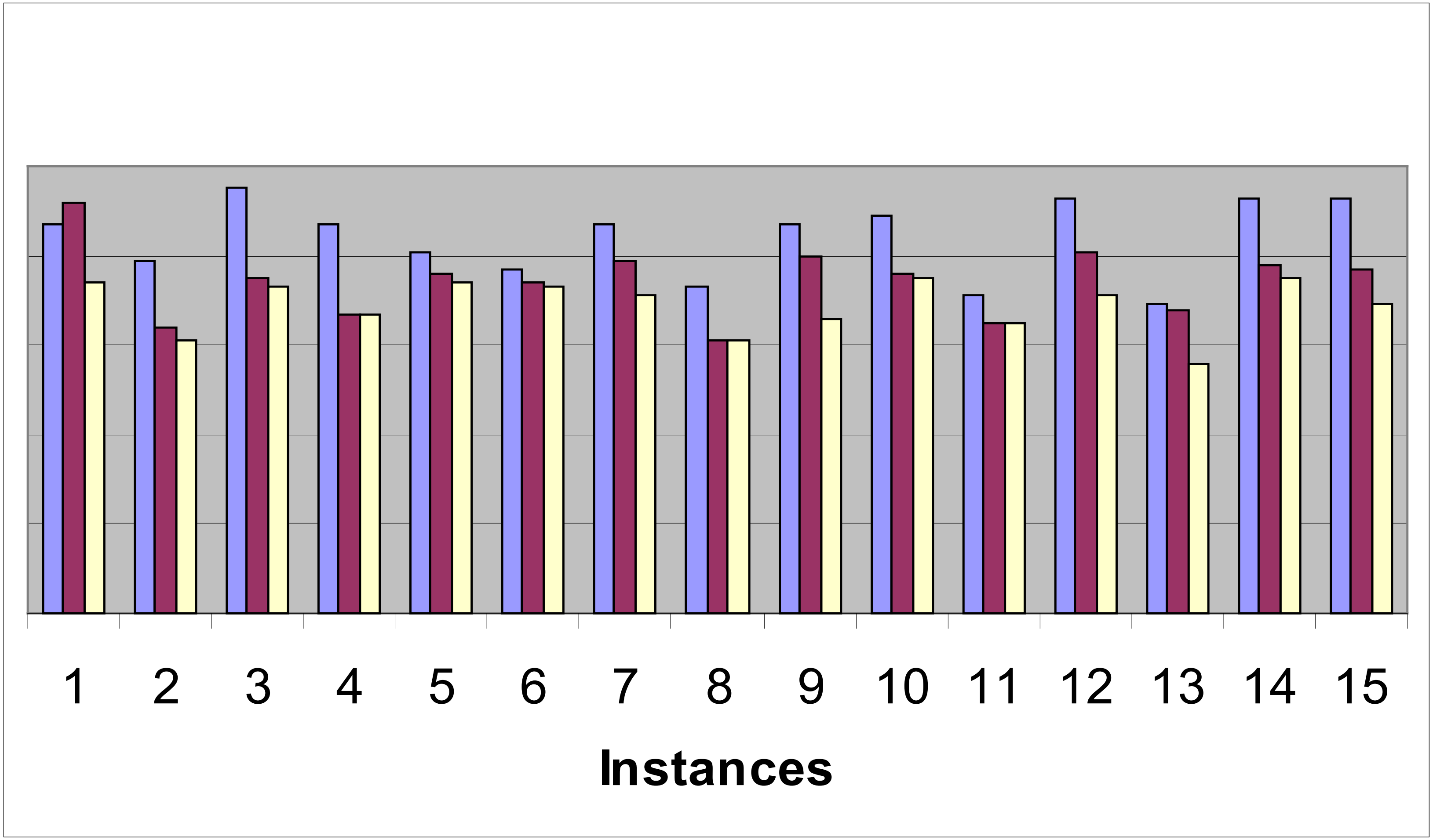
Consequence

Minimum C1-Decomposition Time problem
becomes a network flow problem
with side constraints

$$\sum_{l=0}^{j-1} \sum_{r=j+1}^{n+1} \sum_{e \in E\_(i,l,r)} x_e = I_{ij}$$

Polynomially solvable !

Beam-On-Times of MLC



Integrality is important

$$\sum_{t=1}^{T}\alpha_t + \sum_{t=1}^{T-1} s_{\sigma(t)\sigma(t+1)}$$

minimize delivery time =
beam-on time + set-up time

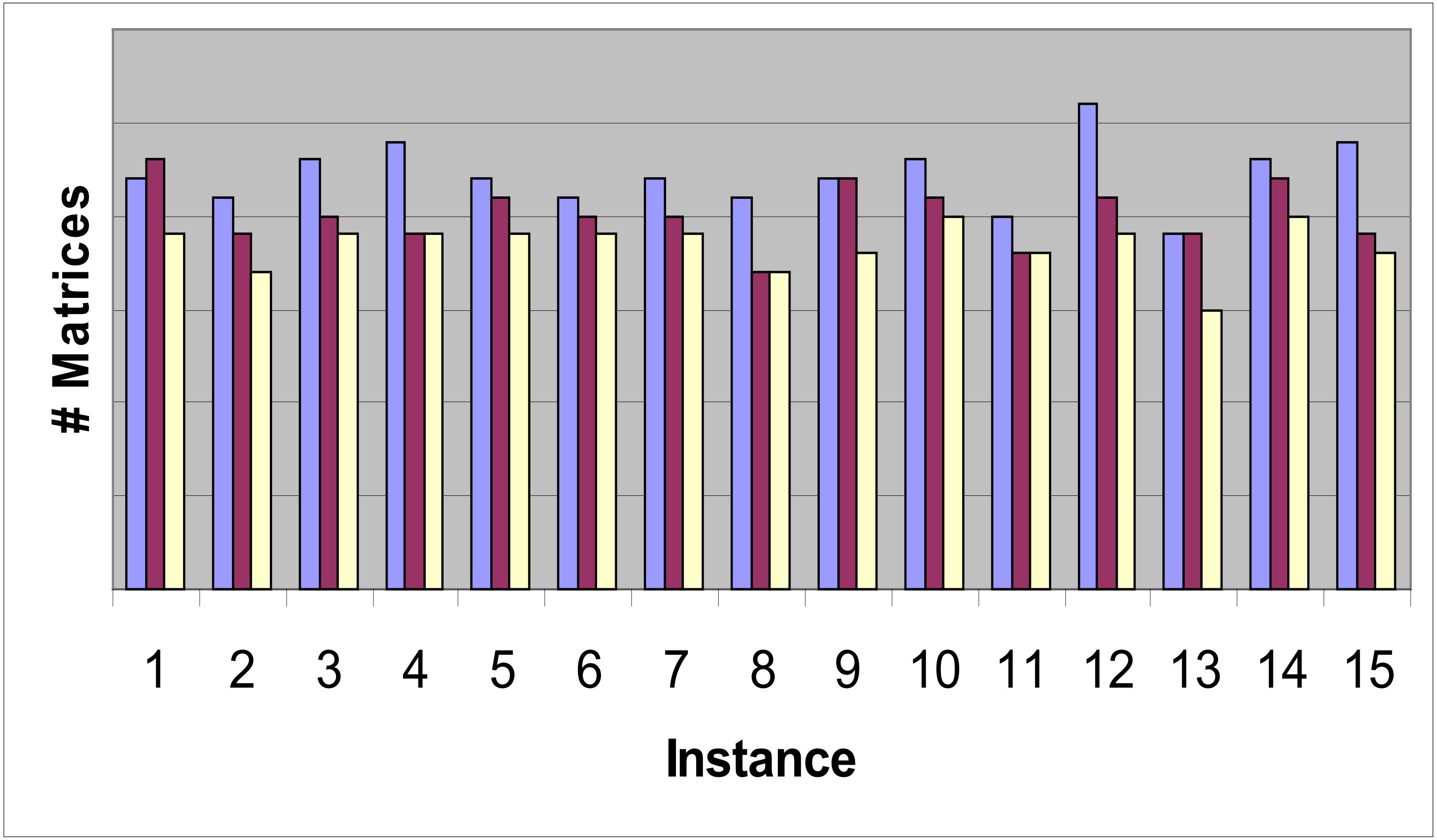
beam-on
time

set-up
time

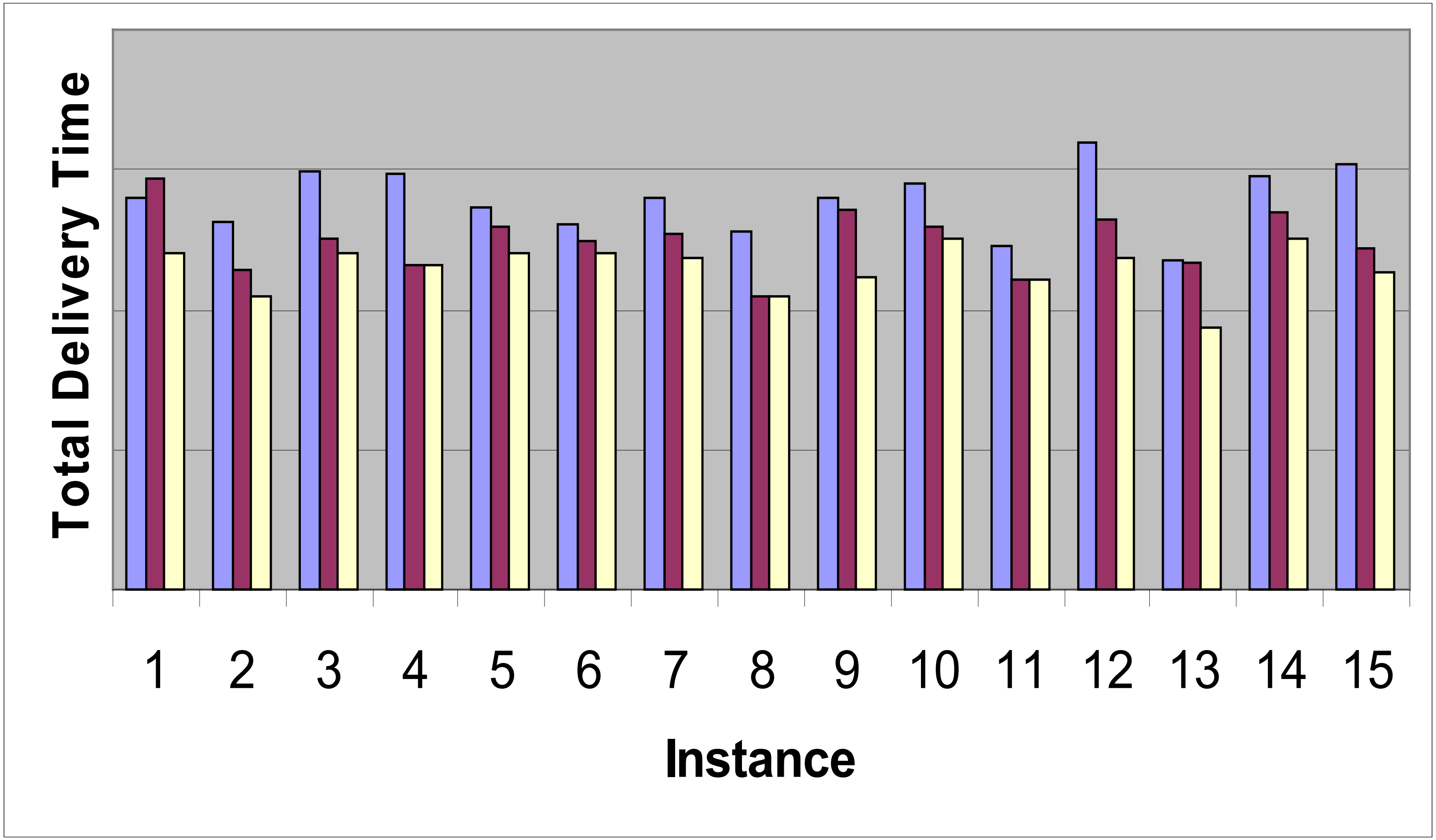
$s_{\sigma(t)\,\sigma(t+1)}$ = constant set up time: $\sum_{t=1}^{T}\alpha_t + \tau(T-1)$

Minimizing T is NP hard (Burkard 2002)

Number of Shape Matrices

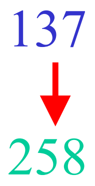


Delivery Time



How about integrality?

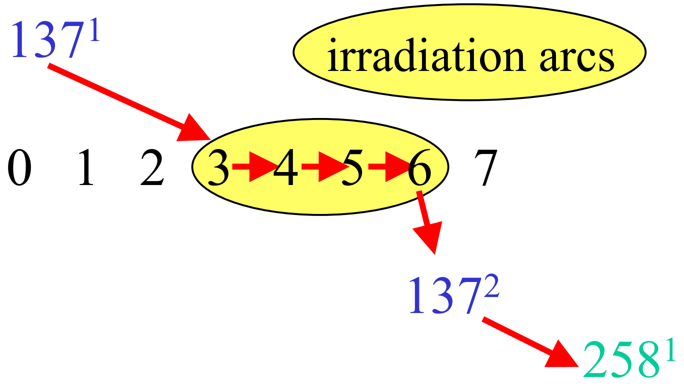
Flow Model I



137

258

Flow Model II



137^1

irradiation arcs

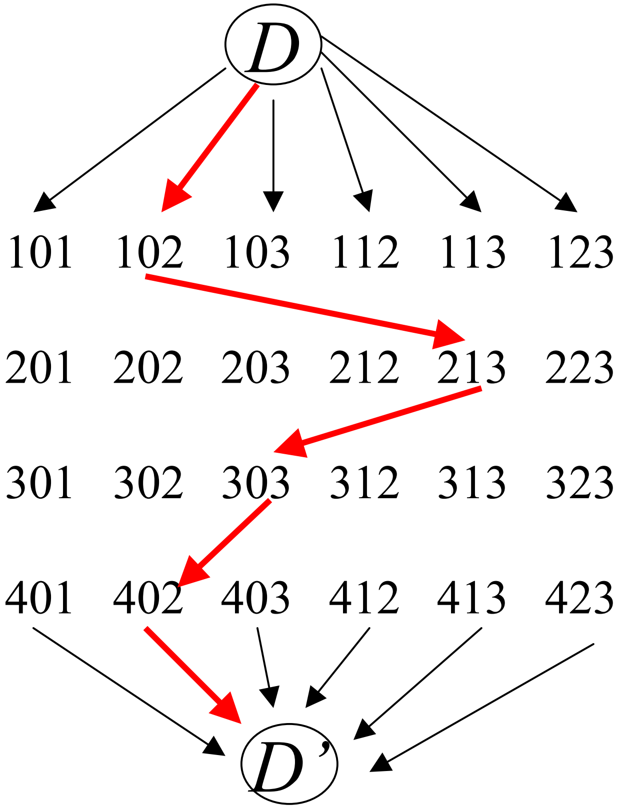
0 1 2 3 4 5 6 7

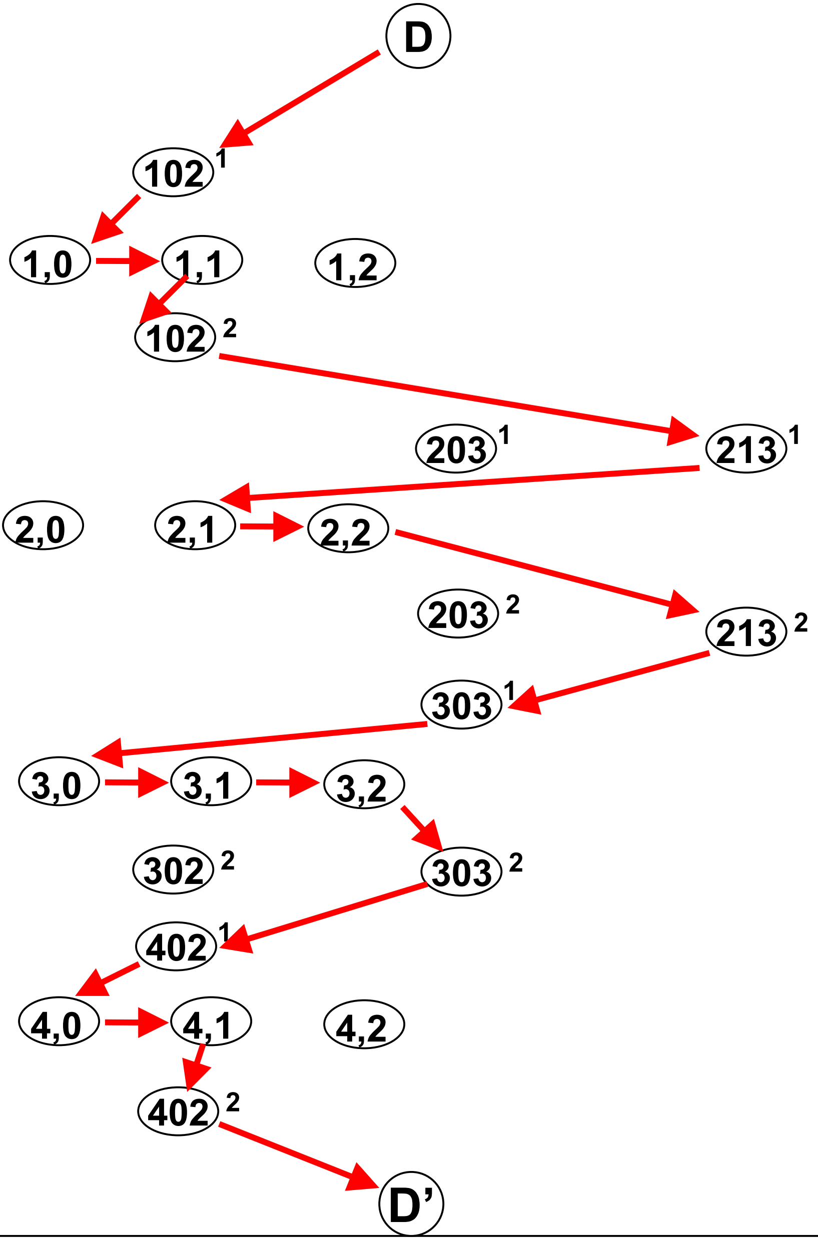
137^2

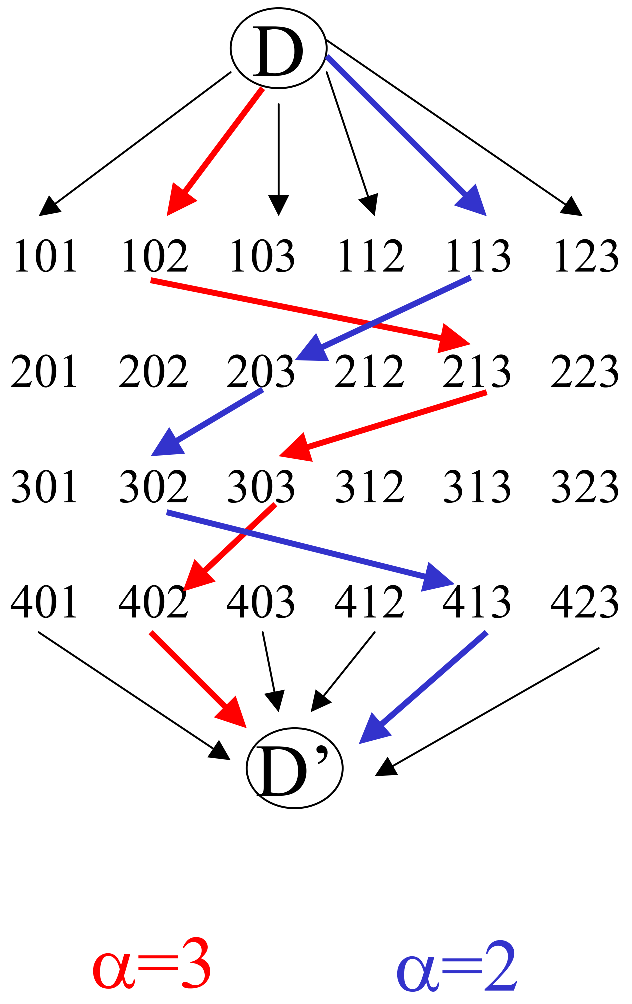
258^1

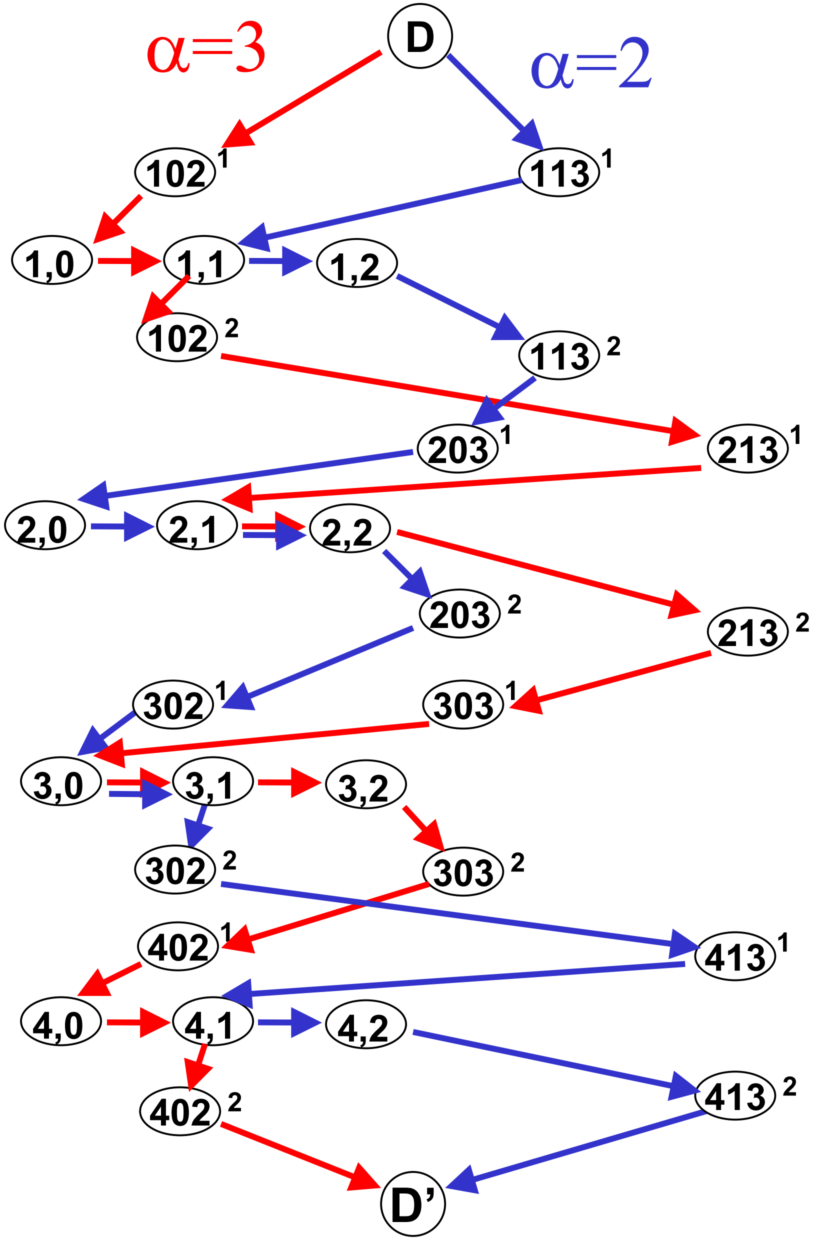
Side constraints are simpler as before:

outfow copy^1 = inflow copy^2


D
101 102 103 112 113 123
201 202 203 212 213 223
301 302 303 312 313 323
401 402 403 412 413 423
D'


D
102^{1}
1,0
1,1
1,2
102^{2}
203^{1}
213^{1}
2,0
2,1
2,2
203^{2}
213^{2}
303^{1}
3,0
3,1
3,2
302^{2}
303^{2}
402^{1}
4,0
4,1
4,2
402^{2}
D'


D
101 102 103 112 113 123
201 202 203 212 213 223
301 302 303 312 313 323
401 402 403 412 413 423
D’
α=3
α=2


α=3
D
α=2
102 1
113 1
1,0
1,1
1,2
102 2
113 2
203 1
213 1
2,0
2,1
2,2
203 2
213 2
302 1
303 1
3,0
3,1
3,2
302 2
303 2
402 1
413 1
4,0
4,1
4,2
402 2
413 2
D’

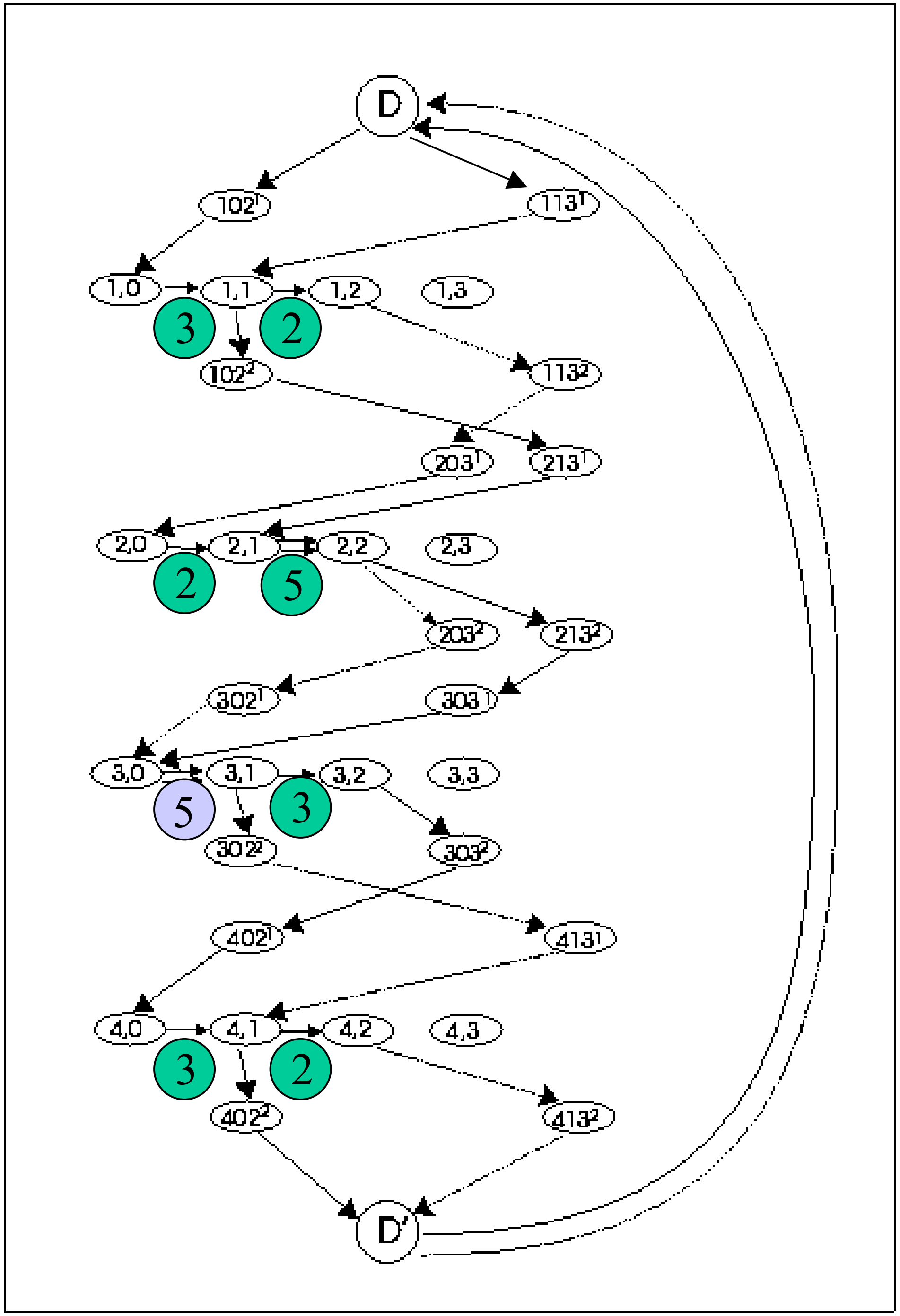
$$\mathbf{I} = \begin{pmatrix} 3 & 2 \\ 2 & 5 \\ 5 & 3 \\ 3 & 2 \end{pmatrix}$$

Introduce

lower = upper bound = I_{ij}

on each irradiation arc

from (i,j-1) to (i,j)!



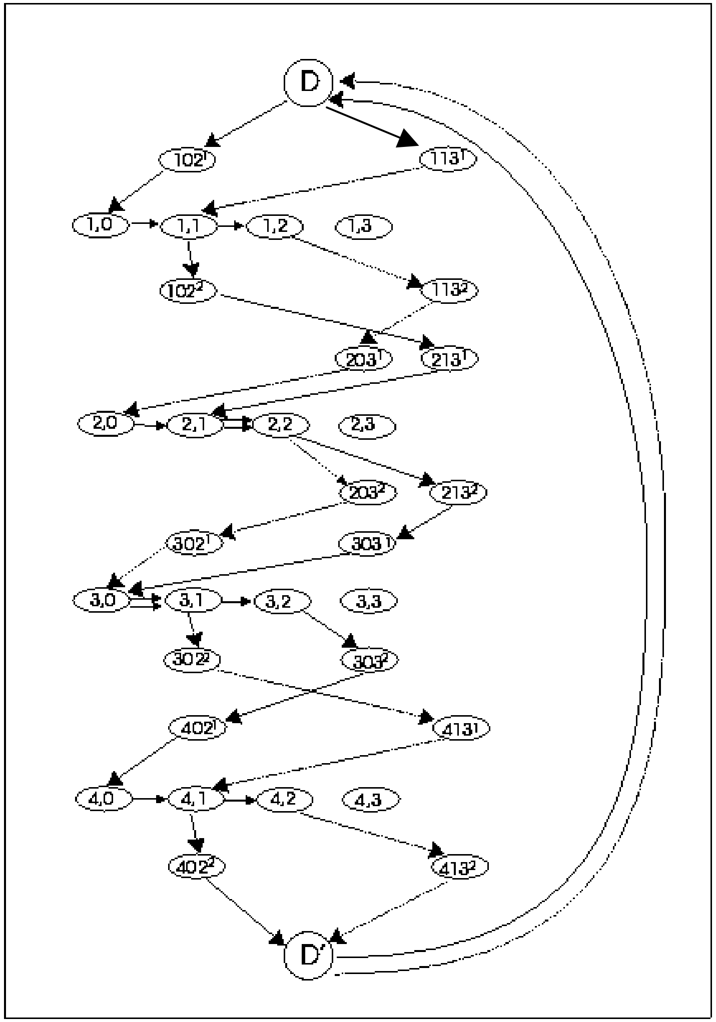
Integral Solvability

Find flow with minimal value satisfying capacities and side constraint

outfow copy^1 = inflow copy^2

Solvable by negative “cycle” argument!

(Existence result - no combinatorial algorithm)



Find Algorithm with Improved Complexity

Algorithm of Baatar and Hamacher (2003)

Idea:

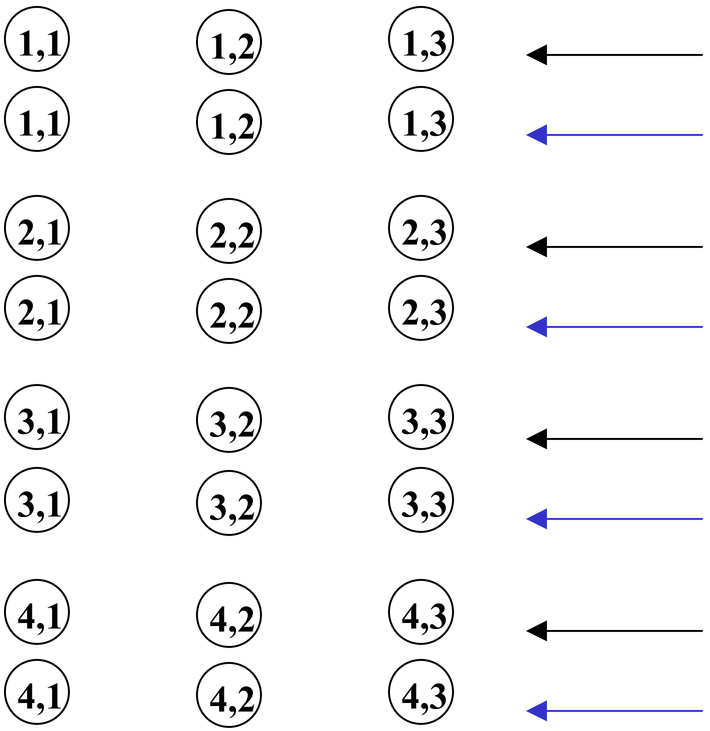
Represent each possible left leaf and each possible right leaf as node of a network (2(m(n+1)) many nodes)

Shape matrices = Paths in the network

Decomposition = Network flow

Example of Baatar Network

nodes:



potential left leaf position
potential right leaf position
in channel 1

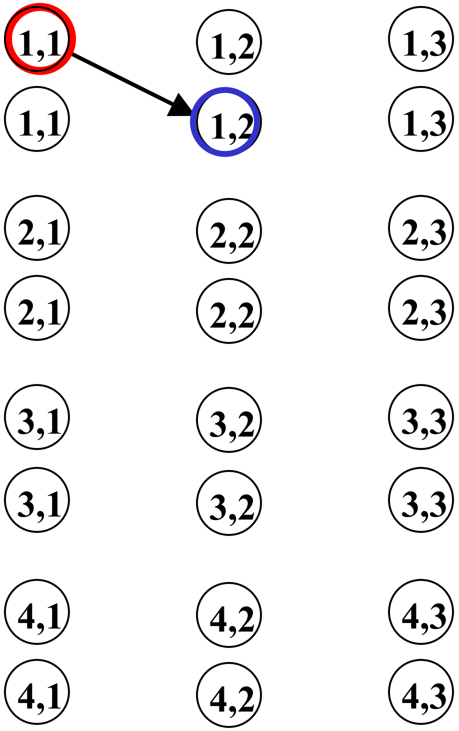
potential left leaf position
potential right leaf position
in channel 2

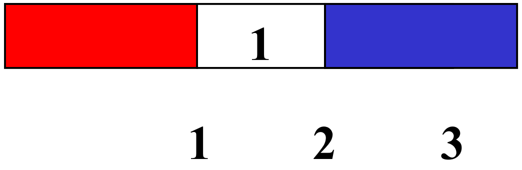
potential left leaf position
potential right leaf position
in channel 3

potential left leaf position
potential right leaf position
in channel 4

Example of Baatar Network

edges:



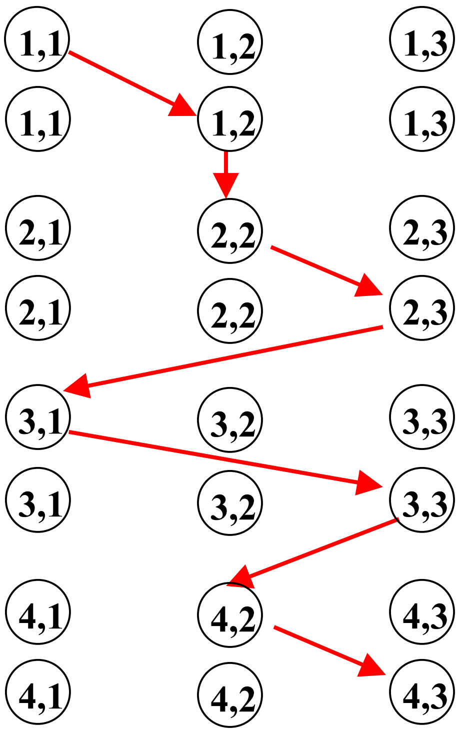


cells

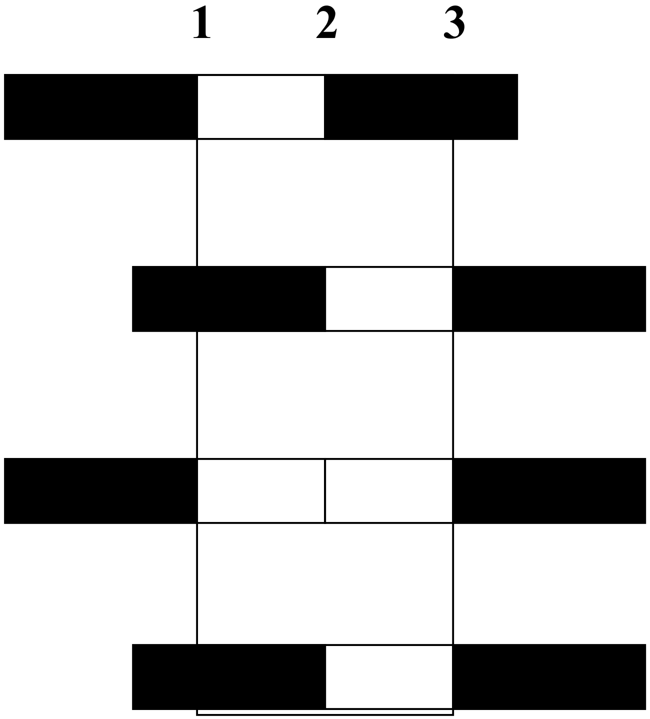
leaf positions

Example of Baatar Network

paths:



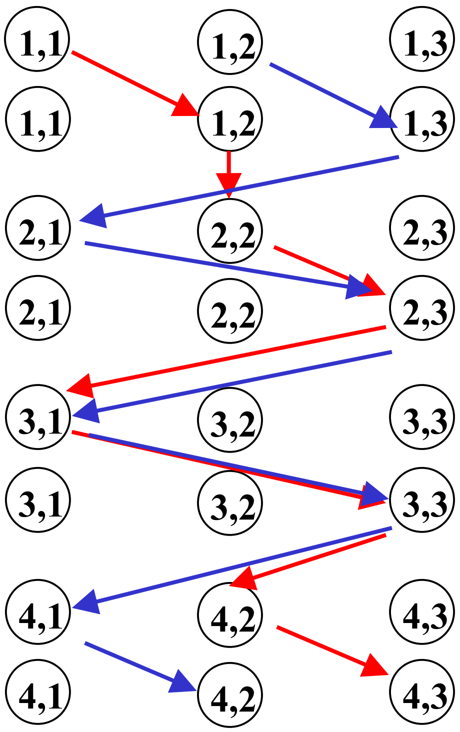
leaf positions

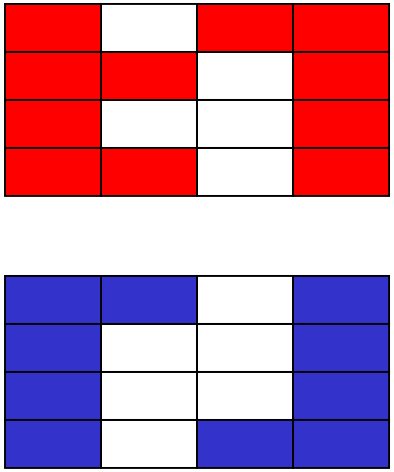


$$= \begin{pmatrix} 1 & 0 \\ 0 & 1 \\ 1 & 1 \\ 0 & 1 \end{pmatrix}$$

Example of Baatar Network

flows:





🟥	⬜	🟥	🟥
🟥	🟥	⬜	🟥
🟥	⬜	⬜	🟥
🟥	🟥	⬜	🟥

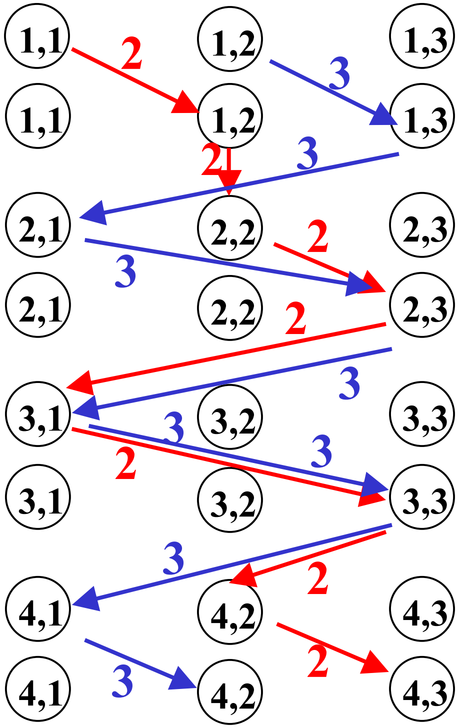
$$= \begin{pmatrix} 1 & 0 \\ 0 & 1 \\ 1 & 1 \\ 0 & 1 \end{pmatrix}$$

🟦	🟦	⬜	🟦
🟦	⬜	⬜	🟦
🟦	⬜	⬜	🟦
🟦	⬜	🟦	🟦

$$= \begin{pmatrix} 0 & 1 \\ 1 & 1 \\ 1 & 1 \\ 1 & 0 \end{pmatrix}$$

Flow ⇒ Intensity Matrix

flows:



$$= 2\begin{pmatrix} 1 & 0 \\ 0 & 1 \\ 1 & 1 \\ 0 & 1 \end{pmatrix} + 3\begin{pmatrix} 0 & 1 \\ 1 & 1 \\ 1 & 1 \\ 1 & 0 \end{pmatrix} = \begin{pmatrix} 2 & 3 \\ 3 & 5 \\ 5 & 5 \\ 3 & 2 \end{pmatrix}$$

Intensity Matrix $\Rightarrow$ Flow

Integer matrix $I = (I_{ij})$ is given.

Compute for all $i=1,\ldots,m$ and all $j=1,\ldots n+1$

$$left_{ij} = \max\{I_{ij} - I_{i,j-1}, 0\}$$

and

$$right_{ij} = \max\{I_{i,j-1} - I_{i,j}, 0\}$$

(with $I_{i0}=I_{i,n+1}=0$)

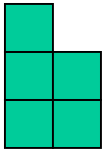
Intensity Matrix ⇒ Flow

$$\mathit{left}_{ij} = \max\{I_{ij} - I_{i,j-1}, 0\}$$

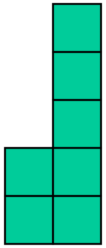
$$\mathit{right}_{ij} = \max\{I_{i,j-1} - I_{i,j}, 0\}$$

$$\begin{matrix} 3 & 0 & 0 \\ 2 & 3 & 0 \\ 5 & 0 & 0 \\ 3 & 0 & 0 \end{matrix} \qquad \begin{pmatrix} 3 & 2 \\ 2 & 5 \\ 5 & 3 \\ 3 & 2 \end{pmatrix} \qquad \begin{matrix} 0 & 1 & 2 \\ 0 & 0 & 5 \\ 0 & 2 & 3 \\ 0 & 1 & 2 \end{matrix}$$

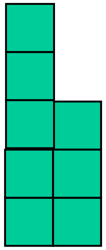
$(3 \quad 2) =$



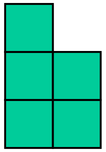
$(2 \quad 5) =$



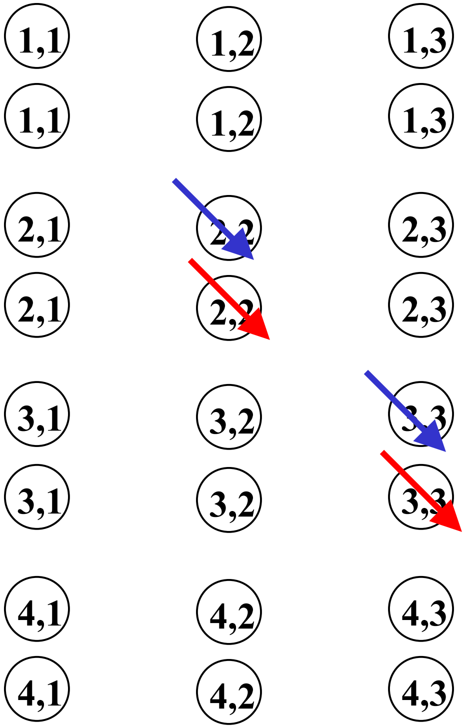
$(5 \quad 3) =$



$(3 \quad 2) =$



Intensity Matrix ⇒ Flow



Result:

Any MLC realization of a given intensity matrix I can be written as flow in the Baatar network with

supply $\text{left}_{ij}+w_{ij}$

and

demand $\text{right}_{ij}+w_{ij}$

satisfying additional side constraints forbidding interleaf motion.

Intensity Matrix $\Rightarrow$ Flow

$$\min T$$

subject to

$$T = left_{i1} + \sum_{j=2}^{n} (left_{ij} + w_{ij}), \qquad \forall i = 1, \dots, m$$

$$\sum_{j=2}^{k} (right_{ij} + w_{ij}) \leq left_{i+1,1} + \sum_{j=2}^{k} (left_{i+1,j} + w_{ij}), \quad \forall i = 1, \dots, m-1, \ k = 2, \dots, n$$

$$left_{i1} + \sum_{j=2}^{k} (left_{ij} + w_{ij}) \geq \sum_{j=2}^{k} (right_{i+1,j} + w_{i+1,j}), \qquad \forall i = 1, \dots, m-1, \ k = 2, \dots, n$$

$$w_{ij} \geq 0, \qquad \forall i = 1, \dots, m, \ \ j = 2, \dots, n$$

$$T \geq 0$$

Intensity Matrix $\Rightarrow$ Flow

Result: Minimizing $\sum_j w_{ij}$
such that flow exists satisfying side constraints
yields minimal beam-on-time decomposition.

Solvable by a linear program with mn many variables!

- Solvable in polynomial time
- Faster than Boland-Hamacher network flow approach

Modifications Including Set-Up Times

$$\sum_{t=1}^{T} \alpha_t + \sum_{t=1}^{T-1} s_{\sigma(t)\sigma(t+1)}$$

minimize delivery time with constant set-up time (i.e. $s_{\sigma(t)\sigma(t+1)}$ = const)

Use same approach with integer variables counting the number of shape matrices used.

Modifications Including Set-Up Times

$$\sum_{t=1}^{T} \alpha_t + \sum_{t=1}^{T-1} s_{\sigma(t)\sigma(t+1)}$$

minimize delivery time with
sequence dependent set-up time

Use arc-path formulation of flow

Use $s_{\sigma(t)\sigma(t+1)}$ as data of a traveling salesman problem.

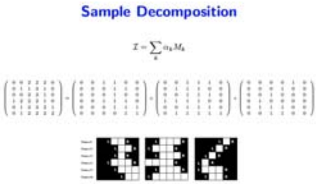
Current Research

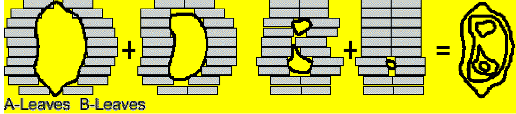
Summary of Part I

- Several subproblems of radiation therapy have been successfully tackled
  - choice of radiation angle
  - representative system of Pareto solutions
  - minimizing beam on time

- Several results are interesting independent of application
  - integer solvability of C1 decomposition
  - NP completeness of cardinality decomposition

- Lots of open problems, e.g.
  - integrated system (angles + intensity profiles + realization)
  - efficient algorithms for (constant and variable) set-up time





KL - Literature:

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”A mixed integer programming approach to the multileaf collimator problem”, in Wolfgang Schlegel and T. Bortfeld (edts.) *The use of Computers in Radiation Therapy*, Springer

- Boland, N. , H.W. Hamacher, and F. Lenzen, 2002:
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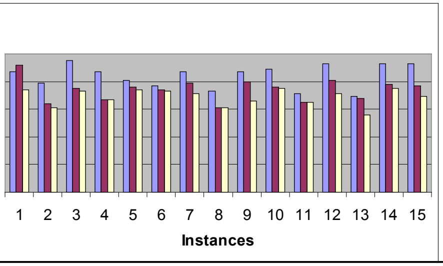
- Bataar, D. and Hamacher, H.W., 2002: “New models for multileaf collimators”, Report, Fachbereich Mathematik, Universität Kaiserslautern



Part II:
Algorithms and Numerics
Online Treatment Planning - A Decision Support Tool
show transparencies