Algorithmics II (H)

Lecture 17

Integer programming and kidney exchange

Kidney failure

- Treatment
  - Dialysis
  - Transplantation
- Need for donors
  - 6,939 on UK transplant list as of 31 March 2025
  - Median waiting time: 503 days (adults), 387 days (children) [based on patient registrations during 1 April 2018 – 31 March 2022]
  - 3,301 transplants but 4,669 new patient registrations between 1 April 2024 and 31 March 2025
  - 2,337 transplants from deceased donors between 1 April 2024 and 31 March 2025
  - Living donors
    - 964 transplants from living donors between 1 April 2024 and 31 March 2025
    - 29% of all donations from living donors
    - But: blood type incompatibility (e.g. $A \not\rightarrow B$)
    - Positive crossmatch (tissue-type incompatibility)
- Source of figures: [NHS Blood and Transplant, 2025]

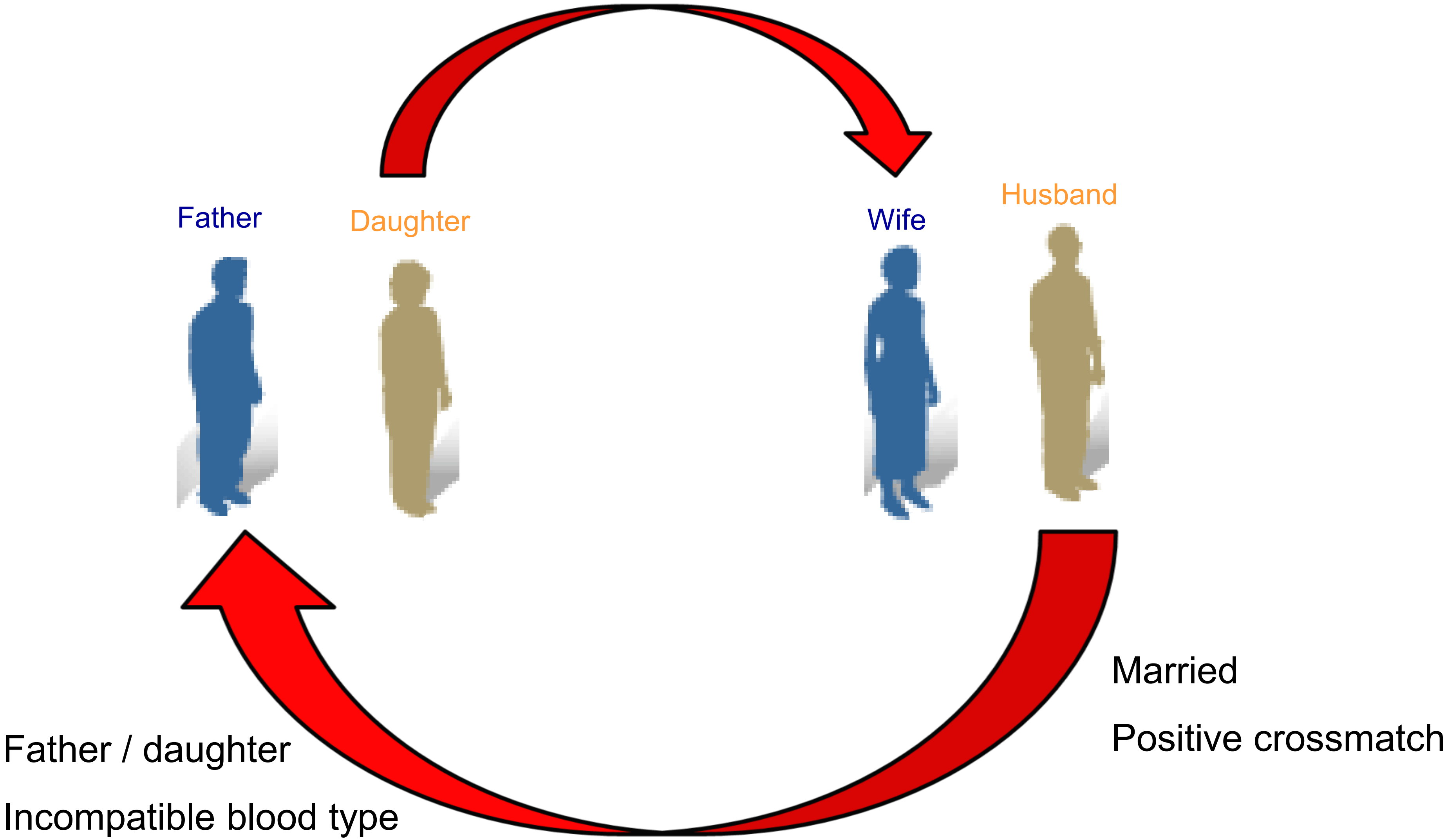
NHS Blood and Transplant

Human Tissue Act

- Prior to 1 September 2006, transplants could only take place between those with a genetic or emotional connection
- Human Tissue Act 2004 and Human Tissue (Scotland) Act 2006:
  - legal framework created to allow transplants between strangers
- New possibilities for live-donor transplants:
  - *Paired kidney donation*: a patient with a willing but incompatible donor can swap their donor with that of another similar patient
  - *Non-directed* (altruistic) donors
    - they can donate directly to the *deceased donor waiting list* (DDWL)
    - they can trigger *non-directed donor chains*
- UK Living Kidney Sharing Scheme (UKLKSS)
  - in operation since 2007
  - matching runs every quarter

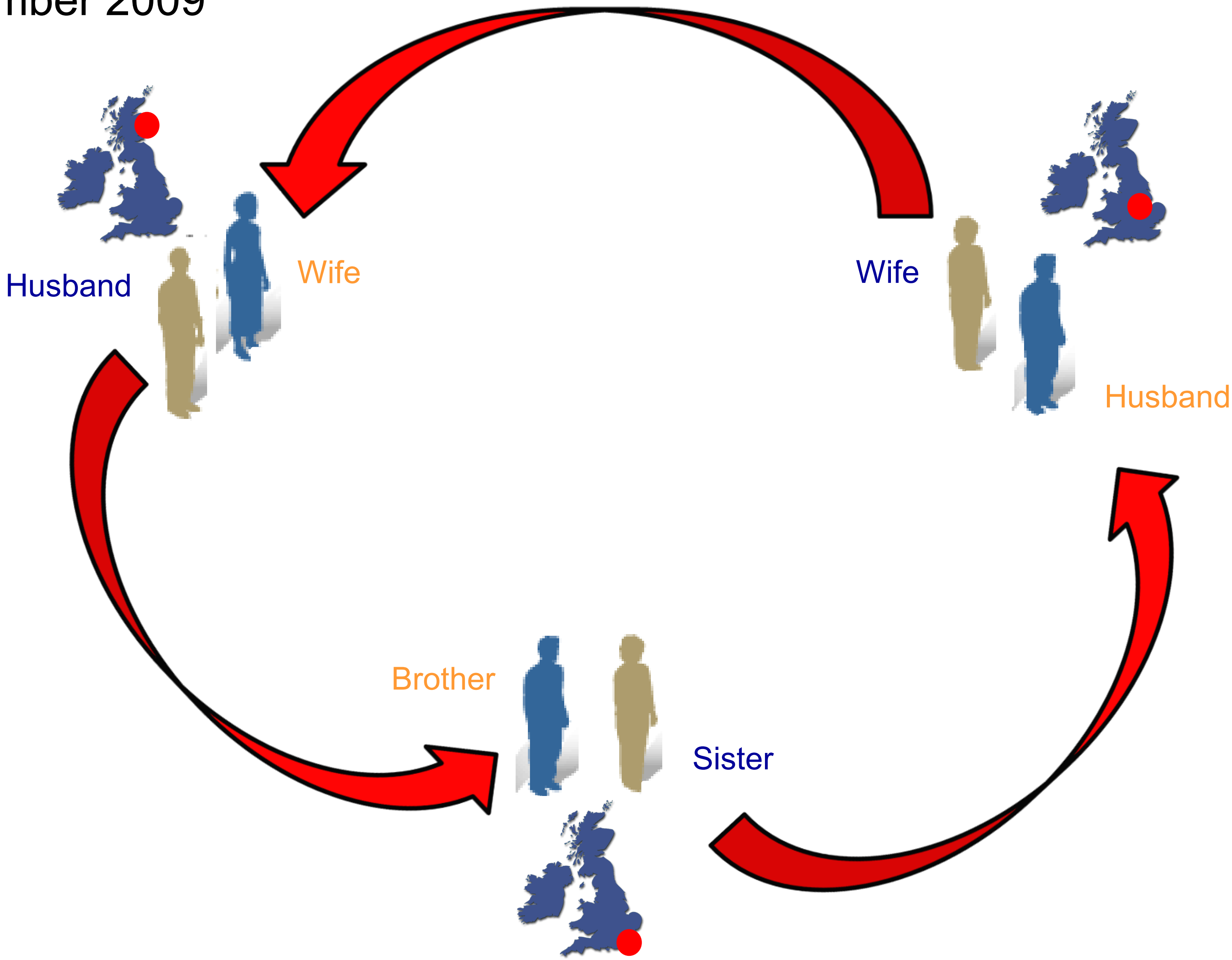
Pairwise exchange

- Portsmouth / Plymouth 2007



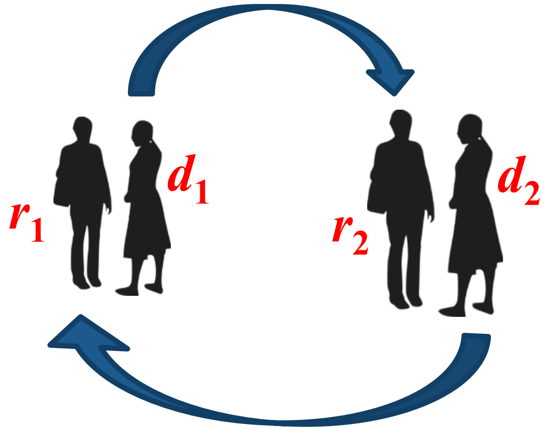
3-way exchange

- 4 December 2009

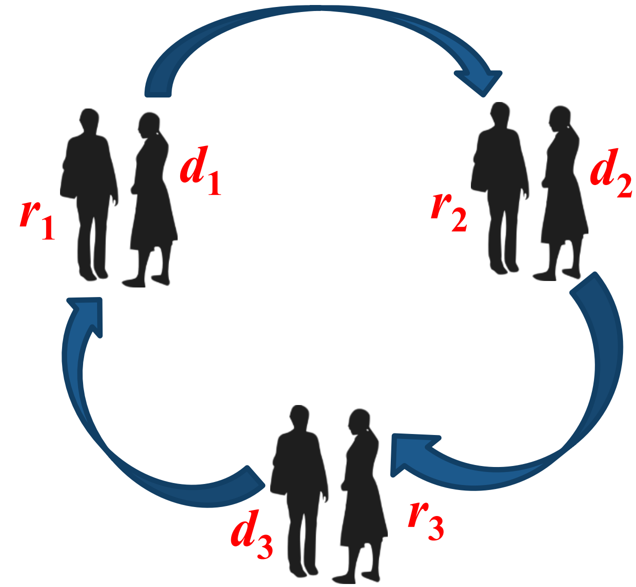


Kidney exchanges in the UKLKSS

Cyclic exchanges

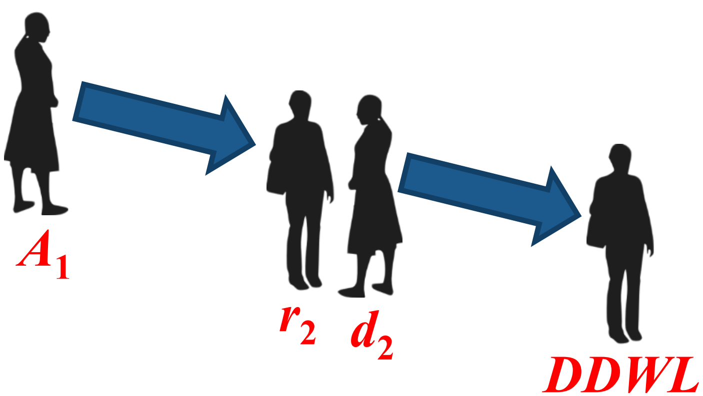


2-way exchange

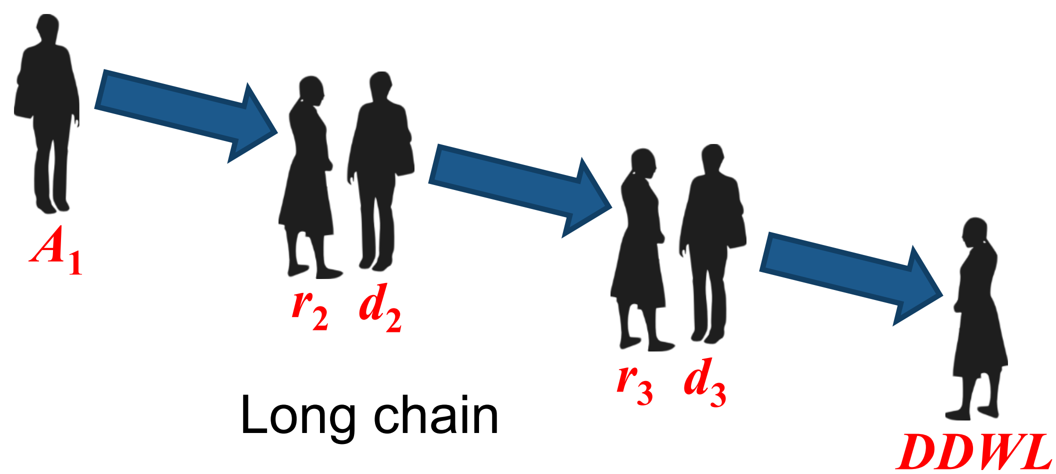


3-way exchange

Non-directed donor chains



Short chain



Long chain

http://news.bbc.co.uk/1/hi/health/8552162.stm

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Three-way kidney transplant success

By Graham Satchell
BBC News Breakfast reporter

Step back to nine in the morning on 4 December 2009.

Six patients are ready for surgery at three different hospitals across the UK.

It is the culmination of months of preparation and a remarkable event in the history of live organ donation in this country.

This is a three-way kidney swap between couples who've never met.

In Aberdeen, 54-year-old Andrea Mullen suffered sudden kidney failure three years ago.

It had a devastating impact on her life. She had to have dialysis three times a week.

She said: "It was just an existence, it really was.

"It was terrible being ill all the time. As far as I was concerned it just ruined my life. It just totally ruined my life and I hated it."

Her husband Andrew, 53, was prepared to donate one of his healthy kidneys but he wasn't a match.

Chris Brent with his sister Lisa Burton

"It's a threefold thing really so it's a real good feelgood factor all round"

Lisa Burton, who donated a kidney

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Kidney Exchange in Europe

- Countries with national or international kidney exchange programmes (KEPs)

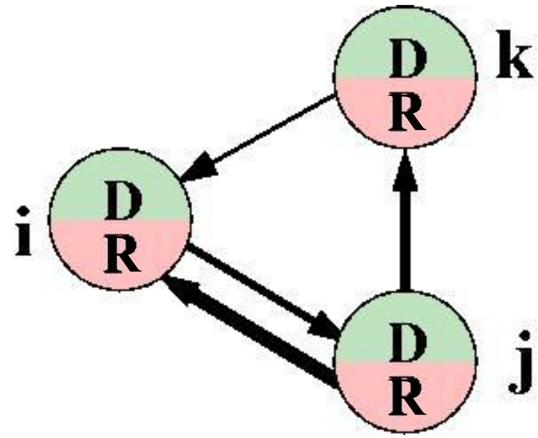
International KEPs in Europe

- KEPSAT (Italy, Portugal, Spain)
- Austria, Czech Republic, Israel
- STEP (Denmark, Finland, Iceland, Norway, Sweden)

EURO-KEP project

Modelling the problem

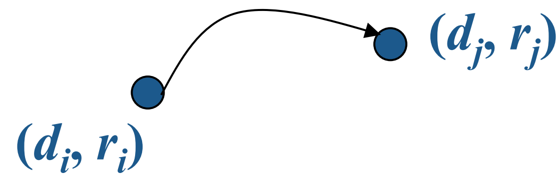
- We consider recipient-donor pairs as single vertices of a directed graph $D=(V,A)$



- $(i,j)\in A$ if and only if donor i is compatible with recipient j
- **2**-cycles and **3**-cycles in D correspond to pairwise and **3**-way exchanges (in the UK, no cycles of length **>3** permitted)
- Arc weights can likelihood of success of corresponding transplants (HLA mismatch levels), and recipient priorities (waiting time, sensitisation levels, age difference) etc.

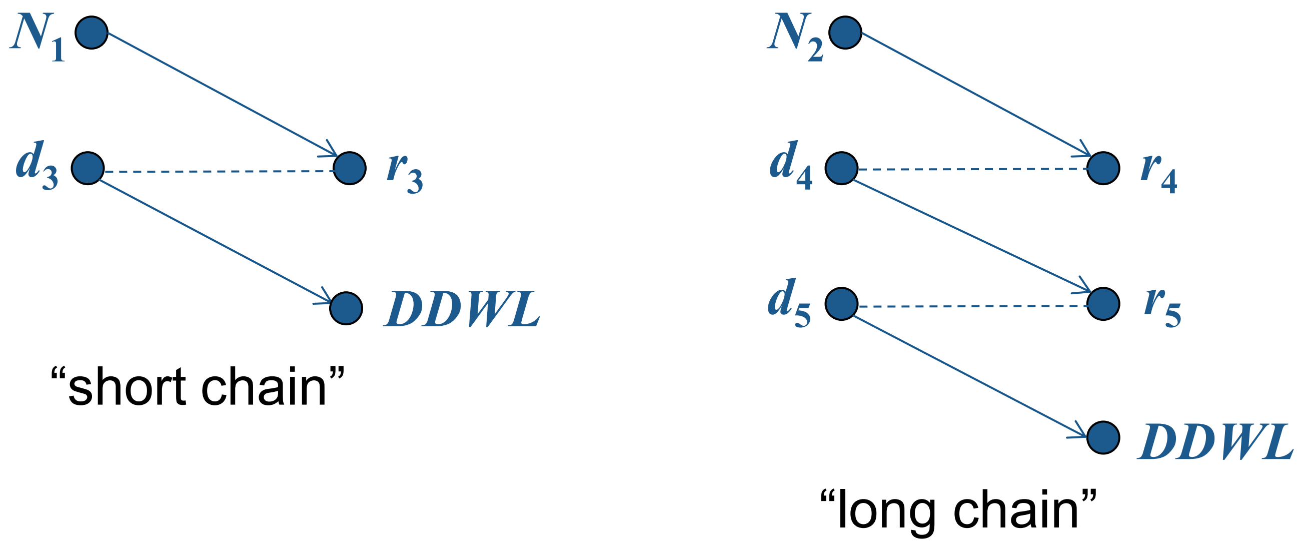
UKLKSS scoring system

A score ≥ 0 is given to each arc (i,j):



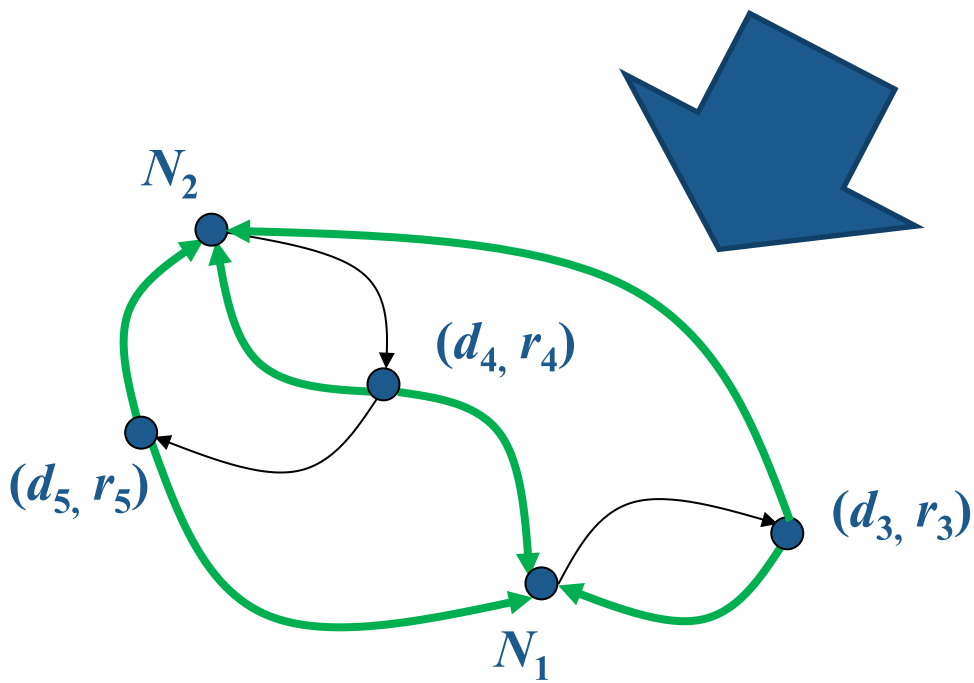
- Waiting time
  - $50 \times$ number of previous matching runs that r_j has been involved in
- Sensitisation points (0-50)
  - Based on calculated sensitisation ("panel reactive antibody") test % for r_j divided by 2
- HLA mismatch points (0, 5, 10 or 15)
  - HLA ("Human Leukocyte Antigen") mismatch levels determine tissue-type incompatibility between d_i and r_j
- Donor-donor age difference (0 or 3)
  - 3 points if $|\text{age}(d_i) - \text{age}(d_j)| \leq 20$ years, 0 otherwise
- "Final discriminator" involving *actual* donor-donor age difference

- Non-directed donors can trigger chains



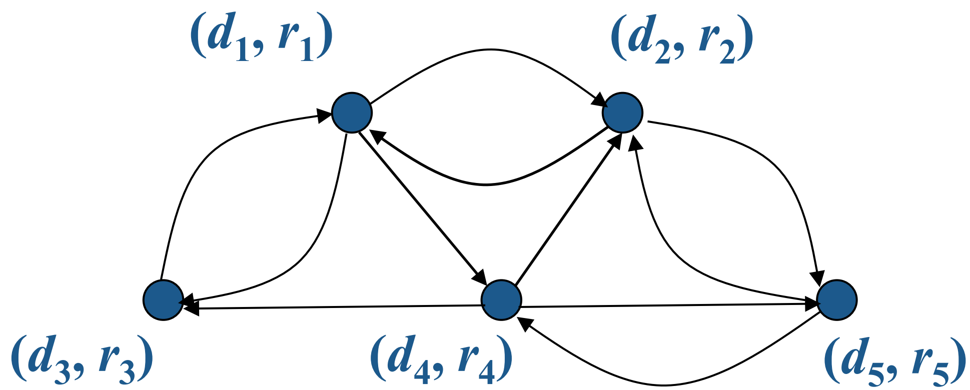
Modelling non-directed donor chains

- Non-directed donors can trigger chains

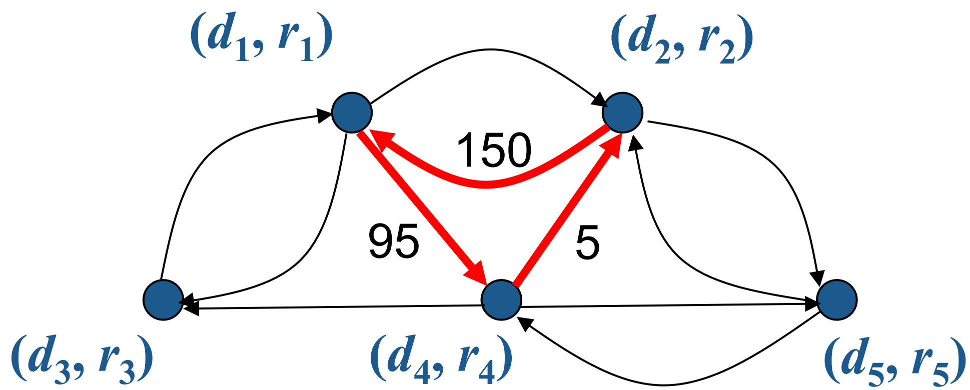


- At most one non-directed donor per cycle!

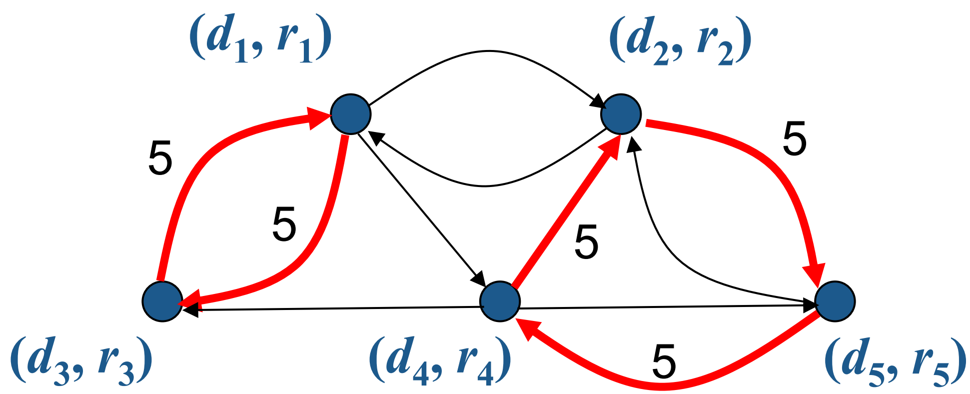
What to optimise?



What to optimise?



3 transplants
Total weight 250



5 transplants
Total weight 25

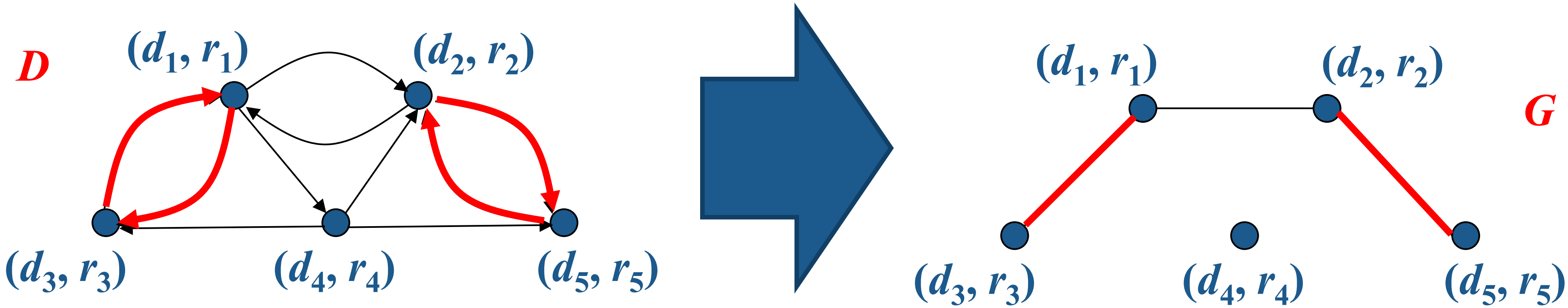
Base optimisation problems

- A *set of exchanges* is a packing S of vertex-disjoint cycles in D
- A vertex $v \in V$ is *covered* by S if v is incident to a cycle of S
- A set of exchanges is *optimal* if
  1. the number of vertices covered by S is maximum (i.e., the number of transplants is maximum);
  2. subject to (1), the sum of the weights is maximum (i.e., the total score is maximum)

- We study 3 cases:
  - Only 2-cycles (pairwise exchanges) are possible
  - The cycle lengths are unrestricted
  - 2- and 3-cycles (pairwise and 3-way exchanges) are allowed

Pairwise exchanges ⇒ matching problem

- We transform the directed graph D to an undirected graph G

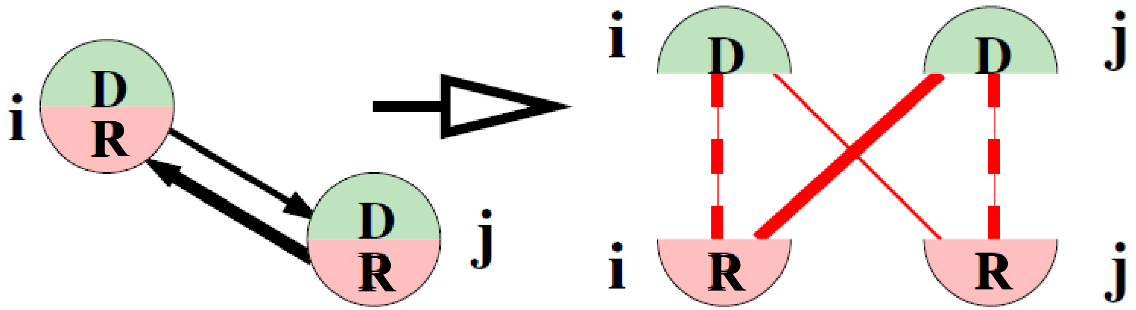


- A set of pairwise exchanges in D corresponds to a *matching* in G with the same weight, since $w(\{i,j\}) = w(i,j) + w(j,i)$ for every edge $\{i,j\}$ of G

- The problem of finding a maximum weight maximum cardinality matching in G (general graph) can be solved in polynomial time [Gabow and Tarjan, 1991]

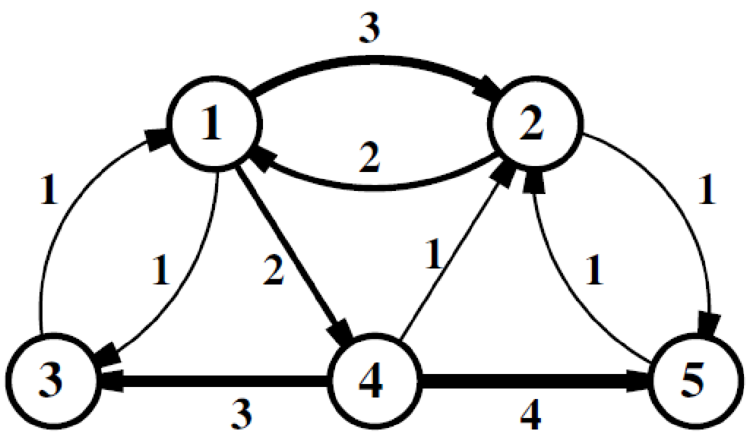
Unrestricted exchanges ⇒ matching problem

- We transform the directed graph ***D*** to an undirected graph ***G***



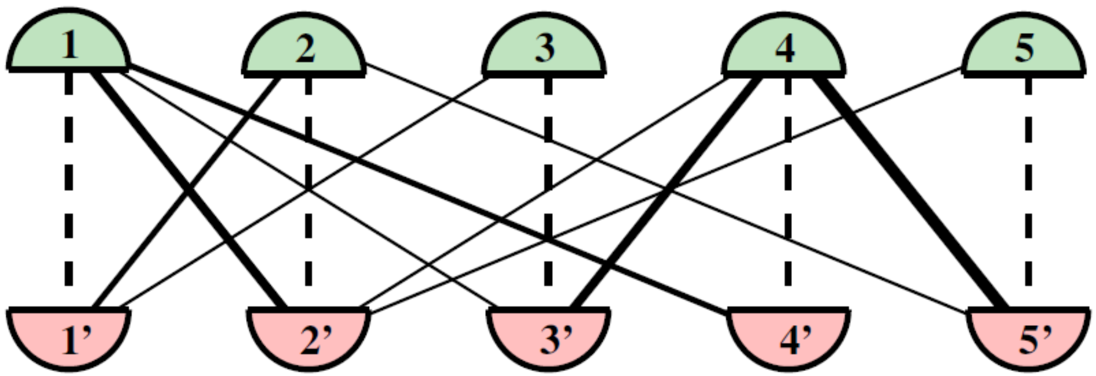
- With an edge of weight **0** between each recipient and his/her donor
- A set of exchanges in ***D*** corresponds to a *perfect matching* in ***G*** with the same weight
- The problem of finding a *maximum weight perfect matching* in ***G*** (bipartite graph) can be solved using an efficient algorithm [Gabow and Tarjan, 1989]

The transformation in an example

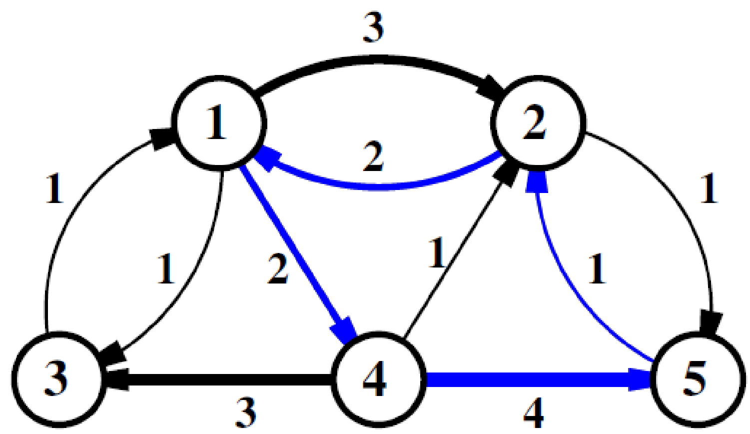


From a directed graph ***D***

we create a bipartite graph ***G***

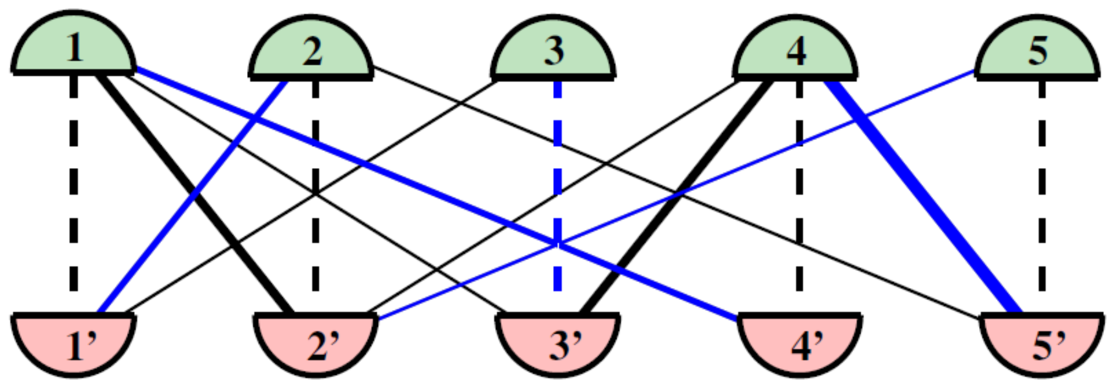


The transformation in an example



From a directed graph ***D***, maximum weight unrestricted set of exchanges

we create a bipartite graph ***G***, maximum weight perfect matching



Pairwise and 3-way exchanges: hard problem

- The problem of finding an optimal set of exchanges involving only 2- and 3-cycles is NP-hard [Abraham, Blum and Sandholm, 2007]

- Heuristics or approximation algorithms are not acceptable
  - must find an optimal solution

- Exact algorithm
  - Will run in exponential time in the worst case
  - Integer programming is a common solution technique [Roth, Sönmez and Unver, 2007]

Introduction to integer programming

- Involves optimising an objective function subject to a system of linear inequalities
  - $\max\ \mathbf{c}^{\mathrm{T}}\mathbf{x}$ subject to $A\mathbf{x} \leq \mathbf{b}$

    Objective function

    Constraints

    Variables
  - where $\mathbf{c}=(c_1, c_2,\ldots, c_n)^{\mathrm{T}}$, $\mathbf{x}=(x_1, x_2,\ldots, x_n)^{\mathrm{T}}$, $\mathbf{b}=(b_1, b_2,\ldots, b_m)^{\mathrm{T}}$
    $A=(a_{ij})$ $(1\leq i\leq m,\ 1\leq j\leq n)$, the c_i, a_{ij} and b_j are real-valued known coefficients and the x_i are integer-valued variables
- Linear programming: relaxation in which x_i are real-valued
  - solvable in polynomial time
- The general integer programming problem is NP-hard
  - e.g., SAT can be modelling by an IP formulation
  - but there are some powerful solvers

Example: knapsack problem

- *Knapsack problem*
  - Instance: n items, where item i has a weight w_i and a profit p_i, knapsack capacity C
  - Output: A subset S of $\{1,\ldots,n\}$ for which $\Sigma_{r \in S}\, p_r$ is maximum subject to $\Sigma_{r \in S}\, w_r \leq C$
  - That is, choose a subset of the items of maximum total profit such that the knapsack capacity is not exceeded
  - NP-hard in general

- Example:
  - Knapsack capacity C=65, n=5 items
  - Weights: w_1=23, w_2=15, w_3=15, w_4=33, w_5=32
  - Profits: p_1=33, p_2=23, p_3=11, p_4=35, p_5=11
  - Choosing all the items gives total weight $118 > C$
  - Choosing items 1, 4 gives total weight $56 \leq C$ and total profit 68
  - Choosing items 2, 3, 4 gives total weight $63 \leq C$ and total profit 69 (optimal)

Example integer programming model

- Define the following binary variables:

$$x_i = \begin{cases} 1, & \text{if item } i \text{ is selected} \\ 0, & \text{otherwise} \end{cases} \qquad (1 \le i \le n)$$

- Define the following integer programming model:

$$\max \sum_{i=1}^{n} p_i x_i \qquad \text{subject to}$$

Objective function

$$\sum_{i=1}^{n} w_i x_i \le C$$

Knapsack capacity must not be exceeded

$$x_i \in \{0,1\} \quad (1 \le i \le n)$$

Variables are binary-valued

Example: knapsack problem

$$\max \sum_{i=1}^{n} p_i x_i \qquad \text{subject to}$$

$$\sum_{i=1}^{n} w_i x_i \leq C$$

$$x_i \in \{0,1\} \quad (1 \leq i \leq n)$$

- Solve using an optimization tool such as Gurobi
- Example:
  - Knapsack capacity C=65, n=5 items
  - Weights: w_1=23, w_2=15, w_3=15, w_4=33, w_5=32
  - Profits: p_1=33, p_2=23, p_3=11, p_4=35, p_5=11
  - Solution: x_1=0, x_2=1, x_3=1, x_4=1, x_5=0
  - Objective value: 69

Integer programming for kidney exchange

- The classical *cycle-formulation* is as follows:
  - first formulated by [Roth, Sönmez and Ünver, 2007]
  - investigated computationally by [Abraham, Blum and Sandholm, 2007]
  - list all the possible cycles (exchanges) of lengths **2** and **3** in the directed graph as $\mathcal{C}=\{C_1, C_2, \ldots, C_m\}$
  - use binary variables $x_1, x_2, \ldots, x_m$
  - where $x_i = 1$ if and only if C_i belongs to an optimal solution
  - build an $n \times m$ matrix A where $n = |V|$ and $A_{i,j} = 1$ if and only if v_i is incident to C_j
  - let b be an $n \times 1$ vector of **1**s
  - let c be a $1 \times m$ vector of values corresponding to the optimisation criterion, e.g., c_j could be the length of C_j
  - solve $\max\ cx$ such that $Ax \le b$, subject to $x \in \{0,1\}^m$

$$\max \sum_{i=1}^{n} |C_i| x_i$$

such that

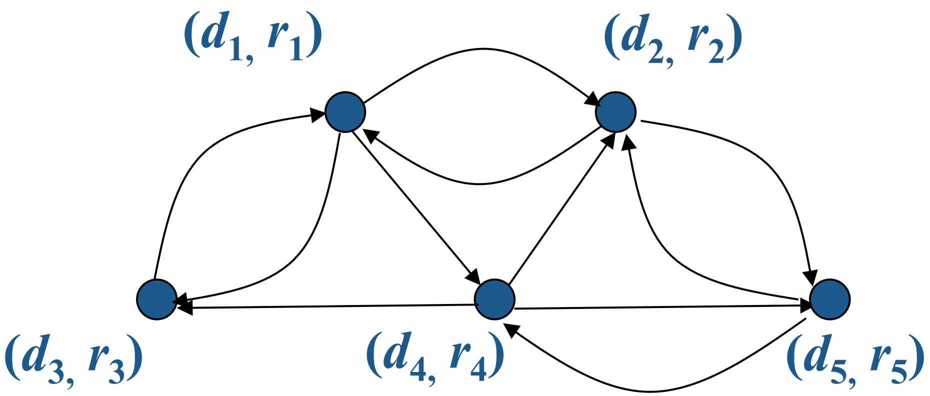
$$\sum_{C_j \in \mathcal{C}:\, v_i \in C_j} x_j \le 1 \qquad 1 \le i \le n$$

$$x_i \in \{0,1\} \qquad 1 \le i \le n$$

Integer programming model: example

max cx
s.t. $Ax \leq b$
and $x_i \in \{0, 1\}$

where

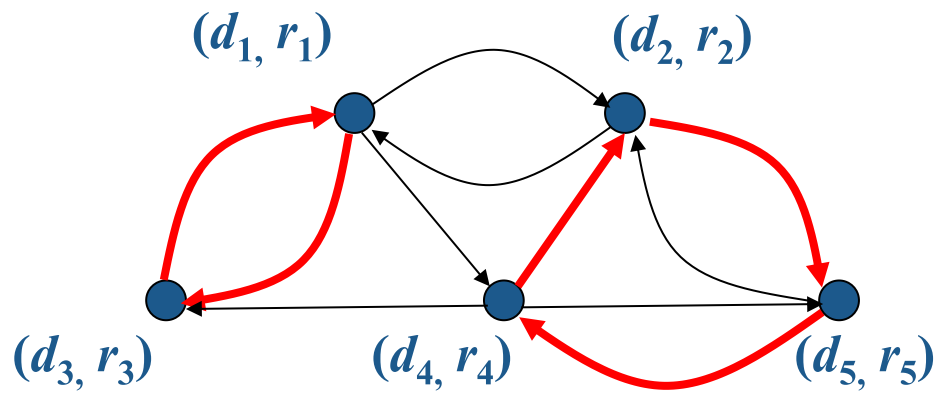


$$A = \left[\begin{array}{cccc|ccc} 1 & 1 & 0 & 0 & 1 & 1 & 0 \\ 1 & 0 & 1 & 0 & 1 & 0 & 1 \\ 0 & 1 & 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 & 1 & 1 & 1 \\ 0 & 0 & 1 & 1 & 0 & 0 & 1 \end{array}\right], \quad b = \begin{bmatrix} 1 \\ 1 \\ 1 \\ 1 \\ 1 \end{bmatrix}, \quad x = \begin{bmatrix} x_1 \\ x_2 \\ x_3 \\ x_4 \\ x_5 \\ x_6 \\ x_7 \end{bmatrix} \text{ and}$$

$$c_s = \left[\begin{array}{cccc|ccc} 2 & 2 & 2 & 2 & 3 & 3 & 3 \end{array}\right]$$

Integer programming model: example

$$\max\ cx$$
$$\text{s.t. } Ax \leq b$$
$$\text{and } x_i \in \{0, 1\}$$



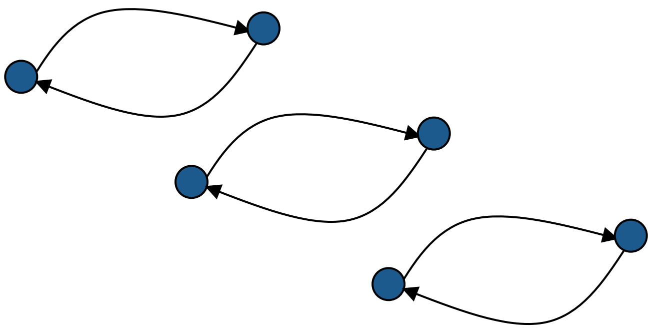
where

$$A = \left[\begin{array}{cccc|ccc} 1 & 1 & 0 & 0 & 1 & 1 & 0 \\ 1 & 0 & 1 & 0 & 1 & 0 & 1 \\ 0 & 1 & 0 & 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 & 1 & 1 & 1 \\ 0 & 0 & 1 & 1 & 0 & 0 & 1 \end{array}\right] \quad b = \begin{bmatrix} 1 \\ 1 \\ 1 \\ 1 \\ 1 \end{bmatrix} \quad x = \begin{bmatrix} 0 \\ 1 \\ 0 \\ 0 \\ 0 \\ 0 \\ 1 \end{bmatrix} \text{ and}$$

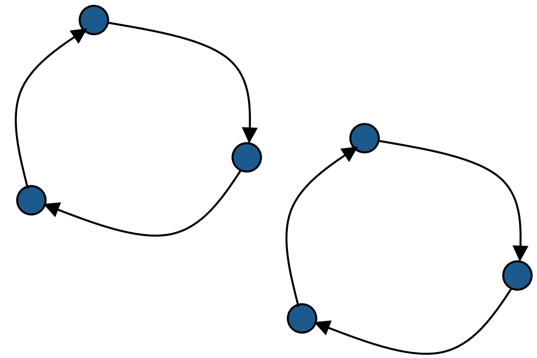
$$c_s = \left[\begin{array}{cccc|ccc} 2 & 2 & 2 & 2 & 3 & 3 & 3 \end{array}\right] \qquad \max\ c_s x = 5$$

Extension: mitigating the risk of 3-ways

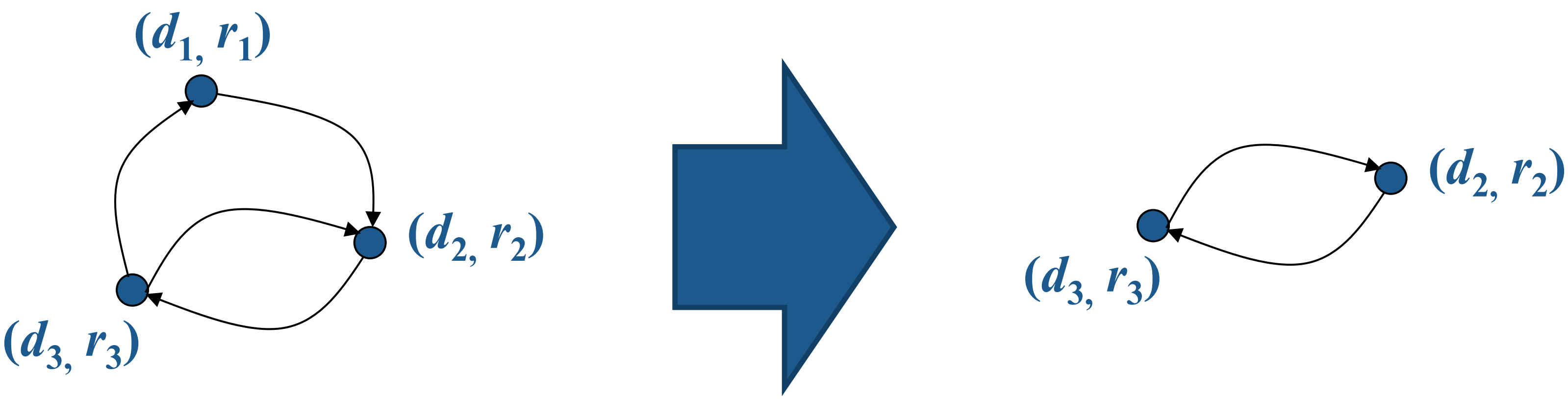
- Minimising the number of 3-way exchanges



is less risky than



- A 3-way exchange with a *back-arc* has an embedded pairwise exchange



  – If (d_1, r_1) drops out then the embedded pairwise exchange could still proceed

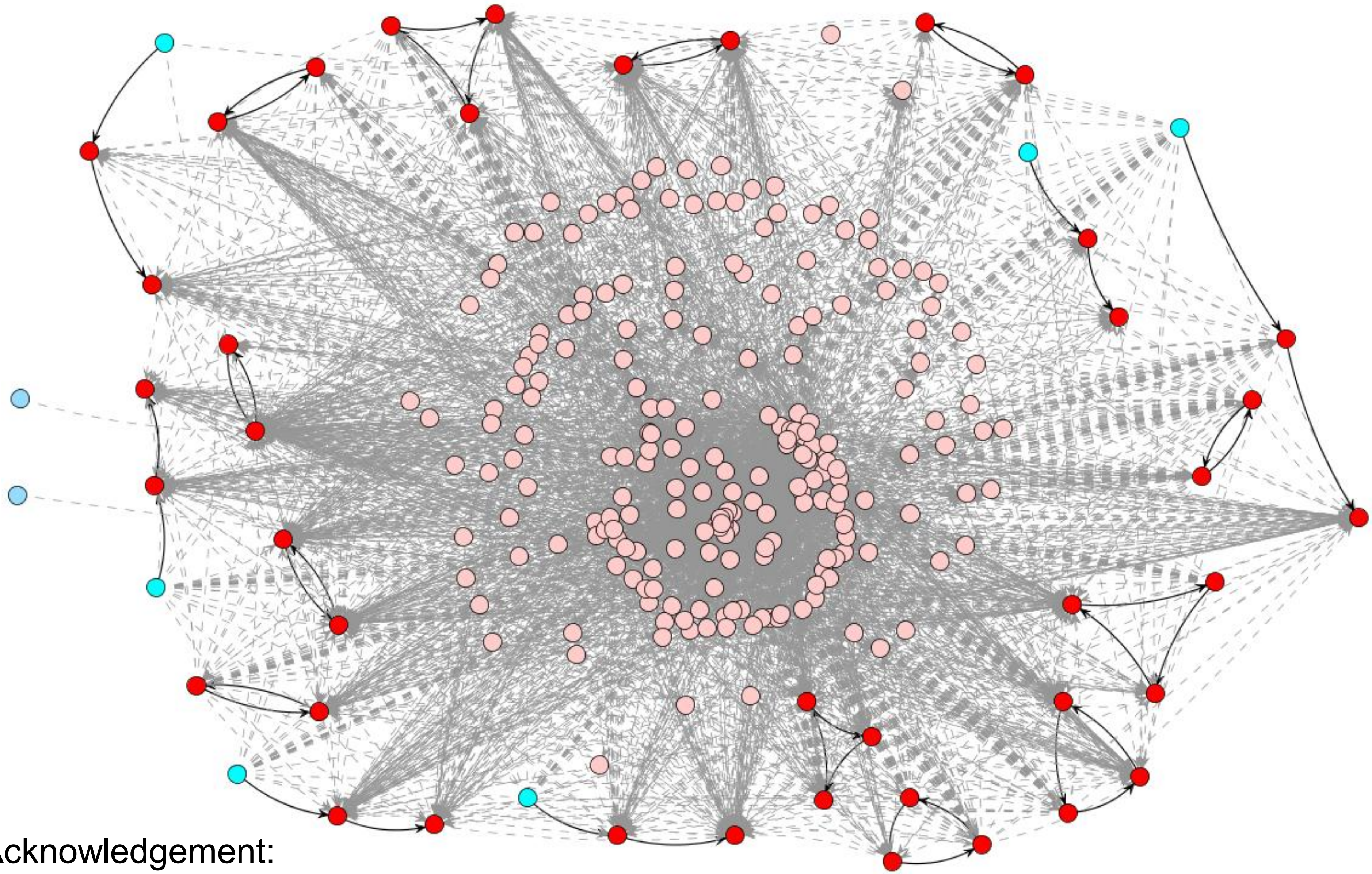
The optimisation problem in the UK

- A *set of exchanges* is a packing S of vertex-disjoint cycles in D, where each cycle has length ≤ 3
- A set of exchanges is *optimal* if

1. the number of *effective pairwise exchanges* (i.e., no. pairwise exchanges plus no. 3-way exchanges with a back-arc) is maximised
2. subject to (1), the number of vertices covered by S (i.e., the total number of transplants) is maximised
3. subject to (1)-(2), the number of 3-way exchanges is minimised
4. subject to (1)-(3), the number of back-arcs in the 3-way exchanges is maximised
5. subject to (1)-(4), the overall weight is maximised.

D. Manlove and G. O'Malley, Paired and altruistic kidney donation in the UK: Algorithms and experimentation. ACM Journal of Experimental Algorithmics, vol. 19, no. 2, article 2.6, 2014

Visualisation of July 2015 solution



- Acknowledgement: Tommy Muggleton

Results from UKLKSS matching runs

Since scheme began:

- Number of transplants identified: 3,439
- Number of actual transplants: 2,239
- Number of two-way exchanges: 255
- Number of three-way exchanges: 248
- Number of short chains: 212
- Number of long chains: 187