Implications of data-driven transplantation in welfare

Press Start

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In Canada

1 in 10	Canadians have kidney disease and millions more are at risk.
36%	grow since 2007 on the number of Canadians living with end-stage disease.
47%	of new patients are under the age of 65.
Diabetes	is the leading cause of kidney failure.
11^{th}	leading cause of death in 2014.
48 000	Canadians are being treated for kidney failure.
$50 billion	per year is the approximate cost to the health care system for chronic kidney disease.

The Kidney Foundation of Canada: https://www.kidney.ca/facing-the-facts, visited 21-02-2019

Treatments

- Dialysis
- Transplantation

Dialysis vs Transplantation

- Transplantation yields longer survivability.
- Transplantation yields a better quality of life.
- Dialysis is more expensive than transplantation.

Transplantation

In Canada

Treatment for those with end-stage kidney disease:

- **58.4%** are on dialysis with three-quarters receiving hemodialysis (the most expensive treatment)
- **41.4%** have a functioning transplant

77% of the 4 500 Canadians on the waiting list for an organ transplant are waiting for a kidney.

1 731 kidney transplants performed in 2016.

4 years is the median waiting time for a deceased-donor kidney transplantation. (shortest Nova Scotia: 3 years; longest Manitoba: 5.7 years).

Dialysis costs between $56 000 and $107 000 per patient per year.

The Kidney Foundation of Canada: https://www.kidney.ca/facing-the-facts, visited 21-02-2019

Transplantation

Deceased donation

- Patients are registered in a waiting list (provincial level).
- A patient and physician together decide whether to accept or refuse a kidney offer.

No reliable tool to support their decision.

Living donation

- Transplantation from a **compatible** living donor: typically, relative or friend, or through the Kidney Paired Donation Program (federal level).

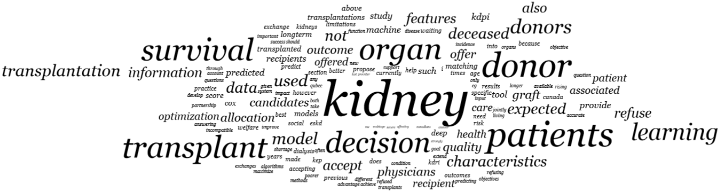
Optimization for exchange of donors.

Facts:

42% of kidney transplants are made possible by living donors

54% of living donors are unrelated to the recipient.

5-year survival rate for adults with transplanted kidneys is 90% from living donors are 82% from deceased donors.


kidney
donor
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survival
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kidneys
limitations
waiting
because
into
objective
question
practice
however
impact
best
dialysis
shortage

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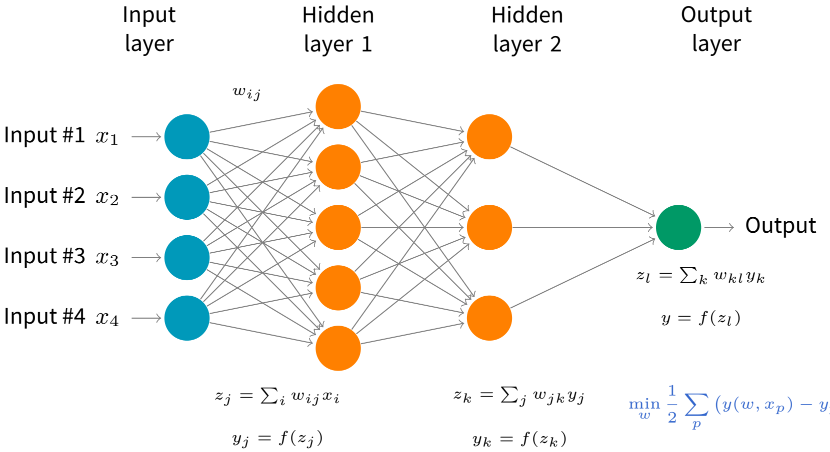
Machine learning for graft survival prediction

M. Luck, T. Sylvain, H. Cardinal, A. Lodi, Y. Bengio and J. P. Cohen

Deep Learning

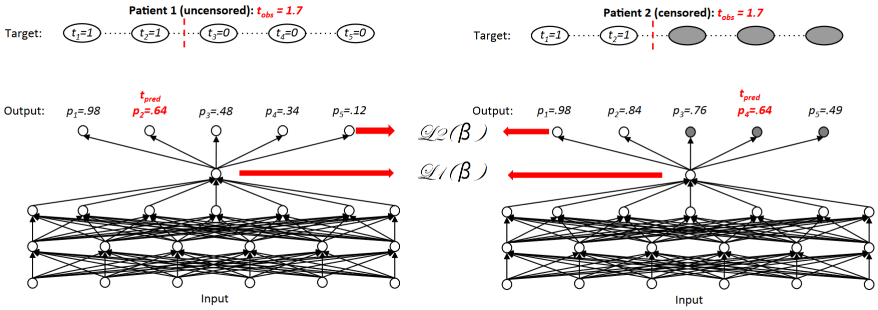
- Algorithm is fed with raw data in order to learn the representations needed for performing
  - regression: estimation of the relationships among variables or
  - classification: identification of the category to which data points belong (e.g., patient sick or patient healthy).
- Multiple layers of representation, each transforming the representation at one level (starting with the raw input) into a representation at a higher, slightly more abstract level.

Deep Learning



$$\min_w \frac{1}{2} \sum_p (y(w, x_p) - y_p)^2$$

Goal: Predict graft survival time for specific patient-donor pairs



Scientific Registry of Transplant Recipient (SRTR) - a large database that comprises donor and recipient information for all solid organ transplantations that are performed in the United States.
A limitation: long-term kidney graft survival is inferior in the US when compared to other industrialized countries. Our current mode may not be directly applicable to Canadian patients.

Margaux Luck, Tristan Sylvain, Héloïse Cardinal, Andrea Lodi, Yoshua Bengio. *Deep Learning for Patient-Specific Kidney Graft Survival Analysis*. arXiv:1705.10245. 2017
Margaux Luck, Tristan Sylvain, Joseph Paul Cohen, Heloise Cardinal, Andrea Lodi, Yoshua Bengio. *Learning to rank for censored survival data*. arXiv:1806.01984. 2018

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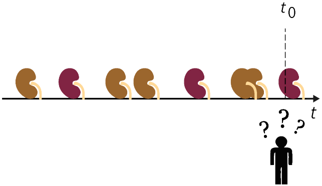
Decision tool for deceased donation

J-N Weller, H. Cardinal and A. Lodi.

Accept or refuse an organ from a deceased donor?

How long is the kidney from this specific donor expected to last in someone like me? ✓

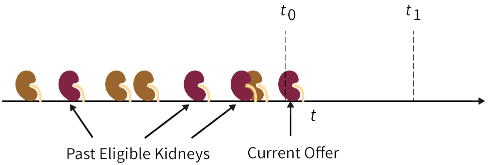
If I refuse this specific donor, how much longer am I expected to wait?



Accept or refuse an organ from a deceased donor?

Predict the time for the next offer with quality greater or equal than the current one.

Estimation of eligible donors distribution (Poisson process with varying parameter).



$$\mu_0 = \frac{N_{eligible}}{\Delta T} \times \left(1 - \frac{cPRA}{100}\right)$$

Jean-Nöel Weller. Predicting next kidney offer for a kidney transplant candidate declining current one. *Master Thesis*. École Polytechnique Montréal. 2018.

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Decision tool for living donation
Kidney Exchange Game

Transplantation

Deceased donation

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- A patient and physician together decide whether to accept or refuse a kidney offer.

No reliable tool to support their decision. ✓

Living donation

- Transplantation from a **compatible** living donor (typically, relative or friend).
- Canadian Kidney Paired Donation program.

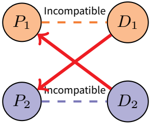


Figure 1: 2-way kidney exchange

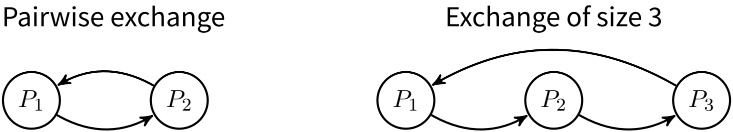


Figure 2: Kidney exchanges.

Model

Vertex-disjoint cycle packing formulation (Abraham et al. 2007)

$$\max_{x} \sum_{c \in C(L)} x_c w_c$$

$$\text{s.t.} \sum_{c \in C(L): n \in c} x_c \leq 1 \ \forall\, n \in N$$

$$x \in \{0,1\}^{|C(L)|}$$

where $C(L)$ is the set of cycles with size at most L and x_c is 1 if cycle $c \in C(L)$ is selected, 0 otherwise.

Canadian Kidney Paired Donation program

- Maximum length for cycles is 5.
- Since 2009, the Kidney Paired Donation program has completed 637 tranplants.
- 378 of 637 transplants come from chains.

https://professionaleducation.blood.ca/en/organes-et-tissus/programmes-et-services/kidney-paired-donation-kpd-program, visited 21-02-2019

Multi-agent kidney exchange

Motivation

Context: Some countries have regional (or hospital) pools, where the matches are performed internally with no collaboration between the different entities.

Goal: It became relevant to study kidney exchange programs involving several hospitals or even several countries, since there is potential to increase the number of transplants.

Strategic behaviour: These entities aim is to maximize the transplant benefit for their patients.

Our contribution: Analysis of the problem from the non-cooperative game theory point of view.

2-way exchanges

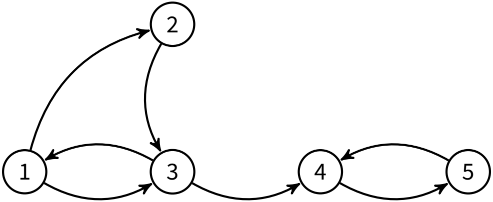


Figure 3: Kidney exchanges.

2-way exchanges

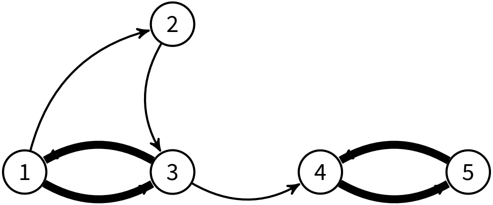


Figure 4: Kidney exchanges.

Replace cycles of length 2 by edges

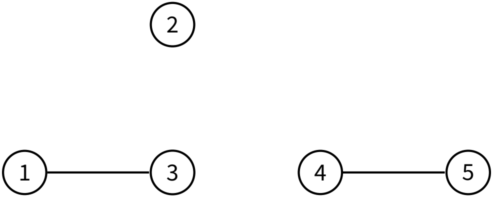
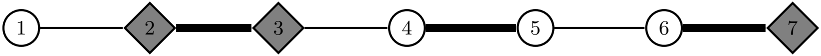


Figure 5: Kidney exchanges.

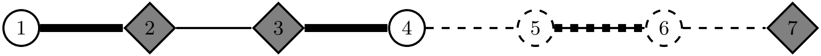
A subset M of E is called a *matching* of graph $G = (V, E)$ if no two edges in it share the same vertex

Literature

Literature concentrates on the search of a strategyproof mechanism that decides all exchanges to be performed in a multi-hospital setting.
An optimal matching:



might not be strategyproof:



I. Ashlagi, F. Fischer, I. A. Kash, and A. D. Procaccia, Mix and match: A strategyproof mechanism for multi-hospital kidney exchange, Games and Economic Behavior 91 (2015), 284–296.

Game instructions

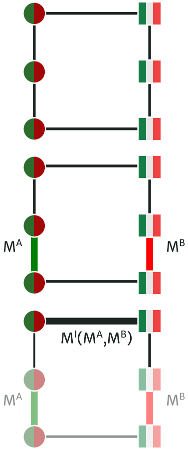
Players

Player A controls the incompatible patient-donor nodes

Player B controls the incompatible patient-donor nodes

Edges between patient-donor nodes represent a compatible exchange.

The players feasible strategies are matchings among their nodes, i.e., a set of internal edges such that no two edges share a common node.



Nash Equilibrium

A Nash equilibrium (NE) is a matching M^A in G^A for player A and a matching M^B for player B such that

$$2|M^A|+|M^I(M^A,M^B)| \geq 2|R^A|+|M^I(R^A,M^B)| \quad \forall \text{matching } R^A$$

$$2|M^B|+|M^I(M^A,M^B)| \geq 2|R^B|+|M^I(M^A,R^B)| \quad \forall \text{matching } R^B.$$

Multi-Player Kidney Exchange Game

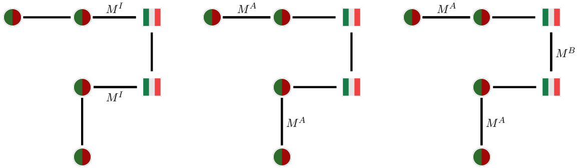
Theorem

There exists at least one pure Nash equilibrium and it can be computed in polynomial time.

Proof.

The game has a potential function
$\Phi(M^A, M^B) = 2|M^A| + 2|M^B| + |M^I(M^A, M^B)|$ □

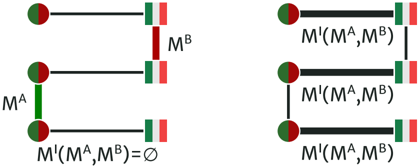
$\Phi = 2$ $\Phi = 4$ $\Phi = 6$



The game can have multiple equilibria

$$\Phi(M^A, M^B) = 2|M^A| + 2|M^B| + |M^I(M^A, M^B)|$$

$\Phi = 4$ $\Phi = 3$



A *social welfare equilibrium* (SWE) is an NE that is also a social optimum.

Theorem

There is always a ***social welfare equilibrium*** *and it can be computed in polynomial time.*

Are Social Welfare Equilibria rational outcomes?

Multi-Player Kidney Exchange Game

Lemma

Any social welfare equilibrium is Pareto efficient.

Theorem

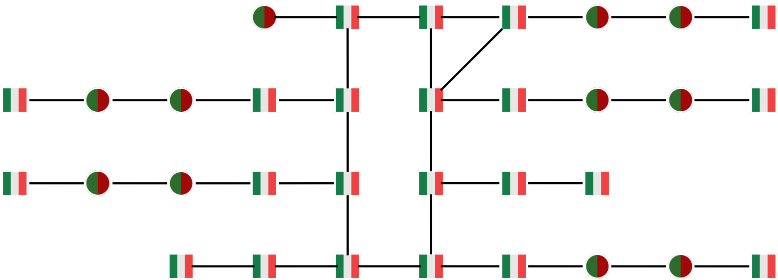
There is an algorithm that after a finite number of steps finds a SWE that dominates a given NE.

Dominant SWE over a NE

Algorithm

Input: A 2-KEG instance G and an NE M of G.
Output: M if it is an SWE, else an SWE dominating it.

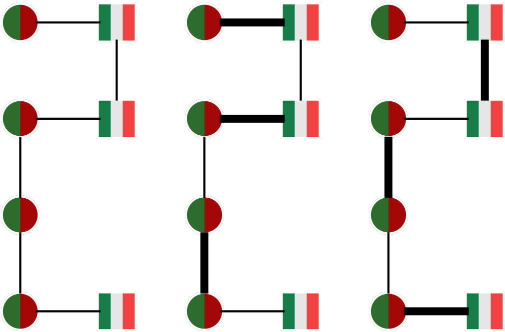
Computes a maximum matching dominating a NE.
Then, iteratively removes a player incentive to deviate by removing alternating paths of type *ii*.



Instance

$\Pi^A = 4$
$\Pi^B = 2$

$\Pi^A = 3$
$\Pi^B = 3$



Refinement of NE

Algorithm

Input: A 2-KEG instance G.
Output: An SWE that minimizes the number of external exchanges.

Solves a weighted matching problem in G where the internal edges weigh $2+2|V|$ and external edges weigh $1+2|V|$.

Lemma

Algorithm

- *runs in polynomial time*
- *outputs a social optimum*
- *outputs a Nash equilibrium*
- *minimizes the number of external exchanges among the social welfare equilibria*
- *guarantees uniqueness in terms of the players utilities*
- *outputs the SWE minimizing the difference between players' utilities.*

M. Carvalho, A. Lodi, J. P. Pedroso, A. Viana, *Nash Equilibria in the Two-Player Kidney Exchange Game*, Mathematical Programming, Volume 161, Issue 1-2, 389–417, January 2017.

Interpretation of the results

Theorem (M. Carvalho, A. Lodi (2018))

For any game with a set of players N and any deterministic algorithm $\mathcal{A}$ for the IA, there is a SWE and it can be computed in polynomial time.

Good news: Our approach to this multi-agent setting shows why a simple maximization of number of transplantations among agents can make all players happy (i.e., be an *equilibrium*).

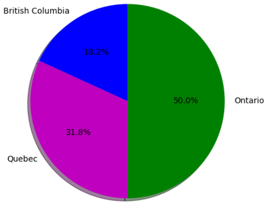
Literature

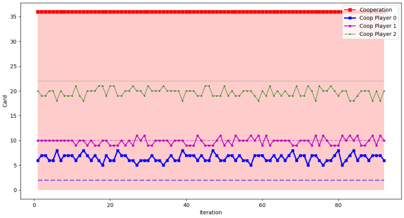
(...) market failures cause the loss of hundreds of transplants per year (...) the market is highly fragmented, with 65% of transactions happening in small platforms, often within hospitals, as opposed to in large, national platforms.

The hospitals that do participate don't perform all their kidney exchanges through the national platform and register particularly hard-to-match patients and donors at the platform (...) within hospital exchanges match a much larger fraction of O donors with non-O patients (...)

Nikhil Agarwal, Itai Ashlagi, Eduardo Azevedo, Clayton Featherstone, Omer Karaduma. Market Failure in Kidney Exchange.

Working Paper, (last version) Sep 2017.





	# nodes	OPT_{alone}	Best OPT_{coop}	Worst OPT_{coop}
British Columbia	13	2	9	3
Quebec	22	10	13	8
Ontario	35	22	23	16

Maximum Matching: 36 transplants

From **10 000** maximum matchings, **6** are Nash equilibria.

Instances: M. Constantino, X. Klimentova, A. Viana, A. Rais. New insights on integer-programming models for the kidney exchange problem. EJOR, 2013.

Uniform generation of Matchings with Maximum Cardinality

Motivation: Deterministic algorithms are used to compute a matching of maximum cardinality, i.e., for the same input order, the same optimal solution is determined.

Uniform generation of lattice point in polytopes implies counting them.

Counting matchings of maximum cardinality is *hard*.

Uniform generation of Matchings with Maximum Cardinality

INS	NUM	TIME	Max Card	$\lvert E \rvert$
30-instance-30	138	0.33	6	29
30-instance-31	56	0.71	7	30
30-instance-32	8	0.21	7	20
30-instance-33	120	0.98	6	30
30-instance-34	2928	1.26	4	36
30-instance-35	42	0.18	6	21
30-instance-36	5	0.01	4	13
30-instance-37	4072	23.43	8	44
30-instance-38	252	0.29	5	26
30-instance-39	120	4.11	8	37
30-instance-40	28	0.05	5	19
30-instance-41	12094	10.98	5	45
30-instance-42	1684	80.09	8	50
30-instance-43	27	1.02	7	31
30-instance-44	2803	2.91	5	42
30-instance-45	12	0.01	4	11
30-instance-46	3444	2.45	5	46
30-instance-47	220	0.22	4	26
30-instance-48	222	0.34	5	27
30-instance-49	6	0.00	3	9
30-instance-50	12	0.01	5	14

Computations done in Julia 1.0.0 using dynamic programming approach.

Uniform generation of Matchings with Maximum Cardinality

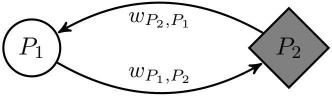
INS	NUM	TIME	Max Card	$\vert E\vert$
40-instance-30	9915	175.79	9	52
40-instance-31	5150	21.57	7	48
40-instance-32	128669	386.98	8	75
40-instance-33	2272	65.00	8	45
40-instance-34	1475772	5054.43	9	87
40-instance-35	348	1.77	7	31
40-instance-36	72	3.08	9	26
40-instance-37	5680	502.24	10	55
40-instance-38	1344	785.65	11	62
40-instance-39	4	0.00	3	6
40-instance-40	288	2.13	8	24
40-instance-41	196	11.39	9	38
40-instance-42	7847	14.97	7	38
40-instance-43	41	0.01	3	16
40-instance-44	5639	47.04	7	55
40-instance-45	1260	3.85	6	40
40-instance-46	126	0.19	5	26
40-instance-47	1440	0.67	5	30
40-instance-48	14	0.01	2	15
40-instance-49	102	0.11	3	24
40-instance-50	360150	476.73	8	70

Computations done in Julia 1.0.0 using dynamic programming approach.

Adding Machine Learning...

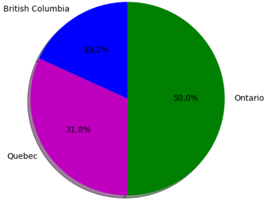
Adding Machine Learning graft quality predictions

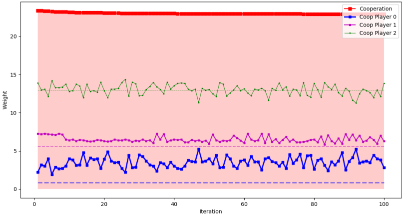
The goal becomes the maximization of a weighted matching



★ Verifying if a matching is an equilibrium is NP-complete.
★ Moreover, our computational experiments show that (pure) equilibria for the game with weighted matchings are rare.

Computational Experiments





	# nodes	OPT_{alone}	Best OPT_{coop}	Worst OPT_{coop}
British Columbia	13	0.84	5.66	1.12
Quebec	22	5.56	8.40	4.96
Ontario	35	12.91	15.00	9.32

Maximum Weighted Matching: 23.38

From the best **10 000** maximum weighted matchings, **0** were Nash equilibria.

Conclusions and Ongoing work

⋆ Deep learning approach.

Conclusions:

- Predicts time of an event (survival time) and C-index (score indicative of the time of graft failure);
- Achieves state-of-the-art performance.

Ongoing work:

- Improve deep learning architecture (usable with loss of features);
- Introduce new learning objects.

Conclusions and Ongoing work

⋆ Decision tool for patients in the waiting list.

Conclusions:

- Promote shared decision making;
- Decision making framework integrating graft survival information.
- The approach was validated with data from Transplant Quebec.

Ongoing work:

- Personalized estimates of patient and kidney graft survival time if the offer is accepted and estimates if an average donor was accepted.
- No question Vs Yes question

Conclusions and Ongoing work

⋆ Kidney Exchange game.

Conclusions:

- There is a social welfare equilibrium when number of transplants is considered;
- Introducing graft quality information makes the game hard to solve and socially satisfactory solutions might fail to exist.

Ongoing work:

- Evaluation of the game using data from the Canadian Kidney Exchange program.
- Integration of the qualitative graft information in the game.
- Redesign the game in order to achieve social optimal solutions (consider dynamic case).

Questions

Thank you for your attention