Kidney Exchange Problem

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Abstract

The demand of kidney transplants on the waiting list in US keeps increasing drastically every year. It lead to a good alternative: living donors (without compensation). However, a critical problem with living donors is the compatibility between the recipient and the donor. To overcome this problem, more kidney donors and recipients turn to kidney exchange. The purpose of this talk is to introduce readers to the mathematical formulation of kidney exchange problem, the complexity of the kidney exchange problem and some algorithms capable of solving the problem. In the end, some further advance to kidney exchange will be discussed.

1. Introduction

The function of kidneys is to filter waste from our blood. Kidney failure leads to accumulation of such waste in our blood, which causes death in months. One feasible treatment is dialysis, in which the patient has his/her blood filtered by an external machine in a hospital. Several visits are required every week, and each visit takes several hours. The quality of life on dialysis can be extremely low, and actually many patients choose to withdraw from dialysis, leading to natural death. Only about ten percent of dialysis patients survive 10 years. Instead, a preferred treatment is kidney transplant. Kidney transplant is by far the most common and sometimes the only effective way to cure end stage renal disease, impacting one out of thousand European and U.S. citizens. The usual process to get a kidney transplant is wait for a compatible deceased donor but waiting for such one can be really time-consuming and uncertain. According to relevant statistics, there have been over 100,000 patients on the waitlist in the U.S. since 2014. In 2014, 4537 of them died while waiting and only 11,559 of them received one from the deceased donor waitlist. Under such circumstances, the best alternative is living donor, which means a healthy person willing to donate one of his/her two kidneys. Although there are marketplaces for living donors, the commercialization of human organs is almost universally regarded as unethical, and the practice is often explicitly banned, such as in the US. However, in most countries, live donation is legal, provided it occurs as a gift with no financial compensation. In 2005, there were 6,563 live donations in the US.

However, a critical concern with living donor transplant is compatibility, more specifically, if a donor and the recipient are blood-type and tissue-type compatible. The number of live donations would have been much higher if it were not for the fact that, with a probability of approximately 40%, a potential live donor and his/her intended recipient are blood-type or tissue-type incompatible. In the past, the incompatible donor was usually sent home, leaving the patient waiting for a deceased-donor kidney. Recently, there are more and more regional kidney exchange programs independently developed in several countries, such as the United States. In such a program, a recipient with an incompatible living donor can "swap" his/her original donor with another patient in a similar position. More generally, an exchange may involve several incompatible donor-patient pairs by permutation of donors, creating cycles of donation. A Kidney Exchange Program aims for an optimal result. The objective of the kidney exchange problem can be defined by different criteria (maximizing number of transplants, maximizing weight of exchanges, maximizing probability of success...).

2. Formulation

The kidney exchange problem (KEP) discussed in this talk is to find a maximum-weight exchange consisting of cycles with length at most some small constant L. This cycle-length constraint arises naturally for the following reasons. First, for example, in a kidney exchange program, all operations in a cycle have to be performed simultaneously; otherwise a donor might withdraw after his original incompatible recipient has received a kidney. This gives rise to a logistical constraint on cycle size: even if all the donors are operated on first and the same personnel and facilities are used to then operate on the recipients, a k-cycle requires between 3k and 6k doctors, around 4k nurses, and exactly 2k operating rooms, which is quite demanding for regional hospitals. Therefore, due to such resource constraints, the regional kidney exchange programs will likely allow only cycles of length 2. Another reason for short-length cycles is that if cycle fails to exchange, fewer agents will be affected. For example, last-minute testing often reveals new incompatibilities that were not detected in the initial testing. More generally, an living donor exits a cycle if he/she simply fails to fulfill the obligations due to forgetfulness or change in preferences.

2.1 Cycle Formulation

The first way to formulate the problem is based on the classical model for solving the directed cycle cover problem with cycles' of length 2. Given a directed graph, $G = (V, E)$, where each $v \in V$ represents incompatible donor-patient pairs, there is an directed edge $e(uv) \in E$ connecting $u, v \in V$ if the recipient in the pair v would accept the kidney from pair u with $w(uv)$ donating the medical benefit of the transplant.

Define C to be the set of all cycles of size at most L in G, x_c to be the binary decision variable $= 1$ if walk c is chosen in the solution, 0 otherwise. The objective is to maximize the total weight of selected cycles and the constraints are that each vertex must be selected in at most one cycle. The Cycle Formulation is then:

$$
\begin{aligned}
max \sum_{c \in \mathcal{C}} w_c x_c & \\
st \sum_{c \in \mathcal{C}: v \in c} x_c \leq 1 & \qquad \forall v \in V \\
x_c \in \{0, 1\} & \qquad \forall c \in \mathcal{C}
\end{aligned}
$$

2.2 Edge Formulation

An alternative way to formulate the problem with one variable for each edge. This formulation method is to consider an optimization over edges. Given a directed graph, $G = (V, E)$, where each $v \in V$ represents incompatible donor-patient pairs, there is an directed edge $e \in E$ connecting $u, v \in V$ if the recipient in the pair v would accept the kidney from pair u with $w(uv)$ donating the medical benefit of the transplant.

First, define $s_{u,v}$ to be a binary decision variable that indicates whether $e(uv)$ is in some cycle. $s_{u,v} = 1$ if $e(uv)$ is in some cycles, , = 0 otherwise. The Edge Formulation is then:

$$
\begin{aligned}
&\max \textstyle\sum_{s_{i,j}, \forall e_{i,j} \in E} w_{i,j} s_{i,j} && \text{Sum Weight of Edges in cycles} \\
&\text{s.t. } s_{i,j} \in \{0,1\}, \forall e_{i,j} \in E && \text{Variables are Binary} \\
&\quad \textstyle\sum_{e_{i,k} \in E} s_{i,k} - \sum_{e_{k,i} \in E} s_{k,i} = 0, \forall v_i \in V && \text{Conservation Constraint} \\
& && \text{(Outgoing minus Incoming Edges)} \\
&\quad \textstyle\sum_{e_{i,k} \in E} s_{i,k} \leq 1, \forall v_i \in V && \text{Capacity Constraint} \\
& && \text{(Only one outgoing edge in a cycle)} \\
&\quad s_{i_1,i_2} + s_{i_2,i_3} + \ldots + s_{i_{L-1},i_L} \leq L - 1, && \text{Path Length Constraint} \\
&\qquad \forall L\text{-length paths} &&
\end{aligned}
$$

Note: a path is defined such that it cannot be a cycle.

3. Complexity

First, I will show the proof that KEP is generally a NP-complete problem.

THEOREM 1. *Given a graph $G = (V, E)$ and an integer $L \geq 3$, the problem of deciding if G admits a perfect cycle cover containing cycles of length at most L is NP-complete.*

PROOF. It is clear that this problem is in NP. For NP-hardness, we reduce from 3D-Matching, which is the problem of, given disjoint sets X, Y and Z of size q, and a set of triples $T \subseteq X \times Y \times Z$, deciding if there is a disjoint subset M of T with size q.

One straightforward idea is to construct a tripartite graph with vertex sets $X \cup Y \cup Z$ and directed edges (x_a, y_b), (y_b, z_c), and (z_c, x_a) for each triple $t_i = \{x_a, y_b, z_c\} \in T$. However, it is not too hard to see that this encoding fails because a perfect cycle cover may include a cycle with no corresponding triple.

Instead then, we use the following reduction. Given an instance of 3D-Matching, construct one vertex for each element in X, Y and Z. For each triple, $t_i = \{x_a, y_b, z_c\}$ construct the gadget in Figure 2, which is a similar to one in Garey and Johnson [5, pp 68-69]. Note that the gadgets intersect only on vertices in $X \cup Y \cup Z$. It is clear that this construction can be done in polynomial time.

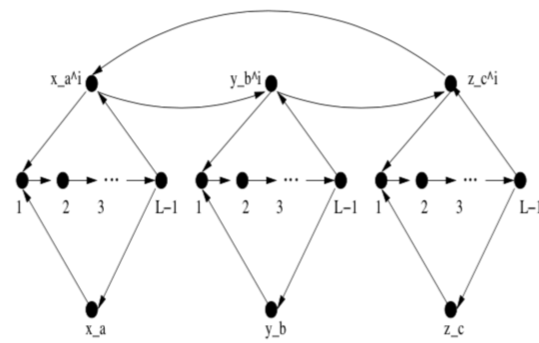

Figure 2: NP-completeness gadget for triple t_i and maximum cycle length L.

Let M be a perfect 3D-Matching. We will show the construction admits a perfect cycle cover by short cycles. If $t_i = \{x_a, y_b, z_c\} \in M$, add from t_i's gadget the three length-L cycles containing x_a, y_b and z_c respectively. Also add the cycle $\langle x_a^i, y_b^i, z_c^i \rangle$. Otherwise, if $t_i \notin M$, add the three length-L cycles containing x_a^i, y_b^i and z_c^i respectively. It is clear that all vertices are covered, since M partitions $X \times Y \times Z$.

Conversely, suppose we have a perfect cover by short cycles. Note that the construction only has short cycles of lengths 3 and L, and no short cycle involves distinct vertices from two different gadgets. It is easy to see then that in a perfect cover, each gadget t_i contributes cycles according to the cases above: $t_i \in M$, or $t_i \notin M$. Hence, there exists a perfect 3D-Matching in the original instance. □

Second, the LP relaxation of the cycle formulation weakly dominates the LP relaxation of the edge formulation, which means that the LP relaxation of the cycle formulation generates results that are in the worst case as good as those provided by the LP relaxation of the edge formulation. This is important because solving the integer programs for a kidney exchange at the nationwide scale is difficult because of memory and computational limitations, and efficient algorithms make use of the LP relaxations. Lastly, for a graph with m edges, the edge formulation requires $O(m^3)$ constraints and the cycle formulation requires $O(m^2)$constraints.

The various algorithms that can be used to solve the KEP in the format of edge formulation and cycle formulation are explicitly illustrated by papers in the reference section.

4. Discussion

Finally, I will briefly talk about an innovative approach that is considered as one of the most exciting achievement to the field of kidney transplant in 25 years, chain transplantation. In our real world, there are always altruistic living donors who do not require a kidney in return for friends or relatives. Such altruistic donors can be utilized to trigger multiple chain transplant instead of only cycles. There are two major advantages of chains approach over traditional paired donation.

First, chains do not rely on reciprocal matching. This enables each donor in the chain to be matched with the recipient that yields the best quality chain. This lack of reciprocity facilitates more transplants and drives better matching performance. For example, the probability of finding a ABO match for a recipient using traditional paired exchange (requiring a reciprocal match) is approximately 21% compared to 46% for a recipient in a chain.

Second, chains approach are more logical than traditional paired approach; and also more efficient in the case of small regional programs. Traditional paired exchange transplants are performed simultaneously to eliminate the possibility of donors withdrawing and resulting in a situation where a patient's donor donates a kidney to a pair and the patient does not get a one in return. Chain transplantation avoids this risky situation perfectly. If a donor withdraws in a chain, the next recipient in the chain suffers no harm as they still have their original incompatible donor and can still get in another chain. The fact that transplantations are performed simultaneously during paired exchanges places a tremendous burden on hospitals, operating rooms, surgeons, nurses, support staff and the patients. For example, a simultaneous 3-way paired exchange requires 3 well-trained donor surgeons, 3 recipient surgeons and 6 operating rooms. Very few transplant programs in the country can provide the surgeons and operating rooms to support this requirement. Conversely, a small center with one donor and recipient surgeon could complete a chain involving the same 6 patients much more easily. The altruistic donor donate to the first recipient on one day, the recipient's original incompatible donor then donate to the second recipient the following day and so forth.

Reference

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