Author's Commentary: The Outstanding Kidney Exchange Papers

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We all use math every day . . .

[start of the opening sequence of episodes of the TV series *Numb3rs*]

Introduction

The 2007 ICM Kidney Exchange Problem arose from discussions in my one-semester-hour seminar in Spring 2006 on the mathematics behind the TV series *Numb3rs*. The specific inspirational episode was "Harvest," which deals with bringing poor Third-World people to the U.S. for black-market sale of their kidneys ["Lady Shelley 2006].

In the "Harvest" episode, one such donor dies after the operation and another potential donor is missing. The mathematician star of the series cites "optimization theory developed at Johns Hopkins University to determine the best matches between organ donors and recipients." He and his colleagues use the blood type and HLA-compatibility of the sister of the missing woman to try to identify potential recipients, despite (according to them) there being only a one-fourth chance that the sister matches the missing woman. The team first checks the database of patients registered to receive a kidney, draws a blank, and then realizes that they are probably looking for a patient "who cannot obtain an organ in the normal way—so they wouldn't be on any official list." (We find out later that the black-marketeer patient has a "blood disorder that disqualifies him from getting a transplant.") Fortunately, the FBI finds a "potential list of customers" (with blood data) on a suspect's computer, the list has

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a unique “positive match,” and the missing girl is rescued just as she is to be operated on.

The remark about Johns Hopkins reminded me of earlier mention of that research in *SIAM News* [Cipra 2004]. Searching on the Web brought me quickly to the Web pages of Sommer Gentry that introduce her research on the mathematics behind optimizing kidney paired donation [2005].

Here I focus on algorithms for matching donors to kidneys, with particular focus on the work of Alvin E. Roth of the Harvard Business School and his associates.

The Problem

The problem involved a variety of tasks that spanned many interdisciplinary aspects—it is a very complex problem—and teams needed to be aware of the contest guideline that “Partial solutions are acceptable.” (In fact, virtually all solutions were by nature partial.) Because of the number of tasks and their difficulty, I did not expect so many teams (273 of the 1222 completing the ICM/MCM) to tackle this problem. But then I also did not expect a 26% increase in participation in the contests, either. The proportion of teams selecting the ICM problem was about the same as in 2006.

Matching Kidneys to Patients

Kidneys from Cadavers

Kidneys become available as people die and must be transplanted very shortly after death. Thus, the problem is dynamic, and a priority scheme is needed to determine the recipient of such a cadaver kidney. Such a scheme could be provided by regulation (e.g., the Organ Procurement and Transplantation Network (OPTN) in the U.S.) or by compensation (e.g., a market for kidneys).

Living Donors

Suppose that we have a group of patients in need of kidneys and a group of altruistic living people each willing to donate a kidney to any patient.

We can model the situation as a bipartite graph, with patients in one part of the graph and donors in the other. An edge joins each donor to each patient for whom the kidney would be suitable. The graph has n vertices (patients plus donors) and m edges (corresponding to feasible donations). A greedy algorithm, using the concepts of *alternating path* and *augmenting path*, finds a matching with the most matches (called a *maximum (cardinality) matching*) in $\mathcal{O}(mn)$ time. Saip and Lucchesi [1993, 5] note other sequential algorithms offering different complexity, as well as parallel algorithms.

This matching "saves" the most patients possible but relies on the altruism of people to become donors.

Quality of Match

A refinement would be to assess the "value" of each match, in terms of a single number incorporating

- medical quality (match on ABO blood type, HLA markers, and Panel Reactive Antibody (PRA)),
- individual desirability (among other aspects, preferences for different quality kidneys and travel distance to the operation), and
- social desirability, perhaps in terms of QALY—quality-adjusted life years [Gold et al. 1996; Phillips and Thompson 2001] and a measure of equity (see Zenios et al. [2000]).

The value of the match can be incorporated into the model as a weight for the edge, and the graph-theoretic problem generalizes to finding a matching that

- maximizes the sum of the edge weights; or, alternatively,
- among all maximum cardinality matchings, maximizes the sum of the edge weights.

The reason to distinguish these two situations is that maximizing the sum of edge weights might result in fewer than the maximum possible number of matches: We might get better matches but "save" fewer patients.

The first kind of matching can be realized through the Hungarian algorithm of Kuhn (1955) in $\mathcal{O}(mn^2)$ time, and the second by an algorithm of Edmonds and Karp (1972) in $\mathcal{O}(mn \log n)$ time. Again, Saip and Lucchesi [1993, 5] note other sequential algorithms offering different complexity, as well as parallel algorithms.

Like a priority scheme for allocation of cadaver kidneys, incorporation of any measure of social desirability of a match is a political question. Mathematicians can only highlight the tradeoffs for various schemes.

Dynamism

Both the cadaver situation and the living donor situation are dynamic, in that the optimal matching may change (perhaps drastically) with entry or withdrawal of a donor or patient.

Kidney Paired Donation (KPD)

In kidney paired donation, a patient with a willing but incompatible donor is matched with another patient/donor pair such that the donor of each pair is compatible with the recipient of the other pair.

Matching Model

A bipartite graph is not an appropriate model, since the matching now demands that if donor/patient pair i donates to pair j, then j must donate to i. A general graph is called for. Gentry and Segev [2005] display such a graph with the vertices in a circle and edges as chords, which can be weighted.

The algorithms for finding optimal matchings in a bipartite graph require some tweaking to handle a general graph. Edmonds's algorithm (1965) finds a maximum cardinality matching in $\mathcal{O}(mn^2)$ time, while that of Blum (1990) finds one in $\mathcal{O}(mn^{1/2})$ time. An algorithm of Galil, Micali, and Gabow solves the edge-weighted problem in $\mathcal{O}(mn \log n)$ time [Saip and Lucchesi 1993, 14]. In the "Math Behind *Numb3rs*" seminar, we worked through the Edmonds algorithm and its proof but found that hand implementation of it on even small graphs—necessary for really understanding it—was unwieldy.

The idea for kidney paired donation originated with Rapaport [1986] and was first implemented in Korea [Park et al. 1991]. In the U.S., about 150 such transplants have been performed.

How Much Difference Could KPD Make?

How much difference could kidney paired donation make? In June 2007, there were 72,000 individuals awaiting kidneys, at 270 centers, an average of 270 per center [Organ Procurement . . . 2007]. Of those 270, according to the team from Princeton University, 10%–15%, or 27 to 40, have a willing but incompatible donor. A simulation by Roth et al. [2005a] shows that in a population of 25 donor-patient pairs (where the pair may or may not be compatible), on average 12 patients receive a kidney from their own associated compatible donor, but an additional 4 could receive a kidney with paired donation. In a larger population of 100 donor-patient pairs, the corresponding numbers are 47 from their own donor and an additional 23 from paired donation. These data suggest that *one-third to one-half more live kidney transplants could take place with widespread implementation of kidney paired donation*.

Well, how many is that and how much difference would it make? In 2006, there were 17,100 transplants in all, of which 6,435 were live transplants; one-third to one-half more of the latter would be 2,100 to 3,200. That would not be enough to turn the tide: Over the course of 2006, the waiting list for a kidney grew by 6,100 (to 72,200), despite 4,200 leaving the list by dying [Organ Procurement . . . 2007].

Donation Circles

The idea of kidney paired donation generalizes naturally to n-way circular exchanges, in which each donor-patient pair donates to another in the circle and in turn receives a donation from a pair in the circle. A few 3-way exchanges have taken place, and one 5-way exchange has been performed [Ostrov 2006].

Roth et al. [2005b] explain how 3-way exchanges offer further benefits beyond 2-way exchanges, and why going to 4-way exchanges has very limited further value (because of the rarity of the AB blood type). They calculate upper bounds, based on national data for blood types and PRA, for the effect of n-way exchanges. These bounds agree well with their simulations, which used "various integer programming techniques" for optimization in the case of greater than 2-way exchanges. In a population of 25 *incompatible* donor-patient pairs, on average 9 patients can receive a kidney via 2-way exchange, and 2 more via 3-way exchanges. In a population of 100 donor-patient pairs, the corresponding numbers are 50 via 2-way and an additional 10 via 3-way. Allowing 4-way or larger circles has negligible additional benefit.

In fact, Roth et al. prove under mild conditions—mainly, that the population of donor-patient pairs is large—the remarkable result that "4-way exchange suffices": If there is a matching with the maximum number of patient-donor pairs, with no restriction on the size of exchanges, then there is a matching involving the *same* pairs that uses only 2-way, 3-way, and 4-way exchanges. (Perhaps the 5-way exchange in 2006 could not have been reduced to smaller exchanges because of too few donor-patient pairs at that transplant center.)

A Kidney Is Like a House

Roth et al. [2004] cite an analogy between a housing market, as modeled by Shapley and Scarf [1974], and the "kidney transplant environment":

> [There are] n agents, each of whom is endowed with an indivisible good, a "house." Each agent has preferences over all the houses (including his own), and there is no money in the market, trade is feasible only in houses . . . [I]f we consider exchange only among patients with donors, the properties of the housing market model essentially carry over unchanged . . . .

Top Trading Cycles Algorithm

The authors note that Shapley and Scarf attribute to David Gale a particular algorithm for clearing such a market, called the *top trading cycle (TTC)* algorithm:

> Each agent points to her most preferred house (and each house points to its owner). Since the number of houses is finite and since each house has an owner, there is at least one cycle in the resulting directed graph. In each such cycle, the corresponding trades are carried out, i.e. each agent

in the cycle receives the house she is pointing to, and these agents and houses are removed from the market.

The remaining agents express new preferences and the procedure is iterated recursively. This system cannot be "gamed": The algorithm results in an allocation in which no coalition could have done better by trading among themselves, and it is in each agent's best interest to express true preferences [Roth 1982]. Roth et al. [2004] show that the TTC mechanism is the unique mechanism that is "individually rational, [Pareto-]efficient, and strategy-proof."

TTC has further applications to other important current problems of allocation or matching, such as college admissions, student placement, and school choice [Kesten 2004; Sönmez 2005].

Combining Cadavers and Living Donors

The top trading cycles algorithm would suffice for allocating kidneys among patients with willing but incompatible donors, via kidney paired exchange and kidney circles.

A complicating factor is that the kidney transplant environment also contains "unowned" cadaver kidneys. This situation corresponds to what Abdulkadiroğlu and Sönmez [1999] call the *housing allocation problem with existing tenants*—which, to the intrigue of the students in the *Numb3rs* seminar, was exactly the problem that they were facing at the time of our study: room draw for dorm rooms.

Abdulkadiroğlu and Sönmez critique the mechanism commonly used by colleges (including my institution, Beloit College), which they dub *random serial-dictatorship with squatting rights*. Under this system, a student may elect to keep their current dorm room ("squat" it) for next year and thus opt out of the dorm-room lottery. The major deficiency is that a student who foregoes keeping their current room and enters the lottery may wind up with a worse room.

You Request My House—I Get Your Turn

Abdulkadiroğlu and Sönmez consequently generalize the top trading cycles mechanism to a procedure that they call *you request my house—I get your turn (YRMH–IGYT)*. All students indicate their preferences, all are in the lottery, and turns are chosen at random. If a student whose turn comes wants your room (and you have not already had your turn), you get the very next turn before they get to choose. So you can always keep your room if all the "better" rooms are gone.

This seems like a great idea, one that could be completely automated; but the *Numb3rs* students and I had to reflect on the difficulties of changing a procedure well-established at the College. That procedure absorbs several days of staff time sitting for appointments with students coming to select rooms, not to mention students bolting out of classes to meet their appointments. We could see no good way to assess the likely level of improvement in overall student satisfaction, apart from just trying YRMH–IGYT for a year's room draw. However, Chen and Sönmez [2002; 2004] offer results of small-scale experiments.

At first, YRMH–IGYT would seem to be an easy sell to students: You can't be any worse off than you already are or could be under the current system. But it seemed to us that if all students had the same rankings for rooms, then the advantages of YRMH–IGYT accrue to students already in "good" rooms: If instead of "squatting" their current "good" room under the current system, they enter the YRMH–IGYT lottery and do better by taking "top" rooms, it is in some sense at the expense of other students for whom those "top" rooms are then not available. Yilmaz [2005] offers a further critique of the fairness of TTC; shows the incompatibility of fairness ("no justified envy"), individual rationality, and strategy-proofness; and offers his own algorithm.

Kidney Analogy: LPD

The kidney transplantation community independently invented YRMH–IGYT (dubbing it "indirect exchange," now more commonly known as *list paired donation (LPD)*): A patient's willing but incompatible donor donates to the highest-priority compatible patient on the cadaver waitlist; in return, the donor's intended recipient goes to the top of that list [Roth et al. 2004]. However, analogous to a student being reluctant to enter the dorm-room lottery for fear of losing their current "good" room, a donor may be unwilling to donate unless the donor's intended recipient gets a kidney at least as good as the donor's.

Roth et al. itemize the differences between the housing market and the kidney environment. The main difference is the dynamism that we mentioned earlier: No one knows when or what quality kidneys will become available on the cadaver queue, and such kidneys must be allocated and transplanted immediately. "Therefore, a patient who wishes to trade his donor's kidney in return for a priority in the cadaveric waiting list is receiving a *lottery* instead of a specific kidney" [2004].

Top Trading Cycles and Chains

Roth et al. introduce the *top trading cycles and chains (TTCC)* mechanism for kidney exchange, a recursive procedure that generalizes TTC. Each patient points toward a kidney or toward the cadaver queue, and each kidney points a paired recipient. In addition to cycles, this directed graph can also feature *w-chains*. A *w-chain* is a directed path on which kidneys and patients alternate and which starts at a kidney and ends at a patient pointing to the cadaver queue The result is a chain to the "waitlist," hence the "w" in the name "w-chain." Such chains correspond to generalized indirect exchanges: The kidneys can be allocated to their immediate successor patients, with the last patient getting a high place on the cadaver queue. As before with TTC, we can resolve and remove cycles; now we can also resolve and remove w-chains, perhaps preferably w-chains of maximal length (or perhaps not, for logistical reasons). But since a kidney or a patient can be part of several w-chains, there is a policy dimension needed to complete the algorithm, and Roth et al. discuss several conceivable chain-selection rules. They characterize TTCC using a particular class of rules as Pareto-efficient and TTCC with certain specific rules as strategy-proof.

Segev et al. [2005] and Gentry et al. [2005] examine optimal use of kidneys through kidney paired donation in association with list paired donation.

Future Prospects

Kidney paired donation, plus 3-way donations, plus TTCC, offer prospects for reducing the growth of the kidney waiting list and saving the vast cost of dialysis for patients on it.

Roth et al. [2004] offer simulation results that demonstrate for a population of 30 donor-candidate pairs:

- The rate of utilization of potential-donor kidneys goes from 55% to 69% with kidney paired exchange (this result roughly confirms that of the team from Duke University) and to 81–85% under the TTCC mechanism with varying chain-selection rules.

- TTCC decreases the average HLA mismatch from 4.8 to 4.2–4.3.

- The average cycle size is 2.5–3 pairs and the average w-chain size is 1.8–2 pairs.

Larger numbers of pairs (Roth et al. give results for 100 and 300) result in (on average) higher utilization rates, lower HLA mismatch, and longer cycles and chains.

Roth et al. go on to describe the advantages of TTCC over current kidney exchange programs.

Operations researchers (as some economists are, too) must always consider not just the problem of optimization but that of selling an improved solution. In particular, operations researcher Robert E.D. "Gene" Woolsey (Colorado School of Mines) cast as his First Law: "A manager would rather live with a problem he cannot solve than accept a solution he does not understand" [2003]. Implementing new kidney exchange procedures on a wide scale would require suitable legislation, coordination of databases, and education of patients and potential donors.

Finally, different blood types between willing donor and patient may not be an absolute obstacle in the future. In September 2006, a type-A wife donated to a type-B husband, a transplant that "was made possible by desensitization, a process that removed [rejection] antibodies from [the husband's] blood and kept them away with medication" [Wausau couple . . . 2006]. Segev et al. [2006] recommend pursuing desensitization, because

> even in a large-cohort live donor match, approximately half of the patients remain unmatched . . . . There is subsequently little additional benefit to placing difficult-to-match patients into a list exchange program.

What about a market for kidneys? The team from Princeton University explores the economics of this possibility. They dismiss the option of a government-managed program on the basis of their conviction that government management implies bureaucratic inefficiency and slowness; but surprisingly, after touting the relative advantages of a free market in kidneys, in their conclusion they reject that, too, because of the danger of discriminatory pricing. Roth [2007] reflects on general repugnance to certain economic efficiencies, including a market for kidneys.

Conclusion

I previously wrote about the potential and sources for using the *Numb3rs* TV series as a way to draw college students into appreciation of mathematics [Campbell 2006]. Instructors may find doing so more feasible with the advent in fall 2007 of a potential "textbook" for a course or seminar based on the series [Devlin and Lorden 2007].

My experience demonstrated to me that such a course also offers the instructor an opportunity to serendipitously expand horizons—to learn and engage with more mathematics as it manifests itself in life. I am glad that the TV series, its "Harvest" episode, and the course also led to the ICM Kidney Exchange Problem; I have enjoyed learning a great deal about an interdisciplinary congeries of mathematics, algorithms, medical practice, economics, public policy, and ethics.

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