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Decision Models
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A Speed Read:
WHERking to Meet the Need for Kidneys with NEAD Chains

Project: Kidney Exchange

Overview

Of the over 122,000 Americans waiting for an organ transplant, more than 101,000 of these people are end-stage renal disease (ESRD) sufferers and specifically in need of a kidney. Less than 17,000 of ESRD patients receive a kidney each year. Every 24 hours, 12 people die while still waiting for a kidney.[1] With the waiting list increasing at about 7,000 patients per year, ESRD is one of the most expensive health treatments.

Everyone is born with two kidneys, but can survive with just one. Thus, when a patient is in desperate need of a kidney transplant, his or her relatives or friends are often willing to donate. However, the patient's relatives and friends are often not biological matches, in which case, the patient must find another pair — a patient and donor who also failed to match one another — to match with for a kidney swap.

Through operations research, the Alliance for Paid Donation (APD) has successfully developed an alternative method known as non-simultaneous extended altruistic (NEAD) chains in order to optimize the matching of donors to patients, and subsequently, increase the number of kidney transplants each year. NEAD chains begin with a kidney donation from an altruistic non-directed donor (NDD), a living donor who does not have a partner requiring a kidney in return. As a result, NEAD chains eliminate the need to engage in traditional kidney exchanges, which require simultaneous surgeries. As a testament to the effectiveness of NEAD chains, the APD has saved over 220 lives since its implementation of the method.

Overall, the two focuses of our project will be:
1. Determining a network of potential donors
2. Deriving optimal chain lengths

[1] "Organ Procurement and Transplantation Network." *Data*. 2014. Web. 1 Dec. 2015.

The Problem

Availability of Biological Matches

In order for a donor to give a kidney to a recipient, they must be a suitable match. Suitability is initially based on two factors: blood type and tissue type. Both the recipient's blood type and tissue type must be compatible with the donor's blood type and tissue type in order for a transplant to take place (*Figure 1a*, *1b*).

A tissue match depends on human leukocyte antigen (HLA) typing. HLA is a genetic protein marker situated on the outside of white blood cells; each individual has a combination of eight possible HLA markers, and most transplant centers require donors and recipients to have a match of at least six or seven out of the eight[2]. A greater number of matching HLA factors the donor has with the recipient increases the longevity of the donated kidney. Unfortunately, the reality is that 70% of patients in need of a transplant do not have a suitable HLA match within his or her family.

If blood type and tissue type match, then the third factor, antibodies, is evaluated using Panel Reactive Antibody (PRA) scores. PRA is a common immunological test performed on patients awaiting organ transplantation. PRA scores measure matching HLA factors and antibodies between potential donors and recipients; simply put, the higher a patient's PRA, the more likely the patient's immune system will attack and reject the transplanted organ. Thus, a small sample of blood from the donor is often implanted into the recipient to affirmatively test for rejection reactions.[3]

Availability of Kidney Donors

Kidneys are available from deceased donors or from living persons. ESRD patients then have two options: 1) stay on the deceased waitlist and hope for a match, or 2) search for a living donor. It is generally preferred to receive a kidney from a living donor, as the kidney lasts [insert info from the article on how much longer a kidney from a living person lasts].

Traditionally, kidney exchanges with living donors are cycles that function much like a bartering system — a swap must take place in order for the recipients of two pairs to receive the kidneys. In essence, the two pairs must have two matches: given Pair A (Donor A + Recipient A) and Pair B (Donor B + Recipient B), the Recipients will only receive kidneys if Donor A matches Recipient B, and Donor B matches Recipient A. Furthermore, law requires these sorts of

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[2] "HLA Matching." *HLA Matching*. 2015. Web. 1 Dec. 2015.
[3] "The Waiting List." *The Waiting List*. Kidney Link, 2015. Web. 8 Dec. 2015.

transplants to be done simultaneously (Pair A and Pair B would require four surgery rooms and four surgeons) to ensure that no party is left without the kidney he or she was intended to receive.

The need for two matches among two pairs greatly reduces the number of potential transplants that can take place. Additionally, the requirement of simultaneous surgeries makes kidney transplants both costly and inefficient for hospitals.

Size of Paired Kidney Network

The New England Program for Kidney Exchange (NEPKE) was established in 2004 and was one of the first programs to implement algorithms for a kidney exchange. Today, it has been found that the success of finding matches for previously incompatible pairs greatly increases the size of the pool. There are multiple databases that collect different measures for each kidney donor and recipient, but these measures differ for each database.

There is a great need for operations analysts to choose which factors lead to the highest percentage of success in organ transplants and implement only those specific factors into their models.

The Model's Methodology

Generation of Random Pairs

The high sensitivity and privacy of data involving real patients prevented us from working with actual data. Thus, in order to simulate the effects of a NEAD chain, we created our own data by using a custom distribution of blood and tissue type (*Figure 2a, 2b*) on Crystal Ball to generate 20 random pairs and one NDD. To focus the scope of our simulation on live kidney exchanges, we assumed the NDD to be an altruistic, living donor.

Create a Network by Extracting Potential Pair Matches

We wrote a macro to create our network map (i.e. show all potential matches and create a "Donating Pair" and "Receiving Pair" column) based on blood and tissue type compatibility (*Figure 1a, 1b*).

```
Function checkFeasibility(Donor As String, Recipient As String)
   Select Case Donor
      Case "A"
         If Recipient = "A" Or Recipient = "AB" Then checkFeasibility = 1
      Case "B"
         If Recipient = "B" Or Recipient = "AB" Then checkFeasibility = 1
      Case "AB"
         If Recipient = "AB" Then checkFeasibility = 1
      Case "O"
         If Recipient = "A" Or Recipient = "B" Or Recipient = "AB" Or Recipient = "O" Then
checkFeasibility = 1
      Case "Frequent"
         If Recipient = "Frequent" Then checkFeasibility = 1
      Case "Rare"
         If Recipient = "Rare" Or Recipient = "Frequent" Then checkFeasibility = 1
   End Select
End Function
```

Due to the complexity of HLA matches and PRA scores discussed earlier, we simplified the scenario by assigning only two possible tissue types — rare and frequent — with a distribution of 10% and 90% respectively (*Figure 2b*).

Maximum Flow Optimization

Decision variables

$$Y_{i,j} \begin{cases} 1 \text{ if pair } i \text{ donates a kidney to pair } j \\ 0 \text{ if pair } i \text{ does not donate to pair } j \end{cases}$$

Objective function

$$maximize \sum_{i=1}^{no.\ of\ pairs} Y_{i,j} \text{ for all } j$$

Maximize the number of kidneys donated, given the number of generated possible (potential) pair matches

Constraints

$$\sum_{i=1}^{no.\ of\ pairs} Y_{NDD,j} - \sum_{i=1}^{no.\ of\ pairs} Y_{j,NDD} = 1$$ Non-directed donor must donate first

$$\sum_{i=1}^{no.\ of\ pairs} Y_{i,j} - \sum_{i=1}^{no.\ of\ pairs} Y_{j,i} = 0$$ Inter-nodes conservation of flow

$$\sum_{i=1}^{no.\ of\ pairs} Y_{end\ pair,j} - \sum_{i=1}^{no.\ of\ pairs} Y_{j,end\ pair} = -1$$ End of chain — last pair does not donate

$$\sum_{i=1}^{no.\ of\ pairs} Y_i \div \sum_{i=1}^{no.\ of\ pairs} i \leq 1 \div \sum_{i=1}^{no.\ of\ pairs} i$$ Each pair can only donate one kidney

[For the stochastic model, we would also set the constraint that the feasibilities of matching pair i *to pair* j *must be greater than or equal to the decision variables, so the optimization would only run for those matches that the macro deemed feasible.]*

The Implemented Model

*screenshots encompass gist of the implemented model, as it was too long to paste all of it

Pair Generation

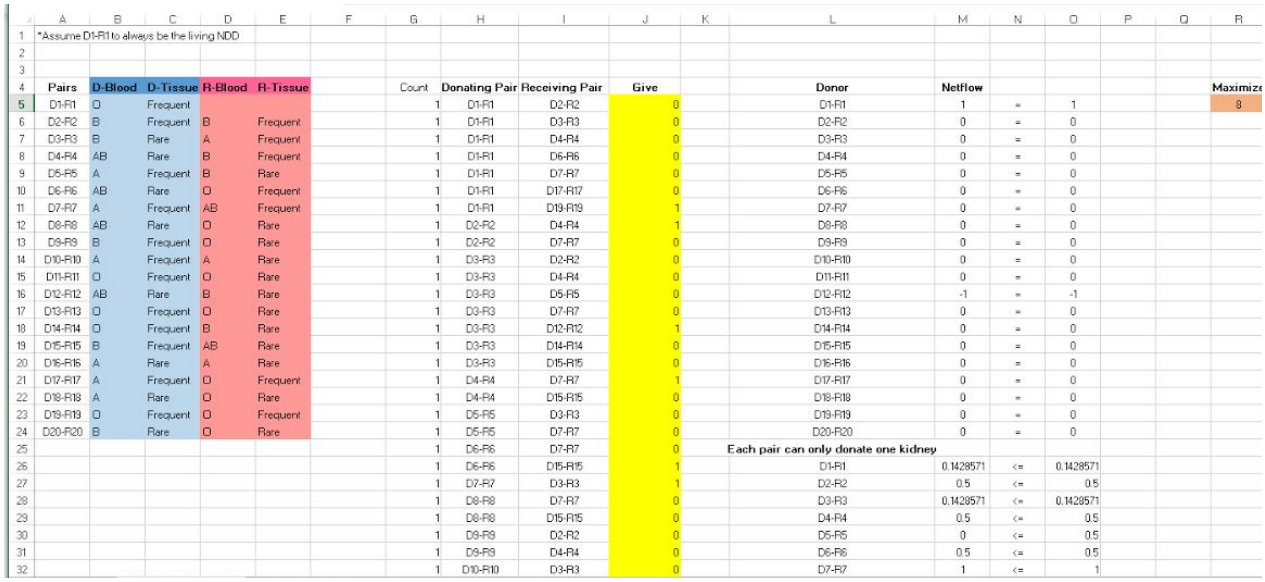
	A	B	C	D	E	F	G	H	I
1	Bucket	Blood Type	Frequency		Bucket	Tissue Type	Frequency		
2	1	O	0.4814		1	Rare	0.1		
3	2	A	0.3373		2	Frequent	0.9		
4	3	B	0.2814						
5	4	AB	0.0385						
6									
7	DonorB	D-Blood	DonorT	D-Tissue		RecipientB	R-Blood	RecipientT	R-Tissue
8	2	A	1	Rare		3	B	1	Rare
9	1	O	1	Rare		1	O	2	Frequent
10	2	A	2	Frequent		4	AB	1	Rare
11	2	A	2	Frequent		4	AB	1	Rare
12	2	A	1	Rare		2	A	2	Frequent
13	3	B	2	Frequent		4	AB	1	Rare
14	1	O	1	Rare		3	B	1	Rare
15	4	AB	1	Rare		2	A	1	Rare
16	1	O	1	Rare		2	A	2	Frequent
17	3	B	1	Rare		1	O	1	Rare
18	2	A	2	Frequent		4	AB	1	Rare
19	3	B	1	Rare		2	A	1	Rare
20	1	O	1	Rare		1	O	2	Frequent
21	2	A	1	Rare		3	B	1	Rare
22	4	AB	1	Rare		4	AB	2	Frequent
23	1	O	2	Frequent		3	B	2	Frequent
24	2	A	2	Frequent		1	O	1	Rare
25	4	AB	2	Frequent		3	B	2	Frequent

Create a Network by Extracting Potential Pair Matches

4	Pairs	D-Bloo	D-Tissu	R-Bloo	R-Tissue		Donor Pair Name	Receiver Pair Name	D-Blood	D-Tissue	R-Blood	R-Tissue	Blood Feasibility	Tissue Feasibility	Pair Feasibility	Total Feasible Pairs
5	D1-R1	B	Frequen	B	Rare		D1-R1	D2-R2	B	Frequent	B	Frequent	1	1	1	147
6	D2-R2	B	Rare	B	Frequent		D1-R1	D3-R3	B	Frequent	B	Frequent	1	1	1	
7	D3-R3	O	Frequen	B	Frequent		D1-R1	D4-R4	B	Frequent	O	Frequent	0	1	0	
8	D4-R4	A	Rare	O	Frequent		D1-R1	D5-R5	B	Frequent	AB	Rare	1	0	0	
9	D5-R5	A	Rare	AB	Rare		D1-R1	D6-R6	B	Frequent	O	Rare	0	0	0	
10	D6-R6	B	Frequen	O	Rare		D1-R1	D7-R7	B	Frequent	AB	Rare	1	0	0	
11	D7-R7	B	Rare	AB	Rare		D1-R1	D8-R8	B	Frequent	B	Rare	1	0	0	
12	D8-R8	AB	Rare	B	Rare		D1-R1	D9-R9	B	Frequent	AB	Rare	1	0	0	
13	D9-R9	A	Frequen	AB	Rare		D1-R1	D10-R10	B	Frequent	O	Frequent	0	1	0	
14	D10-R10	O	Rare	O	Frequent		D1-R1	D11-R11	B	Frequent	AB	Frequent	1	1	1	
15	D11-R11	O	Frequen	AB	Frequent		D1-R1	D12-R12	B	Frequent	A	Rare	0	0	0	
16	D12-R12	A	Frequen	A	Rare		D1-R1	D13-R13	B	Frequent	A	Frequent	0	1	0	
17	D13-R13	B	Frequen	A	Frequent		D1-R1	D14-R14	B	Frequent	O	Rare	0	0	0	
18	D14-R14	B	Rare	O	Rare		D1-R1	D15-R15	B	Frequent	A	Rare	0	0	0	
19	D15-R15	O	Rare	A	Rare		D1-R1	D16-R16	B	Frequent	A	Frequent	0	1	0	
20	D16-R16	B	Frequen	A	Frequent		D1-R1	D17-R17	B	Frequent	A	Rare	0	0	0	
21	D17-R17	B	Frequen	A	Rare		D1-R1	D18-R18	B	Frequent	O	Rare	0	0	0	
22	D18-R18	A	Rare	O	Rare		D1-R1	D19-R19	B	Frequent	B	Rare	1	0	0	
23	D19-R19	A	Rare	B	Rare		D1-R1	D20-R20	B	Frequent	B	Rare	1	0	0	
24	D20-R20	B	Rare	B	Rare		D2-R2	D1-R1	B	Rare	B	Rare	1	1	1	
25							D2-R2	D3-R3	B	Rare	B	Frequent	1	1	1	
26							D2-R2	D4-R4	B	Rare	O	Frequent	0	1	0	
27							D2-R2	D5-R5	B	Rare	AB	Rare	1	1	1	
28							D2-R2	D6-R6	B	Rare	O	Rare	0	1	0	
29							D2-R2	D7-R7	B	Rare	AB	Rare	1	1	1	
30							D2-R2	D8-R8	B	Rare	B	Rare	1	1	1	
31							D2-R2	D9-R9	B	Rare	AB	Rare	1	1	1	
32							D2-R2	D10-R10	B	Rare	O	Frequent	0	1	0	
33							D2-R2	D11-R11	B	Rare	AB	Frequent	1	1	1	

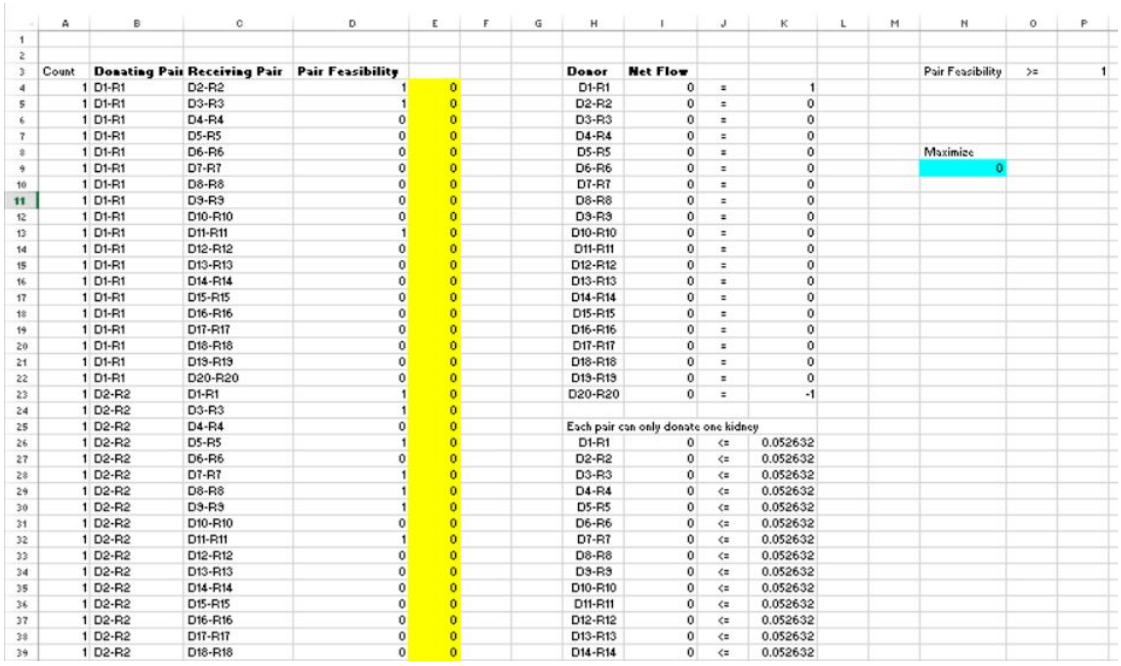
Maximum Flow Optimization

Static Model:



	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R
1	*Assume D1-R1 to always be the living NDD																	
2																		
3																		
4	Pairs	D-Blood	D-Tissue	R-Blood	R-Tissue		Count	Donating Pair	Receiving Pair	Give		Donor	Netflow					Maximize
5	D1-R1	O	Frequent				1	D1-R1	D2-R2	0		D1-R1	1	=	1			8
6	D2-R2	B	Frequent	B	Frequent		1	D1-R1	D3-R3	0		D2-R2	0	=	0			
7	D3-R3	B	Rare	A	Frequent		1	D1-R1	D4-R4	0		D3-R3	0	=	0			
8	D4-R4	AB	Rare	B	Frequent		1	D1-R1	D6-R6	0		D4-R4	0	=	0			
9	D5-R5	A	Frequent	B	Rare		1	D1-R1	D7-R7	0		D5-R5	0	=	0			
10	D6-R6	AB	Rare	O	Frequent		1	D1-R1	D17-R17	0		D6-R6	0	=	0			
11	D7-R7	A	Frequent	AB	Frequent		1	D1-R1	D19-R19	1		D7-R7	0	=	0			
12	D8-R8	AB	Rare	O	Rare		1	D2-R2	D4-R4	1		D8-R8	0	=	0			
13	D9-R9	B	Frequent	O	Rare		1	D2-R2	D7-R7	0		D9-R9	0	=	0			
14	D10-R10	A	Frequent	A	Rare		1	D3-R3	D2-R2	0		D10-R10	0	=	0			
15	D11-R11	O	Frequent	O	Rare		1	D3-R3	D4-R4	0		D11-R11	0	=	0			
16	D12-R12	AB	Rare	B	Rare		1	D3-R3	D5-R5	0		D12-R12	-1	=	-1			
17	D13-R13	O	Frequent	O	Rare		1	D3-R3	D7-R7	0		D13-R13	0	=	0			
18	D14-R14	O	Frequent	B	Rare		1	D3-R3	D12-R12	1		D14-R14	0	=	0			
19	D15-R15	B	Frequent	AB	Rare		1	D3-R3	D14-R14	0		D15-R15	0	=	0			
20	D16-R16	A	Rare	A	Rare		1	D3-R3	D15-R15	0		D16-R16	0	=	0			
21	D17-R17	A	Frequent	O	Frequent		1	D4-R4	D7-R7	1		D17-R17	0	=	0			
22	D18-R18	A	Rare	O	Rare		1	D4-R4	D15-R15	0		D18-R18	0	=	0			
23	D19-R19	O	Frequent	O	Frequent		1	D5-R5	D3-R3	0		D19-R19	0	=	0			
24	D20-R20	B	Rare	O	Rare		1	D5-R5	D7-R7	0		D20-R20	0	=	0			
25							1	D6-R6	D7-R7	0		Each pair can only donate one kidney						
26							1	D6-R6	D15-R15	1		D1-R1	0.1428571	<=	0.1428571			
27							1	D7-R7	D3-R3	1		D2-R2	0.5	<=	0.5			
28							1	D8-R8	D7-R7	0		D3-R3	0.1428571	<=	0.1428571			
29							1	D8-R8	D15-R15	0		D4-R4	0.5	<=	0.5			
30							1	D9-R9	D2-R2	0		D5-R5	0	<=	0.5			
31							1	D9-R9	D4-R4	0		D6-R6	0.5	<=	0.5			
32							1	D10-R10	D3-R3	0		D7-R7	1	<=	1			

Potential Stochastic Model:



	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P
1																
2																
3	Count	Donating Pair	Receiving Pair	Pair Feasibility				Donor	Net Flow					Pair Feasibility	>=	1
4	1	D1-R1	D2-R2	1	0			D1-R1	0	=	1					
5	1	D1-R1	D3-R3	1	0			D2-R2	0	=	0					
6	1	D1-R1	D4-R4	0	0			D3-R3	0	=	0					
7	1	D1-R1	D5-R5	0	0			D4-R4	0	=	0					
8	1	D1-R1	D6-R6	0	0			D5-R5	0	=	0			Maximize		
9	1	D1-R1	D7-R7	0	0			D6-R6	0	=	0			0		
10	1	D1-R1	D8-R8	0	0			D7-R7	0	=	0					
11	1	D1-R1	D9-R9	0	0			D8-R8	0	=	0					
12	1	D1-R1	D10-R10	0	0			D9-R9	0	=	0					
13	1	D1-R1	D11-R11	1	0			D10-R10	0	=	0					
14	1	D1-R1	D12-R12	0	0			D11-R11	0	=	0					
15	1	D1-R1	D13-R13	0	0			D12-R12	0	=	0					
16	1	D1-R1	D14-R14	0	0			D13-R13	0	=	0					
17	1	D1-R1	D15-R15	0	0			D14-R14	0	=	0					
18	1	D1-R1	D16-R16	0	0			D15-R15	0	=	0					
19	1	D1-R1	D17-R17	0	0			D16-R16	0	=	0					
20	1	D1-R1	D18-R18	0	0			D17-R17	0	=	0					
21	1	D1-R1	D19-R19	0	0			D18-R18	0	=	0					
22	1	D1-R1	D20-R20	0	0			D19-R19	0	=	0					
23	1	D2-R2	D1-R1	1	0			D20-R20	0	=	-1					
24	1	D2-R2	D3-R3	1	0											
25	1	D2-R2	D4-R4	0	0			Each pair can only donate one kidney								
26	1	D2-R2	D5-R5	1	0			D1-R1	0	<=	0.052632					
27	1	D2-R2	D6-R6	0	0			D2-R2	0	<=	0.052632					
28	1	D2-R2	D7-R7	1	0			D3-R3	0	<=	0.052632					
29	1	D2-R2	D8-R8	1	0			D4-R4	0	<=	0.052632					
30	1	D2-R2	D9-R9	1	0			D5-R5	0	<=	0.052632					
31	1	D2-R2	D10-R10	0	0			D6-R6	0	<=	0.052632					
32	1	D2-R2	D11-R11	1	0			D7-R7	0	<=	0.052632					
33	1	D2-R2	D12-R12	0	0			D8-R8	0	<=	0.052632					
34	1	D2-R2	D13-R13	0	0			D9-R9	0	<=	0.052632					
35	1	D2-R2	D14-R14	0	0			D10-R10	0	<=	0.052632					
36	1	D2-R2	D15-R15	0	0			D11-R11	0	<=	0.052632					
37	1	D2-R2	D16-R16	0	0			D12-R12	0	<=	0.052632					
38	1	D2-R2	D17-R17	0	0			D13-R13	0	<=	0.052632					
39	1	D2-R2	D18-R18	0	0			D14-R14	0	<=	0.052632					

Analysis

Our model solution optimized our network graph by finding a chain of length 8, a success rate of 8/20 = 40%. By restricting donor pair D1-R1 as the altruistic living donor (flow out 1) and the donor pair D12-R12 as an arbitrary "sole receiver" (flow out -1), we ended up with the following chain:

D1-R1 to D19-R19
D19-R19 to D6 R6
D6-R6 to D15-R15
D15-R15 to D2-R2
D2-R2 to D4-R4
D4-R4 to D7-R7
D7-R7 to D3-R3
D3-R3 to D12-R12

Our dataset was of 20 patients pairs, with each patient pair representing a random blood type and random tissue type picked from custom defined probability distributions described above in the paper.

By generating other random samples, our program can solve for optimal chains in other unique graphs as well. Though we ultimately could not incorporate the stochastic process, we were able to generate stochastic data. From the process, we observed that if we were able to automate this process, we would be able to determine more interesting metrics such as convergence rates for optimal chain lengths, impact of the altruistic donor's blood and tissue types on the creation of the chain (i.e. if the starting donor had blood type A tissue type R instead of blood type O tissue type F, how would it affect the optimal chain choice and success rate?).

Conclusion

Our model demonstrates that it can show the chain length of an optimized network graph. Our main limitation was integrating our stochastic data with our network optimization model. We were able to analyze a snapshot of sample data, but incorporating stochastic data would have allowed us to find even more interesting insights.

The model can be further expanded by adding further layers of complexity we did not incorporate due to limitations in our data and medical knowledge. For example, we could incorporate weights representing pair match difficulty into our graph in order to customize our optimization further. Furthermore, taking tissue compatibility from two discrete variables,

frequent and rare, to a continuous variable, such as PRA percentage, would give even more customization for doctors to generate more data tailored graphs. An interesting mathematical problem posed from such a model would be the comparison of incorporating PRA levels as weights versus deletion of random edges. Though both are consistent with modeling PRA levels into the graph, a deterministic approach rather than a random approach may be more comforting to patients psychologically.

The field of paired kidney exchange can be improved by prolonging the lives of patients who are waiting to receive an organ transplant. This increases the pool of potential matches. Extending the life of patients can be done by novel plasma exchange therapies. The data from paired kidney exchange networks can be used to transfer plasma from a donor to multiple recipients. If one donor matches with three recipients, only one recipient can receive the kidney. However, with plasma exchange, the two other matching recipients can receive the donor's plasma. Data shows that this extends patients' lives up to three years.[4] Limitations to this suggestion are the willingness of patients to change from dialysis to plasma transplants. There are also financial limitations, and the patient must be in a good state of health.

Another suggestion to improve paired kidney exchange is desensitization. When kidneys are correctly matched using blood type, it is possible to override negative crossmatch results caused by antibodies. Immunoadsorption (IA) and anti-CD20 antibody induction can be jointly used to suppress strong donor-specific antibodies. This increases the number of possible matches for donors and can allow recipients with hard-to-match blood types and PRA weights to find a match. An algorithm exists that leads to elimination of donor-specific antibodies with a low chance for side effects.[5] Limitations for this method are that depending on age, health condition, and financial stability, this may not be a suitable solution for all patients.

In conclusion, there are a number of algorithmic and medical considerations that could add to the model.

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[4] Hamilton, Patrick, Olumide Ogundare, Ammar Raza, Arvind Ponnusamy, Julie Gorton, Hana Alachkar, Jamil Choudhury, Jonathan Barratt, and Philip A. Kalra. "Long-Term Therapeutic Plasma Exchange to Prevent End-Stage Kidney Disease in Adult Severe Resistant Henoch-Schonlein Purpura Nephritis." *Case Reports in Nephrology* (2015): 1-5. Print.

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Appendix

Figure 1a: Blood Compatibility

Donor blood type	**Possible recipient blood types**
O	O, A, B, AB
A	A, AB
B	B, AB
AB	AB

Figure 1b: Tissue Compatibility

Tissue Type	**Possible recipient tissue types**
Frequent	Frequent
Rare	Rare, Frequent

Figure 2a: Distributions of Blood Type[6]

Blood Type	**Frequency**
O	48.14%
A	33.73%
B	14.28%
AB	3.85%

Figure 2b: Distributions of Tissue Type [Simplified Assumption]

Tissue Type	**Frequency**
Frequent	90.00%
Rare	10.00%

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