

Efficient and Incentive-Compatible Liver Exchange

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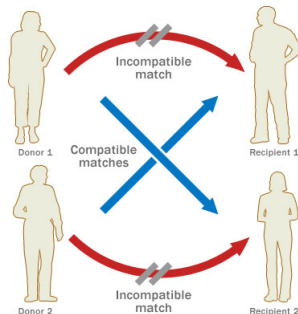
Boston College

Arrow Lecture

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- **Kidney Exchange** became a mainstream transplantation modality within the last fifteen years.
- Annually, more than 700 patients in the US receive kidney transplants through donor exchange.
- In theory **living-donor organ exchange** can be utilized for any organ for which living donation is feasible.
- Liver is the second most transplanted organ following the kidney.
- Living donation of a lobe of liver is widespread, especially in Asia.

Kidney Exchange



- Human organs cannot be received or given in exchange for "**valuable consideration**" (US, NOTA 1984, WHO)
- However, living-donor kidney exchange is not considered as "valuable consideration" (US NOTA amendment, 2007)

- **Kidney Exchange Literature: Plenty...**
- **Liver Exchange Literature:**
 - Hwang et al. [10] proposed the idea and documented the practice in Korea since 03
 - Chen et al. [10] documented the program in Hong Kong
 - Dickerson & Sandholm [14] asymptotic gains from liver+kidney exchange over isolated liver exchange and kidney exchange
 - Ergin, Sönmez, & Ünver [17] proposed and modeled exchange for transplants each of that needs two living donors: lung, simultaneous liver+kidney, dual-graft liver

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- We model liver exchange as a market design problem – different than kidney exchange due to size-compatibility requirement, and the availability of multiple transplant technologies.
- We find the structure of feasible 2-way exchanges and a sequential algorithm to find an efficient matching for two patient/donor sizes.
- The requirement of size compatibility induces an incentive problem for the pair/donor to donate
 - the larger/riskier/easier to match right lobe or
 - the smaller/safer/more difficult to match left lobe
- For any given number of patient/donor sizes, we propose a Pareto-efficient and incentive-compatible mechanism that elicits willingness to donate the right lobe truthfully.
- We introduce a new class of exchange mechanisms for vector-partial-order-induced weak preferences.

Institutions: Living-Donor Liver Transplantation

- Living-donor liver transplantation is the norm in Asian countries, where deceased-donor transplantation is much less common due to cultural reasons and legal non-recognition of **brain death**.

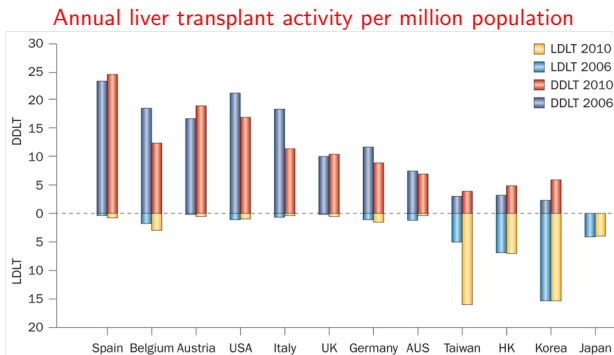
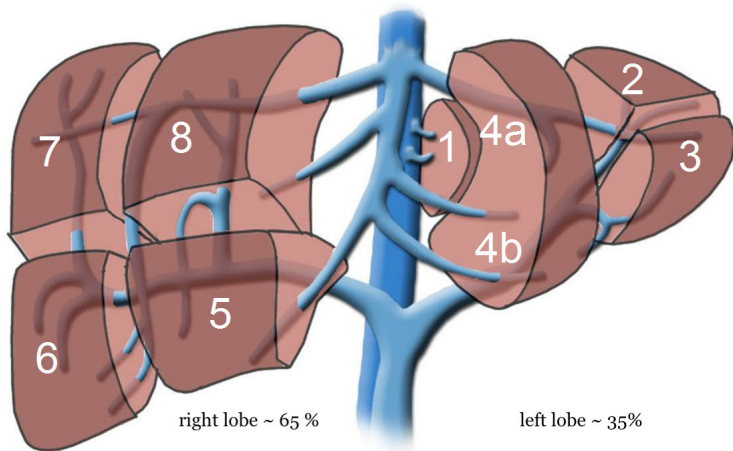


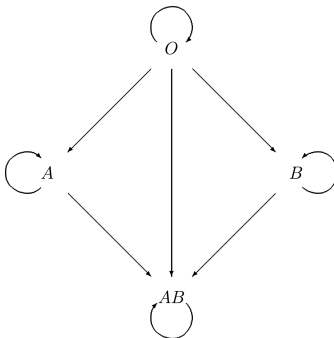
Figure from Chen et al Nature Reviews Gastroenterology & Hepatology 2013

Medical Background: Lobar Liver Donation



Medical Background: Compatibility

- As in kidney transplantation, **blood-type compatibility** is required.



- Different than kidney transplantation,
 - tissue-type compatibility** is **not** required, but instead
 - size compatibility** is required: A patient is in need of a graft that is at least 40% of the volume of his dysfunctional liver.

Institutions: Right-Lobe Liver Transplantation

- Right-lobe transplant has been utilized for size compatibility despite its heightened donor mortality risk.
 - Patient needs at least 40% of his own liver size to survive.
 - Usually right lobe is ~60-70%, left lobe is ~30-40% of the liver.
 - In many occasions, size compatibility is only satisfied through right-lobe transplantation.

Institutions: Living Donor Deaths

TABLE 1. Deaths of Living Donors

Reference	Date	Location	Description
Donor deaths "definitely" related to donor hepatectomy			
11	2003	Japan	A mother in her late 40s donated a right lobe and died 9 months later from complications of hepatic failure.
12	2002	USA	A 57-year-old brother donated a right lobe and developed gastric gas gangrene and <i>Clostridium perfringens</i> infection 3 days after surgery and died.
13	2005	Brazil	A 31-year-old female right lobe donor of unknown relationship to the recipient died 7 days after surgery from a subarachnoid hemorrhage.
14	2003	India	A donor of unknown age and unknown relationship to the recipient donated an unknown lobe and died 10 days after surgery of unknown causes.
15	2003	India	A 52-year-old wife donated an unknown lobe and became comatose 48 hours after surgery from unknown causes and remains in chronic vegetative state.
16-18	1993	Germany	A 29-year-old mother donated a left lateral lobe and died of a pulmonary embolus 48 hours after surgery.
18, 19	2000	Germany	A 38-year-old father donated a right lobe , and 32 days after developing progressive hepatic failure, died during transplantation of acute cardiac failure. The cause of the donor's death was attributed to Berardinelli-Seip syndrome, a lipodystrophy syndrome characterized by loss of body fat, diabetes, hepatomegaly, and acanthosis nigricans.
18, 20	2000	France	A 32-year-old brother donated a right lobe and developed sepsis and multiple organ system failure 11 days after surgery and died of septic shock 3 days later.
18	2000	Europe	A 57-year-old wife donated a right lobe and died of sepsis and multiple organ system failure 21 days after surgery.
21, 22	1999	USA	A 41-year-old half-brother donated a right lobe and died of pancreatitis and sepsis 1 month later.
22, 23	1997	USA	A mother of unknown age donated an unknown lobe to a pediatric recipient and died 3 days after surgery of unknown causes.
24	2005	Asia	A 50-year-old mother donated a right hepatic lobe . She had no history of peptic ulcer disease and received a 2-week course of H2 antagonist. She died 10 weeks after surgery from an autopsy-proven duodenal ulcer with a duodenocaval fistula causing air embolism.
25	2006	Asia	A 39-year-old male "close relative" who donated an unknown lobe died of a myocardial infarction 4 days after donation. The patient reportedly had a preoperative electrocardiogram and treadmill test.
26	2005	Egypt	A brother of unknown age who donated a right lobe died of complications of sepsis from a bile leak 1 month after donation.
Donor deaths "possibly" related to donor hepatectomy			
27	2005	USA	A 35-year-old brother donated a right lobe and died of a self-induced drug overdose 23 months later.
27	2005	USA	A 50-year-old uncle donated a right lobe and died of a self-inflicted gunshot wound to the head 22 months after donation.
Donor deaths "unlikely" to be related to donor hepatectomy			
28	2003	Asia	A donor of unknown age and relationship to the recipient who donated an unknown lobe died of unknown causes during exercise 3 years after donation.
27, 29	2002	USA	A 35-year-old boyfriend donated a right lobe and died in a non-suicidal occupational pedestrian-train accident 2 years after donation. A lone railroad car rolling at high speed struck and killed the donor while he was on duty at his job for the railroad.
16	2003	Germany	A 30-year-old father donated a left lateral segment and died of complications of amyotrophic lateral sclerosis 11 years after successful donation.
30	2003	Japan	A male donor in his 40s of unknown relationship to the recipient donated an unknown lobe died 10 years postoperatively after an apparently unrelated surgery.

- Donor mortality rate is 5 times higher for right-lobe donation than left-lobe donation (0.5% to 0.1%).
- Other significant risks, the morbidity rate, also much higher under right lobe donation (28% to 7.5%).
- In 2001, a high profile death of a living right-lobe liver donor in the US decreased living donation not only for livers, but also for kidneys.
- About half of the living-donor liver transplantations are from right lobes.

Institutions: Living-Donor Liver Exchange

- Liver exchange was first practiced in Korea, followed by Hong Kong and Turkey.
- Liver exchange can have two benefits:
 - (1) It can increase the number of transplants.
 - (2) It can increase donor safety through an increased share of left-lobe transplants.

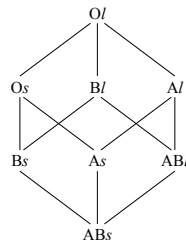
Living-Donor Liver Exchange

- Liver exchange differs from kidney exchange in three key ways:
 - (1) The lack of tissue-type incompatibility,
 - (2) the presence of size incompatibility, and most notably
 - (3) through two different transplant technologies: left-lobe transplantation and right-lobe transplantation.
- In the absence of size incompatibility the scope for liver exchange would be very limited: The only viable exchange would involve
 - a blood-type A patient with a blood-type B donor and
 - a blood-type B patient with a blood-type A donor.

Liver Exchange Model: Two Patient/Donor Sizes

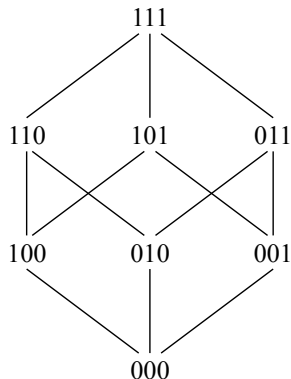
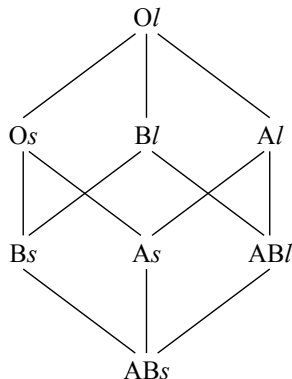
- $\underbrace{\{O, A, B, AB\}}_{\mathcal{B}} \times \underbrace{\{l, s\}}_{\mathcal{S}}$: Set of **individual types**
- **Initial focus:** Left-lobe-only liver transplants.
- **Left-Lobe Compatibility:** A patient can receive a left-lobe transplant from a donor if and only if
 - (1) the patient is blood-type compatible with the donor, and
 - (2) the donor is not smaller than the patient.

Liver Donation Partial Order \trianglelefteq on $\mathcal{B} \times \mathcal{S}$

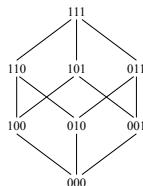
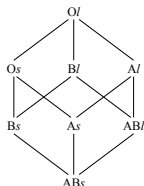


An Equivalent Representation

- Consider the following two partially ordered sets:
 - (1) The liver donation partial order \succeq on $\mathcal{B} \times \mathcal{S}$, and
 - (2) the standard partial order \geq over the corners of the three-dimensional cube $\{0, 1\}^3$.



An Equivalent Representation



- Note that $(\mathcal{B} \times \mathcal{S}, \succeq)$ and $(\{0, 1\}^3, \geq)$ are order isomorphic, where the order isomorphism associates each individual type $\tau \in \mathcal{B} \times \mathcal{S}$ with the following vector $X \in \{0, 1\}^3$:

$$X_1 = 0 \iff \tau \text{ has the } A \text{ antigen}$$

$$X_2 = 0 \iff \tau \text{ has the } B \text{ antigen}$$

$$X_3 = 0 \iff \tau \text{ is small}$$

- For notational convenience, we will work with the equivalent representation $(\{0, 1\}^3, \geq)$.

- The **type** of a patient-donor **pair** is represented through the individual types of its patient and donor, respectively, as $X - Y \in (\{0, 1\}^3)^2$.

Definition

A **liver exchange problem** is a list $\mathcal{E} = \{\mathcal{I}, \tau\}$ where $\mathcal{I} = \{1, 2, \dots, l\}$ is a set of pairs, and for each $i \in \mathcal{I}$, $\tau(i) = X - Y$ is the type of pair i .

Left-Lobe-Only Direct Transplant & 2-way Exchange

- A pair i of type $X - Y$ is **left-lobe compatible**, if

$$Y \geq X$$

- A **(left-lobe-only 2-way) liver exchange** is feasible between a pair i of type $X - Y$ and a pair j of type $V - W$, if

$$Y \geq V \quad \text{and} \quad W \geq X$$

- A **matching** is a collection of mutually exclusive exchanges and direct transplants such that if a pair is left-lobe compatible, then it participates in a direct transplant.

Value of a Pair-Type

- **Value** of a pair type $\underbrace{X_1 X_2 X_3}_X - \underbrace{Y_1 Y_2 Y_3}_Y$ is defined as

$$v(X - Y) = \sum_{k=1}^3 (Y_k - X_k)$$

Observation

In any liver exchange problem, the only types that could be part of an exchange are

$$X - Y \in (\{0, 1\}^3)^2 \text{ such that } X \not\preceq Y \text{ and } Y \not\preceq X.$$

*Therefore, only types of **values** -1, 0, or 1 can be part of an exchange.*

Waste of a 2-way Exchange

- **Waste** of an exchange between a pair of type $X - Y$ and a pair of type $V - W$ is defined as

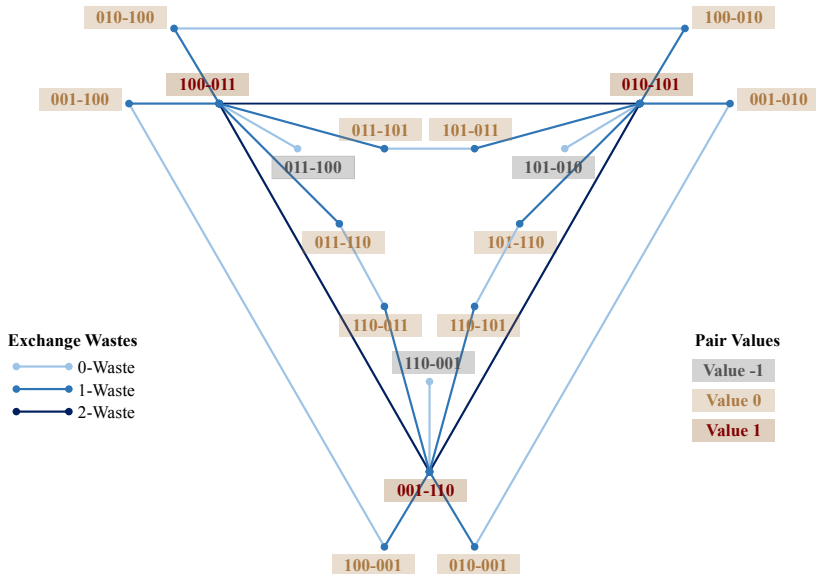
$$v(X - Y) + v(V - W)$$

- All feasible exchanges have non-negative waste.

Observation

All feasible exchanges are either 0-waste, 1-waste, or 2-waste.

Left-Lobe-Only 2-Way Exchange: Feasibility

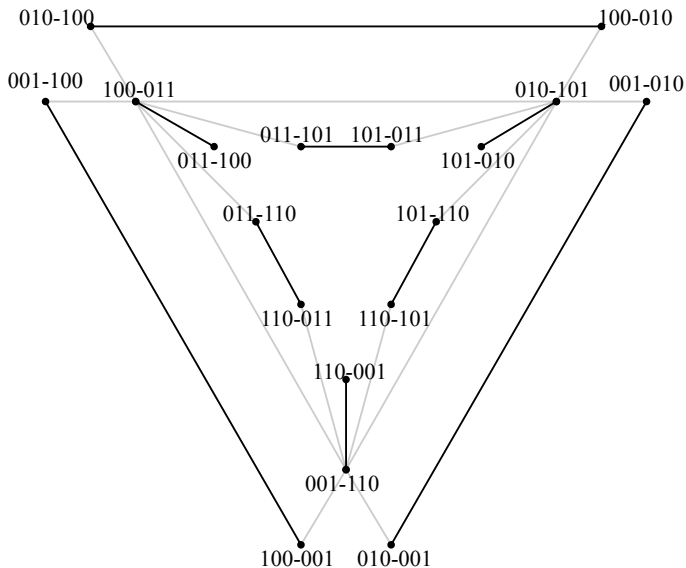


Two-Size Left-Lobe-Only Sequential Exchange Algorithm

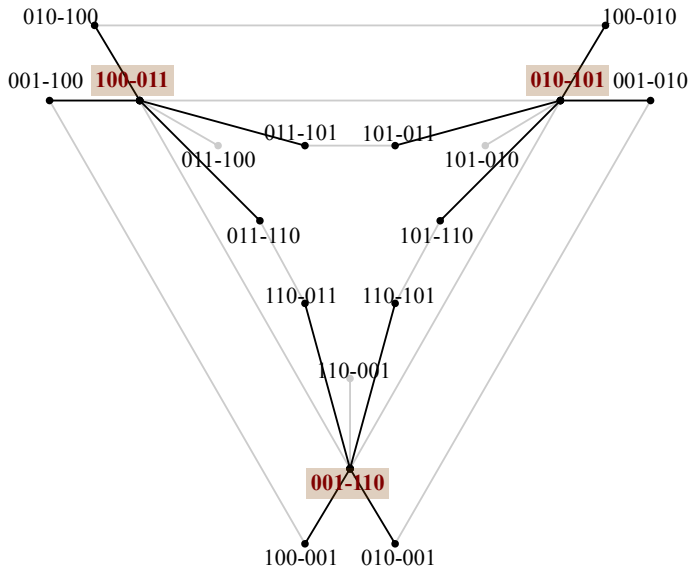
Fix a priority order over pairs.

- Step 0. Clear all feasible direct transplants.
- Step 1. Clear **0-waste** exchanges following the given priority order.
- Step 2. Clear **1-waste** exchanges following the given priority order.
- Step 3. Clear **2-waste** exchanges: Match the maximum number of value 1 types with each other, following the given priority order.

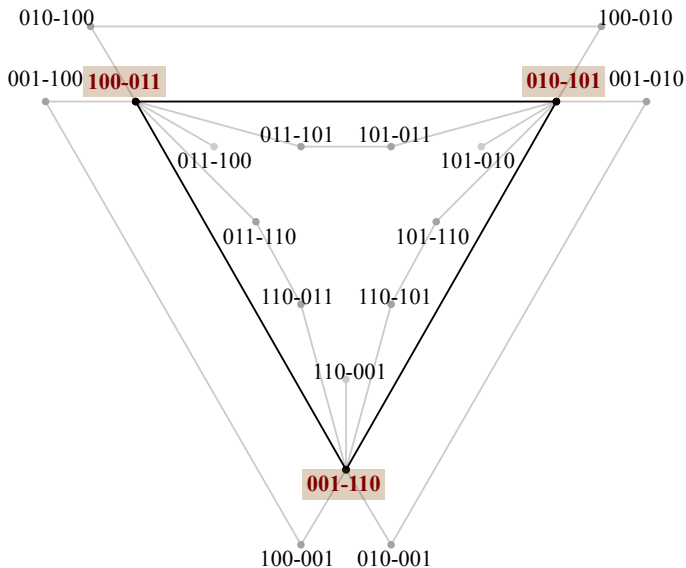
Algorithm Step 1: Clear **0-waste** Exchanges



Algorithm Step 2: Clear **1-waste** Exchanges



Algorithm Step 3: Clear **2-waste** Exchanges



Left-Lobe-Only 2-Way Exchange: Efficiency

Theorem

For any liver exchange problem, the two-size left-lobe-only sequential exchange algorithm maximizes the number of left-lobe-only 2-way exchanges.

- Transplant Technologies:
 - Left-lobe transplant: A patient can receive a left-lobe transplant from a blood-type compatible donor who is at least as large.
 - Right-lobe transplant: A patient can receive a right-lobe transplant from a blood-type compatible donor of any size.
- Pair Preferences:
 - Left-lobe donation is preferred by any pair to right-lobe donation.
 - A willing (w) pair prefers right-lobe donation to no-transplant.
 - An unwilling (u) pair prefers no-transplant to right-lobe donation.

Right-Lobe Donation & Preferences

Willing preferences R_i^w :

Left-Lobe Direct Transplant
Left-Lobe Exchange
Right-Lobe Direct Transplant
Right-Lobe Exchange
 \emptyset

Unwilling preferences R_i^u :

Left-Lobe Direct Transplant
Left-Lobe Exchange
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Right-Lobe Donation & Incentives

- Our focus is on **individual rational** exchanges:
 - A left-lobe compatible pair does not join in any exchange, but only in a left-lobe direct transplant.
 - A right-lobe-only compatible pair participates in an exchange only if its donor donates her left lobe; otherwise,
 - it participates in a right-lobe direct transplant if it is willing, and
 - it receives the no-transplant option if unwilling.
- Willingness (or equivalently preferences) of a pair is private information.
- We inspect direct revelation **mechanisms** to elicit willingness.
- Pairs may have incentives to hide their willingness.

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Transition to Right-Lobe Donation: Transformation

- Fix a willingness profile $R = (R_i)_{i \in \mathcal{I}} \in \{R_i^u, R_i^w\}^{|\mathcal{I}|}$
- A pair of type $X_1 X_2 X_3 - Y_1 Y_2 0w$ is treated as if it is of type $X_1 X_2 X_3 - Y_1 Y_2 1$ when it donates a right lobe.

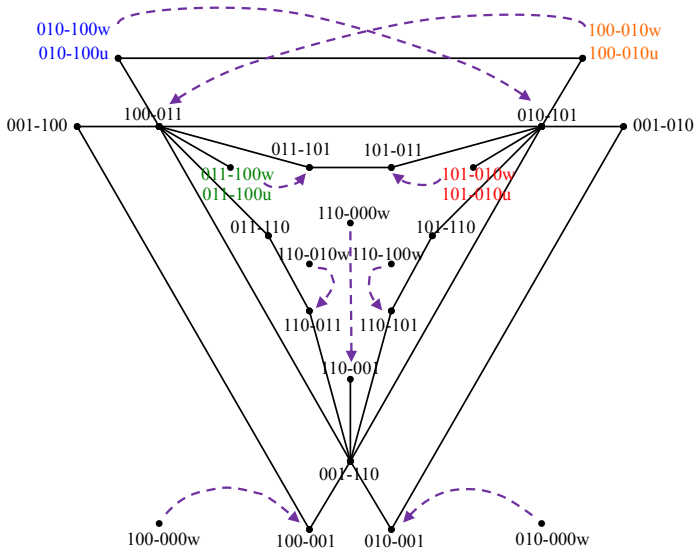
We refer to this transition as a *transformation*.

Lemma (Individually Rational Matchings)

Given both transplant technologies, a pair type $X - Y$ belongs to one of the following seven disjoint groups, based on direct transplant and exchange options available to its members:

- 0. $X > Y_1 Y_2 1$: cannot participate in an exchange or a direct transplant;*
- I. $X \leq Y$: participates in a direct left-lobe transplant;*
- II. $Y_3 = 0$ & $X = Y_1 Y_2 1$: can only participate in a direct right-lobe transplant (if willing);*
- III. $Y_3 = 1$ & $X \not\leq Y$ & $X \not\leq Y$: can only participate in exchange, and only by donating a left lobe;*
- IV. $X_3 = 0, Y_3 = 0$ & $X > Y$: can only participate in exchange, and only by donating a right lobe (if willing);*
- V. $Y_3 = 0$ & $X \not\leq Y$ & $X \not\leq Y_1 Y_2 1$ (010 – 100, 100 – 010, 011 – 100, 101 – 010): can only participate in exchange, either by donating a left lobe or a right lobe (if willing); and*
- VI. $X < Y_1 Y_2 1$ & $X \not\leq Y$ & $X \not\leq Y$: can participate in exchange by donating a left lobe, or receive a direct right-lobe transplant (if willing).*

Left or Right-Lobe Exchange: Feasibility



- A **mechanism** is a systematic procedure that finds a matching for each willingness type profile reported.
- A mechanism is **incentive compatible** if it is a weakly dominant strategy for each pair to reveal its willingness truthfully.
- Since our mechanism will be based on a sequential algorithm, we will attain incentive compatibility by **gradually transforming** willing pairs as their left-lobe transplant prospects are **fully exhausted**.

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Incentive Compatibility Based on Category

- 0. No direct transplant/exchange \implies Irrelevant: Remains w/o transplant
 - I. Direct left-lobe transplant only
 - \implies Irrelevant: Direct l-lobe transplant at the beginning
 - II. Direct right-lobe transplant only
 - \implies Transform for a direct r-lobe transplant at the beginning if willing
 - III. Exchange via left-lobe donation only
 - \implies Irrelevant: Role in the algorithm unaffected
 - IV. Exchange via right-lobe donation only
 - \implies Transform to donate a right lobe at the beginning if willing
 - V. Exchange via left-lobe or right-lobe donation
 - \implies **Gradually transform to donate a right lobe if willing,**
as left-lobe donation prospects are fully exhausted
 - VI. Exchange via left-lobe donation, or direct right-lobe transplant
 - \implies Role in the algorithm unaffected until the end.
If still unmatched, transform for a direct r-lobe transplant if willing

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 \implies Transform to donate a right lobe at the beginning if willing
- V. Exchange via left-lobe or right-lobe donation
 \implies Gradually transform to donate a right lobe if willing,
as left-lobe donation prospects are fully exhausted
- VI. Exchange via left-lobe donation, or direct right-lobe transplant
 \implies Role in the algorithm unaffected until the end.
If still unmatched, transform for a direct r-lobe transplant if willing

Incentive Compatibility Based on Category

- 0. No direct transplant/exchange \implies Irrelevant: Remains w/o transplant
- I. Direct left-lobe transplant only
 \implies Irrelevant: Direct l-lobe transplant at the beginning
- II. Direct right-lobe transplant only
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- Build on the same insight, but integrating with our strategy for incentive compatibility.
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Fix a priority order over pairs.

Step 0. Direct transplant each Category I and Category II w pair.

Step 1. Transform Category IV w pairs.

Clear 0-waste exchanges following the given priority order.

At least one of Category V types 010 – 100 and 100 – 010 is fully depleted. Assume wlog type 100 – 010 pairs are depleted.

Step 2a. Clear all remaining exchanges of type 010 – 100w.

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No exchange remains for Category V type 011 – 100w.

Clear all remaining exchanges of Category V type 101 – 010w.

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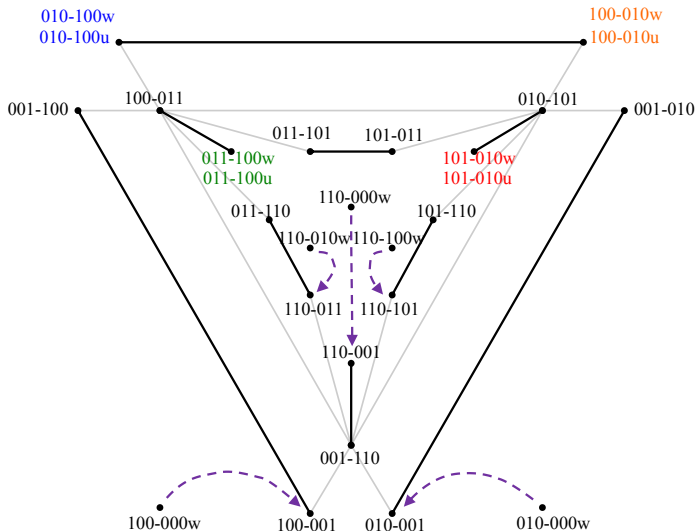
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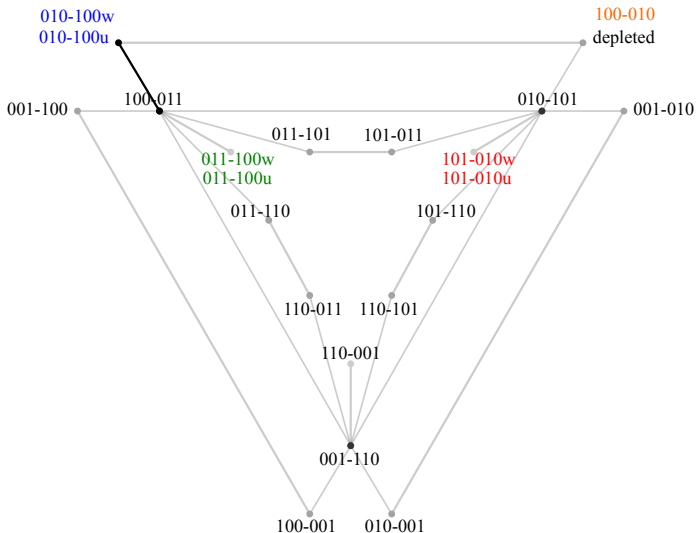
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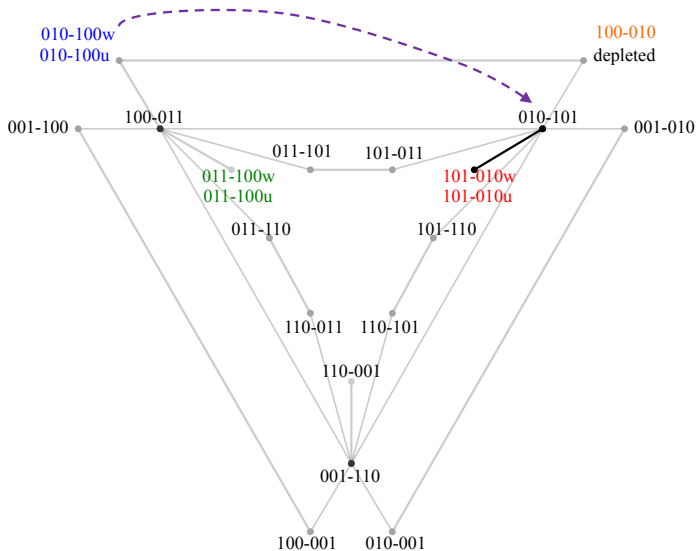
Algorithm Step 1:



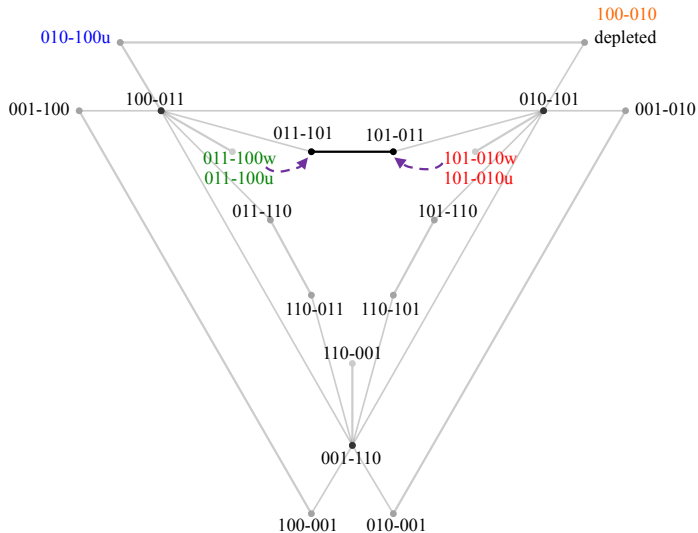
Algorithm Step 2a:



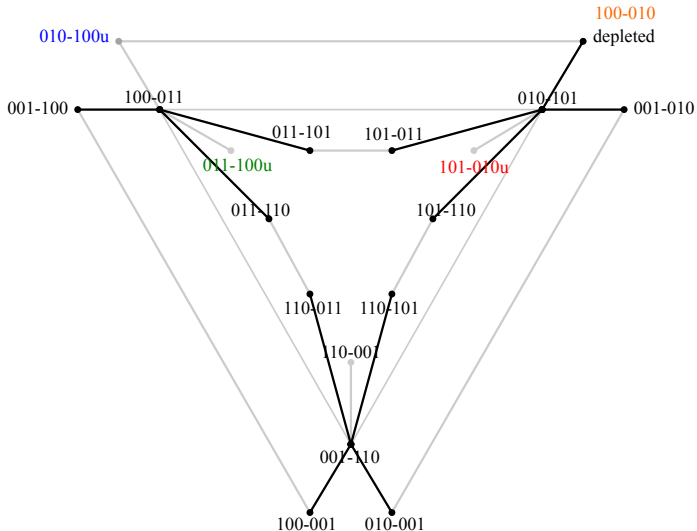
Algorithm Step 2b:



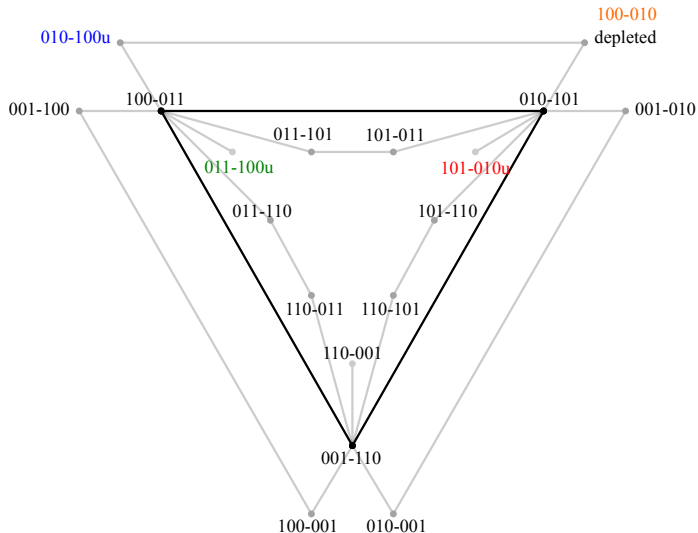
Algorithm Step 2c:



Algorithm Step 2d:



Algorithm Step 3:



Theorem

The left or right-lobe sequential exchange mechanism is individually rational, Pareto-efficient, and incentive compatible.

Generalized Model: Multiple Individual Sizes

- $\mathcal{S} = \{0, 1, \dots, S-1\}$: The set of possible patient/donor sizes
- Individual types: $X, Y \in \{0, 1\} \times \{0, 1\} \times \mathcal{S}$
- Pair types: $X - Y \in (\{0, 1\}^2 \times \mathcal{S})^2$
- Right-lobe donation function: A non-decreasing function $\rho : \mathcal{S} \rightarrow \mathcal{S}$ such that $\rho(s) > s$ for all $s \in \mathcal{S} \setminus \{S-1\}$

A donor of size s size can donate his right lobe to a blood-type compatible patient of any size $s' \leq \rho(s)$.

- Category V pairs: $X - Y$ such that $X \not\preceq Y$ & $X \not\preceq Y_1 Y_2 \rho(Y_3)$

- 1 Sequentially committing to an exchange may compromise efficiency, even for left-lobe-only exchange.
- 2 When right-lobe donation is possible, the transformation order of Category V willing pairs require further analysis.

Transformation Order of Category V Pairs

- We will rely on a priority approach, based on matchability arguments.
- To maintain IC, it is plausible to transform a Category V pair after its left-lobe matchability options are exhausted.

But how does transformation of Category V pairs affect the matchability options of other Category V pairs?

Definition

Define the following **precedence digraph** on the set of Category V pair types, where for any Category V pair types $X - Y$ and $U - V$:

$$X - Y \longrightarrow U - V \iff X \leq V, U \not\leq Y \text{ \& } U \leq \rho(Y).$$

If $X - Y \longrightarrow U - V$, we say that $X - Y$ **precedes** $U - V$.

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Precedence Digraph: 2 Sizes

010-100



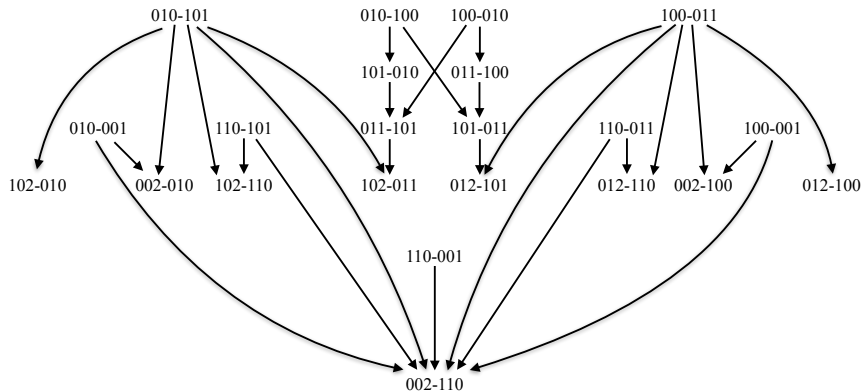
101-010

100-010



011-100

Precedence Digraph: 3 Sizes



Transformation Order of Category V Pairs

Lemma (from graph theory)

Given an *acyclic* digraph, there exists a linear order of all nodes, known as a *topological order*, L , that is consistent with the digraph:

$$x \rightarrow y \implies xLy$$

Lemma

The precedence digraph on Category V pair types is acyclic.

Thus, a topological order of Category V pair types, as well as a topological order of all Category V pairs exist.

The latter can be used as a priority order over transformations.

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Precedence-Order Induced Priority Mechanism

Fix a topological order over Category V pairs as i_1, \dots, i_K and a priority order over all pairs. Given a willingness profile R :

Step 0. Direct transplant Category I and Category III w pairs.
Transform Category IV w pairs.

Step 1. Let \mathcal{I}^0 be the set of remaining pairs, G^0 be the current compatibility graph. Inductive:

Step 1.k. If next Category V Pair i_k together with \mathcal{I}^{k-1} are matchable in G^{k-1} , then $\mathcal{I}^k := \mathcal{I}^{k-1} \cup \{i_k\}$, $G^k := G^{k-1}$.

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Step 2.n. If next pair j_n together with $\mathcal{I}^{K+(n-1)}$ are matchable in G^K , then let $\mathcal{I}^{K+n} := \mathcal{I}^{K+(n-1)} \cup \{j_n\}$. Otherwise, set $\mathcal{I}^{K+n} := \mathcal{I}^{K+(n-1)}$.

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Step 2. Let j_1, \dots, j_N be the remaining pairs in $\mathcal{I}^0 \setminus \mathcal{I}^K$ ordered wrt the priority order. Inductive:

Step 2.n. If next pair j_n together with $\mathcal{I}^{K+(n-1)}$ are matchable in G^K , then let $\mathcal{I}^{K+n} := \mathcal{I}^{K+(n-1)} \cup \{j_n\}$. Otherwise, set $\mathcal{I}^{K+n} := \mathcal{I}^{K+(n-1)}$.

Step 3. Direct transplant willing Category VI pairs in $\mathcal{I}_0 \setminus \mathcal{I}^{K+N}$. Any matching in G^K that matches all pairs in \mathcal{I}^{K+N} in exchanges together with the fixed direct transplants is the outcome.

Theorem

The precedence-order induced priority mechanism satisfies:

- *individual rationality,*
- *Pareto efficiency, and*
- *incentive compatibility.*

Generalized Model: Main Result

Intuition of the Proof.

Individual rationality: By construction.

Pareto efficiency: Obtained by following

- ① topological order for Category V pairs, and
- ② priority order for remaining pairs and transformed Category V pairs.

Incentive compatibility: Acyclicity of the precedence digraph implies that *transformation* a willing Category V pair i_k is independent of the willingness types of its lower-prioritized “graph neighbors.”

Thus, they cannot affect how i_k is matched by manipulating their own willingness types. □

Generalized Model: Main Result

Intuition of the Proof.

Individual rationality: By construction.

Pareto efficiency: Obtained by following

- 1 topological order for Category V pairs, and
- 2 priority order for remaining pairs and transformed Category V pairs.

Incentive compatibility: Acyclicity of the precedence digraph implies that *transformation* a willing Category V pair i_k is independent of the willingness types of its lower-prioritized “graph neighbors.” Thus, they cannot affect how i_k is matched by manipulating their own willingness types. □

Generalized Model: Main Result

Intuition of the Proof.

Individual rationality: By construction.

Pareto efficiency: Obtained by following

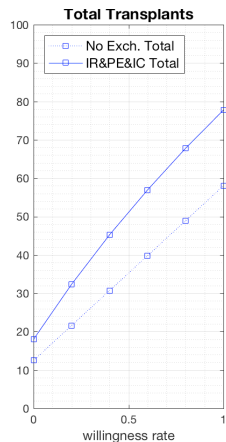
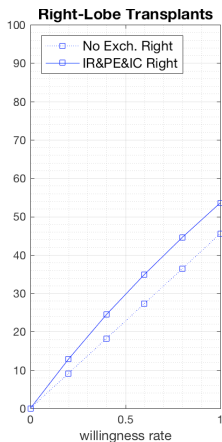
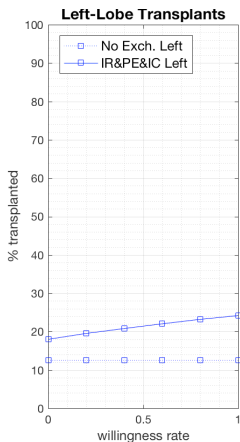
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Thus, they cannot affect how i_k is matched by manipulating their own willingness types. □

Simulations

- Using South Korean population characteristics for $I = 100$
- % of left-lobe transplants higher under IR&PE&IC than no exchange
- IR&PE&IC generates 44%-34% more transplants than no exchange



Conclusion

- We model **living-donor liver exchange** as a market design problem. Information/incentive problems are modeled and solved through a **PE + IC mechanism**.
- Size incompatibility increases the benefit from exchange, more gains plausible with respect to kidney exchange.
- Off-the-shelf-implementable mechanism in Middle East and East Asia: Liver transplants are more complex, two-way may be the way to start the exchange.
- **Implications for matching theory in general:** A new class of bilateral exchange mechanisms for n -dimensional vector partial-order induced weak preferences:
 - Other examples: vacation house exchanges, time/favor exchanges
 - Two-size model with three dimensions is of independent interest: Induces a fully-symmetric model where greedy mechanism design is possible.