Convex rank tests

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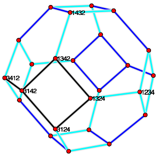
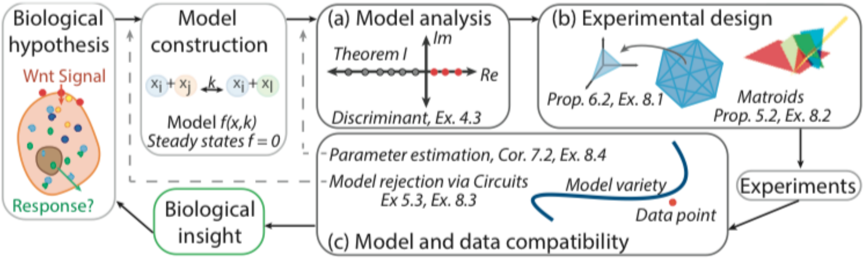




From *Algebraic Systems Biology: A Case Study for the Wnt Pathway* (Elizabeth Gross, Heather Harrington, Zvi Rosen, Bernd Sturmfels 2016).

Outline of talk

- Introduction
- Main Result: *convex rank tests* = *semigraphoids*
- *2 counterexamples*
- Application to biology

Outline of talk

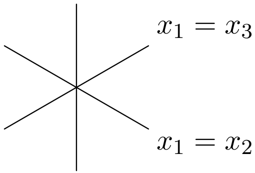
- Introduction
- Main Result: *convex rank tests = semigraphoids*
- *2 counterexamples*
- Application to biology

Joint work with Raymond Hemmecke, Jason Morton, Lior Pachter, Bernd Sturmfels, and Oliver Wienand.

Introduction

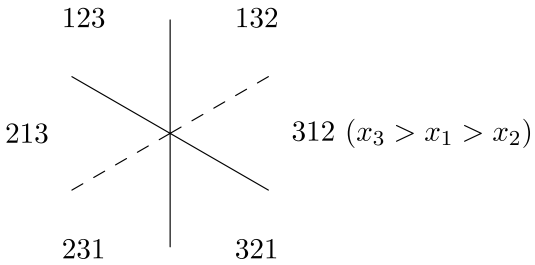
Preliminary definitions

- A **fan** in $\mathbb{R}^n$ is a finite collection $\mathcal{F}$ of polyhedral cones such that:
  - if $C \in \mathcal{F}$ and C' is a face of C, then $C' \in \mathcal{F}$, and
  - if $C, C' \in \mathcal{F}$, then $C \cap C'$ is a face of C.
- The S_n**-arrangement** (the **braid arrangement**) is the arrangement of hyperplanes $\{x_i = x_j\}$ in $\mathbb{R}^n$.
- Example: the *fan* associated to the S_3-*arrangement* has 6 maximal cones.



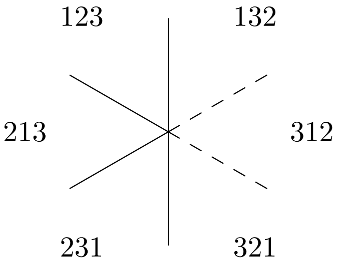
What is a convex rank test?

- A **rank test** is a partition of S_n.
- A **convex rank test** is a partition of S_n defined by a fan that coarsens the S_n-arrangement.
- Example: the following convex rank test partitions S_3 into 4 classes.



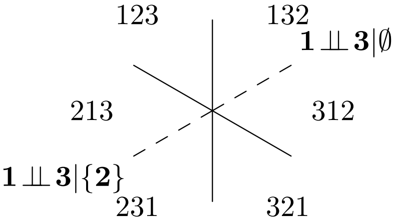
A non-convex rank test

- This partition of S_3 into 4 classes is *not* a convex rank test.



- *Remark*: a convex rank test is determined by the *walls* removed from the S_n-arrangement.

Label walls by conditional-independence statements



- Two maximal cones of the S_n-fan, labeled by permutations δ and δ' in S_n, share a **wall** if δ and δ' differ by an *adjacent transposition*: there exists an index k such that $\delta_k = \delta'_{k+1}$, $\delta_{k+1} = \delta'_k$, and $\delta_i = \delta'_i$ for $i \neq k, k+1$.
- Label wall $\{\delta, \delta'\}$ by the conditional-independence (CI) statement:

$$\delta_k \perp\!\!\!\perp \delta_{k+1} \,|\, \{\delta_1, \ldots, \delta_{k-1}\}.$$

Conditional independence

Consider a collection of n random variables indexed by $[n]$.

$[1 \perp\!\!\!\perp 2|\emptyset]$ $[1 \perp\!\!\!\perp 3|\emptyset]$ $[2 \perp\!\!\!\perp 3|\emptyset]$ $[2 \perp\!\!\!\perp 3|1]$ $[1 \perp\!\!\!\perp 3|2]$ $[1 \perp\!\!\!\perp 2|3]$
$[1 \perp\!\!\!\perp 4|\emptyset]$ $[2 \perp\!\!\!\perp 4|\emptyset]$ $[3 \perp\!\!\!\perp 4|\emptyset]$ $[1 \perp\!\!\!\perp 2|4]$ $[1 \perp\!\!\!\perp 3|4]$ $[2 \perp\!\!\!\perp 3|4]$
$[2 \perp\!\!\!\perp 4|1]$ $[3 \perp\!\!\!\perp 4|1]$ $[1 \perp\!\!\!\perp 4|2]$ $[3 \perp\!\!\!\perp 4|2]$ $[1 \perp\!\!\!\perp 4|3]$ $[2 \perp\!\!\!\perp 4|3]$
$[1 \perp\!\!\!\perp 2|34]$ $[1 \perp\!\!\!\perp 3|24]$ $[1 \perp\!\!\!\perp 4|23]$ $[2 \perp\!\!\!\perp 3|14]$ $[2 \perp\!\!\!\perp 4|13]$
$[3 \perp\!\!\!\perp 4|12]$ $[1 \perp\!\!\!\perp 5|\emptyset]$ $[2 \perp\!\!\!\perp 5|\emptyset]$ ... $[4 \perp\!\!\!\perp 5|123]$ ...

The symbol $[i \perp\!\!\!\perp j \mid K]$ represents the statement,
"the random variables i and j are conditionally independent given the joint random variable K."

Semigraphoids

- *(definition #1)* A set $\mathcal{M}$ of CI statements on $[n]$ is a **semigraphoid** if the following axiom holds[1]:
  (SG) If $[i \perp\!\!\!\perp j \mid K \cup \ell]$ and $[i \perp\!\!\!\perp \ell \mid K]$ are in $\mathcal{M}$
  then also $[i \perp\!\!\!\perp j \mid K]$ and $[i \perp\!\!\!\perp \ell \mid K \cup j]$ are in $\mathcal{M}$.

[1] *Probabilistic Conditional Independence Structures*, Studený 2005

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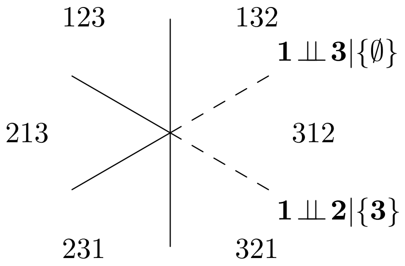
  then also $[i \perp\!\!\!\perp j \,|\, K]$ and $[i \perp\!\!\!\perp \ell \,|\, K \cup j]$ are in $\mathcal{M}$.
- Example:
  (SG) If $[1 \perp\!\!\!\perp 2 \,|\, 3]$ and $[1 \perp\!\!\!\perp 3 \,|\, \emptyset]$ are in $\mathcal{M}$,
  then also $[1 \perp\!\!\!\perp 2 \,|\, \emptyset]$ and $[1 \perp\!\!\!\perp 3 \,|\, 2]$ are in $\mathcal{M}$.
- So, $\mathcal{M} = \{ [1 \perp\!\!\!\perp 3 | \emptyset] , [1 \perp\!\!\!\perp 2 | 3] \}$ is *not* a semigraphoid.



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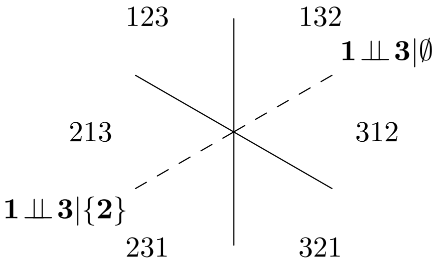
Main result

Main Theorem

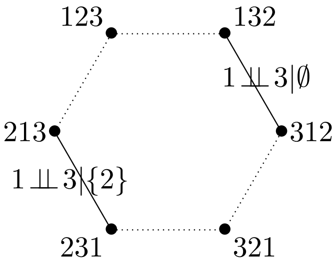
- A convex rank test $\mathcal{F}$ is characterized by the collection of walls $\{\delta, \delta'\}$ that are removed from the S_n-arrangement. Let $\mathcal{M}_{\mathcal{F}}$ denote the CI statements that label those walls.
- **Main theorem:** The map $\mathcal{F} \mapsto \mathcal{M}_{\mathcal{F}}$ is a bijection between convex rank tests and semigraphoids.
- The following convex rank test corresponds to the semigraphoid $\mathcal{M} = \{\ 1 \perp\!\!\!\perp 3|\emptyset,\ 1 \perp\!\!\!\perp 3|2\ \}$.



Restating the Main result via the permutohedron

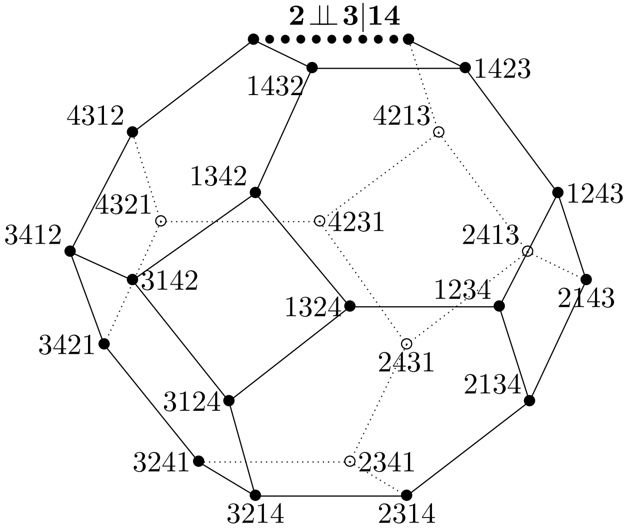
The Permutohedron

- The fan of the S_n-arrangement is the normal fan of the **permutohedron $\mathbf{P}_n$** (the convex hull of the vectors $(\rho_1, \ldots, \rho_n)$, where ρ is in S_n).



- The edges of the permutohedron correspond to walls of the S_n-arrangement.

THE PERMUTOHEDRON $\mathbf{P_4}$

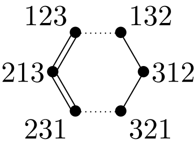


The 2-d faces of P_n are squares and hexagons.

Square and Hexagon Axioms

Lemma: A set **M** of edges of the permutohedron $\mathbf{P}_n$ is a semigraphoid if and only if **M** satisfies the following two axioms:

- **Square axiom:** Whenever an edge of a square is in **M**, then the opposite edge is also in **M**.
- **Hexagon axiom:** When two adjacent edges of a hexagon are in **M**, then the two opposite edges are also in **M**.

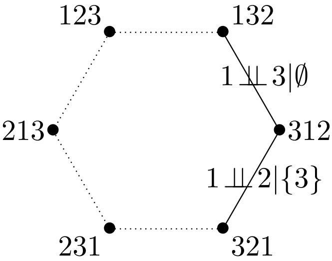


Main theorem, restated.
Coarsenings of the S_n-fan are equivalent to subsets of edges of P_n that satisfy the *Square and Hexagon axioms.*

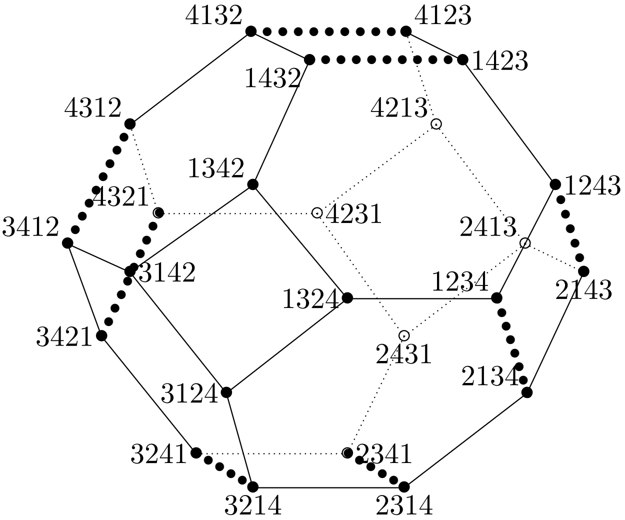
Generalization to other Coxeter arrangemts.
Coarsenings = subsets of edges with the *polygon property.*
(Nathan Reading 2012).

Hexagon axiom illustrated

Consider $\mathbf{M} = \{1 \perp\!\!\!\perp 3|\emptyset, 1 \perp\!\!\!\perp 2|\{3\}\}$ (again).
It is *not* a convex rank test, because it violates the Hexagon axiom:



Main theorem illustrated



$f = (16,\ 24,\ 10)$

2 COUNTEREXAMPLES

Semigraphoids: another definition

- Each CI statement defines a linear form in 2^n unknowns h_I for $I \subseteq [n]$:

$$[i \perp\!\!\!\perp j \mid K] \;\mapsto\; -h_{ijK} + h_{iK} + h_{jK} - h_K .$$

- Non-negativity of these linear forms defines the $(2^n\!-\!n\!-\!1)$-dimensional *submodular cone* in $\mathbb{R}^{2^n}$.
- The linear relations among the forms are spanned by entropy equations:

$$[i \perp\!\!\!\perp j \,|K \cup \ell] + [i \perp\!\!\!\perp \ell \,|K] = [i \perp\!\!\!\perp j \,|K] + [i \perp\!\!\!\perp \ell \,|K \cup j].$$

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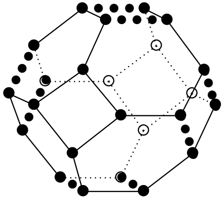
- *(definition #4)* A **semigraphoid** $\mathcal{M}$ specifies the possible zeros for a non-negative solution of the entropy equations.
- A semigraphoid $\mathcal{M}$ is *submodular* if it is the set of actual zeros of a point in the submodular cone.

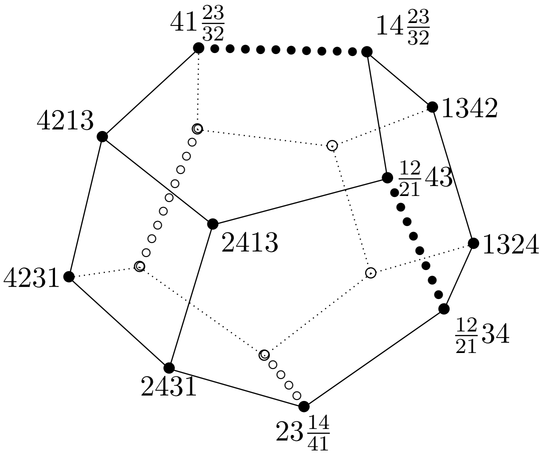
Question 1

- Postnikov, Reiner and Williams (2006) asked:
  Is every simplicial fan which coarsens the S_n-fan the normal fan of convex polytope?
- **Facts.** A convex rank test $\mathcal{F}$ is the normal fan of a polytope if and only if the semigraphoid $\mathcal{M}_{\mathcal{F}}$ is submodular. This polytope is a *generalized permutohedron*. It is simple iff $\mathcal{F}$ is simplicial iff the posets on $[n]$ are trees.
- The answer to the PRW question is no for $n = 4$:
  Proposition. This is simplicial, but *not* submodular:



PROOF: SIMPLICIAL

This simple polytope looks like a generalized permutohedron...



$$\mathcal{M}_{\mathcal{F}} = \{[2 \amalg 3|14], [1 \amalg 4|23], [1 \amalg 2|\emptyset], [3 \amalg 4|\emptyset]\}.$$

Proof: not submodular

... but, it is not a generalized permutohedron.

$$\begin{aligned}
[1 \amalg 2|\emptyset] + [2 \amalg 3|1] &= [1 \amalg 2|3] + [2 \amalg 3|\emptyset] \\
[3 \amalg 4|\emptyset] + [1 \amalg 4|3] &= [3 \amalg 4|1] + [1 \amalg 4|\emptyset] \\
[2 \amalg 3|14] + [3 \amalg 4|1] &= [2 \amalg 3|1] + [3 \amalg 4|12] \\
[1 \amalg 4|23] + [1 \amalg 2|3] &= [1 \amalg 4|3] + [1 \amalg 2|34]
\end{aligned}$$

If $\mathcal{M}_{\mathcal{F}}$ were submodular, there would be a solution where the blue unknowns are zero and the others are positive. Adding both left- and right-hand sides yields

$$[2 \amalg 3|\emptyset] + [1 \amalg 4|\emptyset] + [3 \amalg 4|12] + [1 \amalg 2|34] = 0.$$

Contradiction!

Question 2

For $n = 3$, there are 22 semigraphoids.

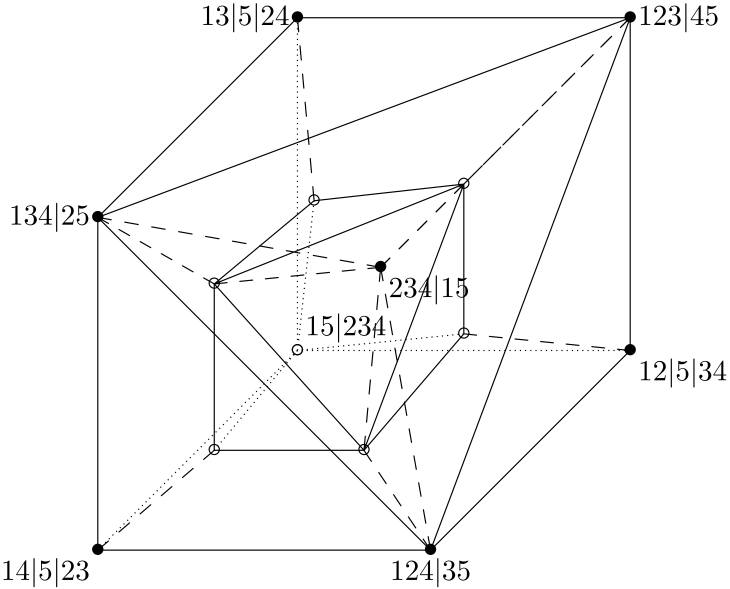
For $n = 4$, there are 26424 semigraphoids
but only 22108 of them are submodular.

For $n \geq 5$, Studený posed many questions, including:

- Is every maximal semigraphoid submodular?

The answer is no.

Non-submodular, but maximal



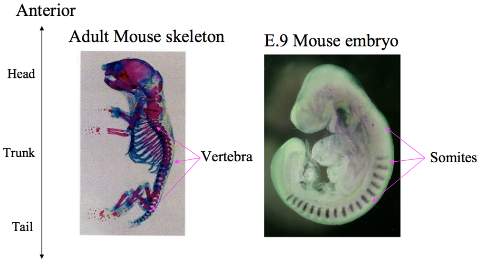
Everyone loves graphs

- We saw:
  submodular semigraphoids = generalized permutohedra.
- In statistics, the most popular semigraphoids are *graphical models*.
- In mathematics, the most popular polytopes are the *graph associahedra* (Stasheff, Bott-Taubes, …)
- **Theorem.** Graphical models = graph associahedra.
- For the biological application which started all this, the corresponding graphical rank tests worked best …

Application: biological clocks

Biological clocks

- *Somitogenesis*: process during embryonic development in vertebrates in which the somites (precursors to the segments of the backbone) are formed

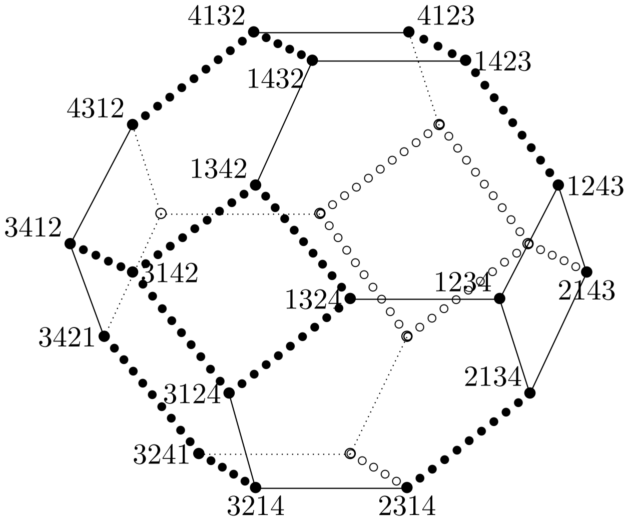


- Which genes control this molecular clock?
- Olivier Pourquié lab at the Stowers Institute, now Harvard
- Dequéant *et al.* A complex oscillating network of signaling genes underlies the mouse segmentation clock. *Science* 314:5805 (2006).

Search for cyclic genes

- Microarray experiments- a microarray chip can measure the gene expression level of tens of thousands of genes simultaneously.
- 17 experiments conducted within one cycle
- Example: the expression level of gene `Axin2`
  (0.34204059, 0.195306068, 0.151584691, 0.215046787, -0.238626783, -0.380163626, -0.431032137, -0.41198219, -0.36420852, -0.317375356, -0.141293099, -0.191303023, 0.085202023, 0.420653258, 0.300682397, -0.002791647, 0.281696744)$\in \mathbb{R}^{17}$
- Its *rank vector*: $(16, 12, 11, \ldots, 14) \in S_{17}$
- Convex rank test as a *statistical test*...

One convex rank test: Up-down analysis



Another test: Cyclohedron

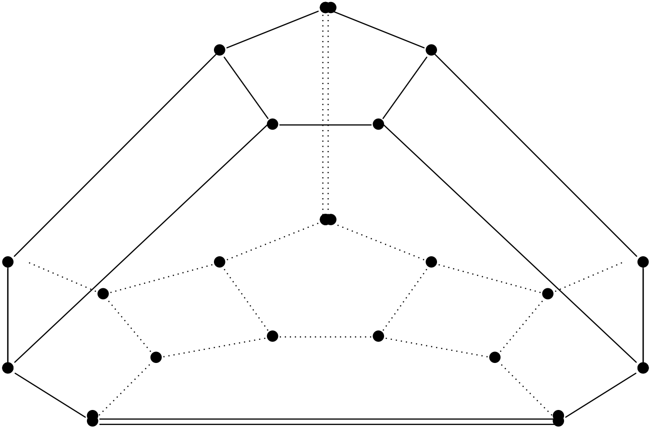


Figure: $\mathcal{M}_{\mathcal{F}} = \{[1 \amalg 3|\emptyset], [2 \amalg 4|\emptyset]\}$.

Cyclohedron test for gene `Obox`

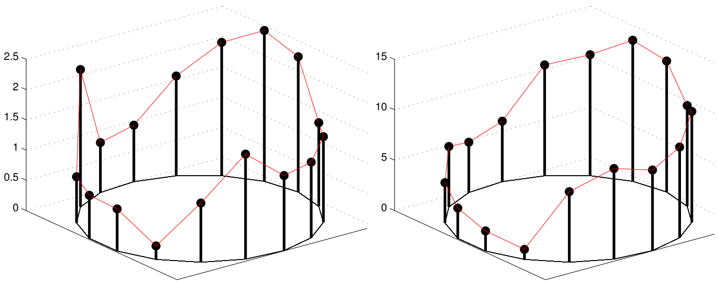
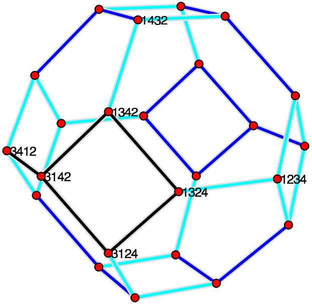


Figure: The cyclohedron test smooths the data; shown are the data vector v and the height vector $h(v)$. How many permutations share a height vector?

Result: We identified this and other genes to be possibly part of the biological clock.

Conclusion

Summary theorem.
Convex rank tests = semigraphoids = edges of the permutohedron that satisfy the square and hexagon axioms.



Combinatorics helped us answer some questions from statistics and biology.

Thank you.

Proof of Theorem

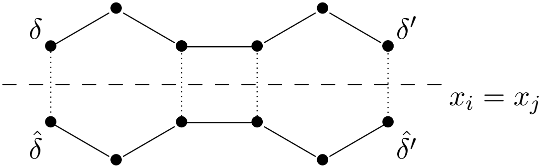
Lemma

If $\mathcal{M}$ is a semigraphoid, then if δ and δ' lie in the same class of $\mathcal{M}$, then so do all shortest paths on $\mathbf{P}_n$ between them.

Lemma $\Rightarrow$ A semigraphoid is a pre-convex rank test.

Proof (continued)

Now, we see that a semigraphoid corresponds to a fan (convex rank test):



Conversely, it is easy to show that a convex rank test satisfies the square and hexagon axioms.