Reverse engineering minimal wiring diagrams

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Algebraic Biology
Broad goals

Suppose we have an unknown Boolean function $f_i : \mathbb{F}_2^3 \rightarrow \mathbb{F}_2$ that satisfies:

$$f_i(1, 1, 1) = 0, \quad f_i(0, 0, 0) = 0, \quad f_i(1, 1, 0) = 1.$$ 

In other words, its truth table looks like

<table>
<thead>
<tr>
<th>$x_1 x_2 x_3$</th>
<th>111</th>
<th>110</th>
<th>101</th>
<th>100</th>
<th>011</th>
<th>010</th>
<th>001</th>
<th>000</th>
</tr>
</thead>
<tbody>
<tr>
<td>$f_i(x)$</td>
<td>0</td>
<td>1</td>
<td>?</td>
<td>?</td>
<td>?</td>
<td>?</td>
<td>?</td>
<td>0</td>
</tr>
</tbody>
</table>

Goals

1. Reverse engineering the wiring diagram: *Which sets of variables can $f_i$ depend on?*
2. Reverse engineering the model space: *Characterize all functions that “fit this data”.*
3. Model selection: *What is the “best fit” function?*

We’ll study the first question in this lecture.

Recall how different types of interactions are indicated in the wiring diagram:

$$f_j = x_i \land x_k \quad f_j = \overline{x_i} \land x_k \quad f_j = x_i + x_k$$

$x_i \rightarrow x_j$ \hspace{1cm} $x_i \rightarrow \overline{x_j}$ \hspace{1cm} $x_i \leftrightarrow x_j$

“$x_i$ activates $x_j$” \hspace{1cm} “$x_i$ inhibits $x_j$” \hspace{1cm} “$x_i$ affects $x_j$ positively & negatively”
Unate functions

Consider the following unknown Boolean function:

<table>
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</tr>
</tbody>
</table>

There are $2^8 = 256$ truth tables, and of these, $2^{8-3} = 32$ fit this data.

Not all of these functions are biologically meaningful.

Definition

A Boolean function $f : \mathbb{F}_2^n \rightarrow \mathbb{F}_2$ is unate if no variable $x_i$ and its negation $\overline{x_i}$ both appear.

Examples

- Conjunctions: $f = x_{i_1} \land \cdots \land x_{i_k}$.
- Disjunctions: $f = x_{i_1} \lor \cdots \lor x_{i_k}$.
- AND-NOT functions: $f = x \land \overline{y} \land z$.
- OR-NOT functions: $f = x \lor \overline{y} \lor \overline{z}$.
- Others: $f = x \land (\overline{y} \lor z)$.

Fact

Most functions that appear in biological networks are unate.
Recall the following unknown Boolean function:

<table>
<thead>
<tr>
<th>$x_1x_2x_3$</th>
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<td>?</td>
<td>0</td>
</tr>
</tbody>
</table>

Of the 256 Boolean functions on 3 variables, $2^{8-3} = 32$ fit this data, and only 4 of these are unate. They are:

$$x_1 \land \overline{x_3}, \quad x_2 \land \overline{x_3}, \quad x_1 \land x_2 \land \overline{x_3}, \quad (x_1 \lor x_2) \land \overline{x_3}.$$  

The wiring diagrams of these functions are shown below, expressed several different ways.

We will call the minimal wiring diagrams (e.g., the first two) min-sets. If we retain the signs of the interactions, we call them signed min-sets.
Finding min-sets using computational algebra

**Figure:** Image courtesy of Alan Veliz-Cuba.
Monomials

We will learn how to reverse-engineer wirgram diagrams using computational algebra.

We will encode the partial data using ideals of polynomials rings generated by square-free monomials.

There is a beautiful relationship between square-free monomial ideals and a combinatorial object called a simplicial complex.

The min-sets can be found by taking the primary decomposition of the ideal.

Notation

Every monomial can be written as \( cx^{\alpha} \), where \( x^{\alpha} := x_1^{\alpha_1} \cdots x_n^{\alpha_n} \) and \( \alpha = (\alpha_1, \ldots, \alpha_n) \in \mathbb{Z}_{\geq 0}^n \).

Example

Consider the following polynomial in \( \mathbb{F}_3[x_1, x_2, x_3, x_4] \), written several different ways:

\[
f = x_1^3 x_2 x_4^2 + 2x_1 x_4^5 = x_1^3 x_2^1 x_3^0 x_4^2 + 2x_1^1 x_2^0 x_3^0 x_4^5 = x^{(3,1,0,2)} + 2x^{(1,0,0,5)}.
\]
Monomial ideals

**Definition**

A monomial ideal \( I \leq \mathbb{F}[x_1, \ldots, x_n] \) is an ideal generated by monomials.

**Proposition (exercise)**

Let \( \mathcal{M}(I) \) be the set of monomials in \( I \). If \( I \) is a monomial ideal, then \( I = \langle \mathcal{M}(I) \rangle \).

Monomial ideals can be visualized by a staircase diagram. Here is an example for the monomial ideal \( I = \langle y^3, xy^2, x^3y^2, x^4 \rangle \).

**Question:** Are any of these monomials not needed to generate \( I \)?
Square-free monomial ideals

Definition

A monomial \( x^\alpha := x_1^{\alpha_1} \cdots x_n^{\alpha_n} \) is square-free if each \( \alpha_i \in \{0, 1\} \).

A square-free monomial ideal is any ideal generated by square-free monomials.

The exponent vector \( \alpha = (\alpha_1, \ldots, \alpha_n) \) of a square-free monomial \( x^\alpha \) canonically determines a subset of \( [n] = \{1, \ldots, n\} \).

Notations

- Given \( x^\alpha \), we may speak of \( \alpha \) as a subset of \( [n] \) rather than a vector.
- We will write subsets as strings, e.g., \( xz \) for \( \{x, z\} \).

Key property

Let \( I \) be a square-free monomial ideal of \( \mathbb{F}[x_1, \ldots, x_n] \), and \( \alpha, \beta \subseteq [n] \). Then

\[
\begin{align*}
 x^\alpha \in I & \quad \text{and} \quad x^\beta \in I \quad \implies \quad x^{\alpha \cup \beta} \in I, \\
 x^\alpha \not\in I & \quad \text{and} \quad x^\beta \not\in I \quad \implies \quad x^{\alpha \cap \beta} \not\in I.
\end{align*}
\]
Simplicial complexes

**Definition**

A **simplicial complex** over a finite set $X$ is a collection $\Delta$ of subsets of $X$, closed under taking subsets. That is,

\[ \beta \in \Delta \quad \text{and} \quad \alpha \subset \beta \implies \alpha \in \Delta. \]

Elements in $\Delta$ are called **simplices** or **faces**.

**Example 1**

\[ X = \{a, b, c, d, e, f\} \]
\[ \Delta = \{\emptyset, a, b, c, d, e, f, bc, cd, ce, de, cde, df, ef\} \]

A $k$-dimensional face (size-$(k + 1)$ subset) is called a **$k$-face**. For small $k$, we also say that:

- 0-face is a vertex, or node,
- 1-face is an edge,
- 2-face is a triangle,
- 3-face is a (solid) triangular pyramid.
Simplicial complexes

We will often be interested in the non-faces of a simplicial complex, i.e., $\Delta^c := 2^X \setminus \Delta$.

**Key property**

Let $\Delta$ be a simplicial complex.

(i) **Faces** of $\Delta$ are closed under intersection: $\alpha, \beta \in \Delta \Rightarrow \alpha \cap \beta \in \Delta$.

(ii) **Non-faces** of $\Delta$ are closed under unions: $\alpha, \beta \in \Delta^c \Rightarrow \alpha \cup \beta \in \Delta^c$.

**Remark**

- $\Delta$ is determined by its maximal faces.
- $\Delta^c$ is determined by its minimal non-faces.

**Example 1 (continued)**

- 14 faces in $\Delta = \{\emptyset, a, b, c, d, e, f, bc, cd, ce, de, cde, df, ef\}$.
- 50 non-faces in $\Delta^c$.
- **Maximal faces**: $a, bc, cde, df, ef$.
- **Minimal non-faces**: $ab, ac, ad, ae, af, bd, be, bf, cf, def$. 
Example 2

Consider the following simplicial complex $\Delta$ over $X = \{x, y, z\}$.

Faces: $\Delta = \{\emptyset, x, y, z, xz\}$ (maximal: $y, xz$)
Non-faces: $\Delta^c = \{xy, yz, xyz\}$ (minimal: $xy, yz$)

The faces $\Delta$ and non-faces $\Delta^c$ form a down-set and a up-set on the Boolean lattice.
An interplay between algebra and combinatorics (Example 1)

Consider the following square-free monomial ideal $I$ in $\mathbb{F}[a, b, c, d, e, f]$:

$$I = \langle ab, ac, ad, ae, af, bd, be, bf, cf, def \rangle.$$

The monomials not in $I$ are closed under intersection, and so they form a simplicial complex

$$X = \{a, b, c, d, e, f\}$$

$$\Delta_{I^c} = \{\emptyset, a, b, c, d, e, f, bc, cd, ce, de, cde, df, ef\}$$

Note that $\Delta_{I^c}$ is determined by its maximal faces: $a, bc, cde, df, ef$.

The unique minimal generating set of $I$ are the minimal non-faces: $ab, ac, ad, ae, af, bd, be, bf, cf, def$.

In summary:

- Every square-free monomial ideal $I$ defines a canonical simplicial complex, $\Delta_{I^c}$.
- Every simplicial complex $\Delta$ defines a canonical square-free monomial ideal $I_{\Delta^c}$.

This process is bijective, and is called Alexander duality.
An interplay between algebra and combinatorics (Example 2)

Let’s see another example, this time the square-free monomial ideal \( I \) in \( \mathbb{F}[x, y, z] \):

\[
I = \langle xy, yz \rangle.
\]

The monomials \emph{not} in \( I \) are closed under intersection, and so they form a simplicial complex

\[
X = \{ x, y, z \}
\]

\[
\Delta_{I^c} = \{ \emptyset, x, y, z, xz \}
\]

Note that \( \Delta_{I^c} \) is determined by its \textbf{maximal faces}: \( y, xz \).

The unique minimal generating set of \( I \) are the \textbf{minimal non-faces}: \( xy, yz \).

Also, note that

\[
I = \langle xy, yz \rangle = \{ xy \cdot h_1(x, y, z) + yz \cdot h_2(x, y, z) : h_1, h_2 \in R \} = \langle y \rangle \cap \langle x, z \rangle.
\]

This is called the \textbf{primary decomposition} of \( I = \langle xy, yz \rangle \). The ideals \( \langle y \rangle \) and \( \langle x, z \rangle \) are called the \textbf{primary components}.
Let's see that last example again

But this time we'll start with the simplicial complex $\Delta$.

**Example 2**

Faces: $\Delta = \{\emptyset, x, y, z, xz\}$ (maximal: $y, xz$)

Non-faces: $\Delta^c = \{xy, yz, xyz\}$ (minimal: $xy, yz$)

$I_{\Delta^c} = \langle xy, yz \rangle = \langle y \rangle \cap \langle x, z \rangle$
Now let's see those examples together

Example 2 (continued)

Faces: $\Delta = \{\emptyset, x, y, z, xz\}$ (maximal: $y, xz$)

Non-faces: $\Delta^c = \{xy, yz, xyz\}$ (minimal: $xy, yz$)

Complements of maximal faces: $xz, y$

$I_{\Delta^c} = \langle xy, yz \rangle = \langle x, z \rangle \cap \langle y \rangle$

---

Example 1 (continued)

$\Delta = \{\emptyset, a, b, c, d, e, f, bc, cd, ce, de, cde, df, ef\}$

Maximal faces: $a, bc, cde, df, ef$

Complements of max'l faces: $bcdef, adef, abf, abce, abcd$

Minimal non-faces: $ab, ac, ad, ae, af, bd, be, bf, cf, def$

$I_{\Delta^c} = \langle ab, ac, ad, ae, af, bd, be, bf, cf, def \rangle$

$= \langle b, c, d, e, f \rangle \cap \langle a, d, e, f \rangle \cap \langle a, b, f \rangle \cap \langle a, b, c, e \rangle \cap \langle a, b, c, d \rangle$
Summary so far

Key property

A square-free monomial ideal $I$ is completely determined by the subsets $\alpha$ for which $x^\alpha \in I$.

- If $\alpha \subseteq \beta$ and $x^\alpha \in I$, then $x^\beta \in I$.
- If $\alpha \subseteq \beta$ and $x^\beta \not\in I$, then $x^\alpha \not\in I$.

In other words,

(i) As subsets, exponents of square-free monomials in $I$ are closed under unions.
(ii) As subsets, exponents of square-free monomials not in $I$ are closed under intersections.

Key property

We can describe a square-free monomial ideal $I$ combinatorially as a collection of subsets, closed under intersections.

These subsets have two interpretations, one algebraic and one combinatorial.

- algebraically: the monomials $x^\alpha$ not in $I$;
- combinatorially: the faces $\alpha$ of a simplicial complex, that we will denote by $\Delta_I^c$. 
Alexander duality

Definition

Given an ideal \( I \) in \( \mathbb{F}[x_1, \ldots, x_n] \), define the simplicial complex

\[
\Delta_I^c := \{ \alpha \mid x^\alpha \not\in I \}.
\]

Given a simplicial complex \( \Delta \), define a square-free monomial ideal

\[
I_{\Delta^c} := \langle x^\alpha \mid \alpha \not\in \Delta \rangle.
\]

This is called the Stanley-Reisner ideal of \( \Delta \).

Theorem

The correspondence \( I \mapsto \Delta_I^c \) and \( \Delta \mapsto I_{\Delta^c} \) is a bijection between:

(i) simplicial complexes on \([n] = \{1, \ldots, n\}\),
(ii) square-free monomial ideals in \( \mathbb{F}[x_1, \ldots, x_n] \).

This correspondence is called Alexander duality.
Primary decomposition (motivation)

In grade-school, everybody learns how to factor integers into products of primes, e.g.,

$$6 = 2 \cdot 3, \quad \text{and} \quad 45 = 3^2 \cdot 5.$$ 

Ideals in the ring $R = \mathbb{Z}$ behave similarly.

Since $\mathbb{Z}$ is a principal ideal domain (PID), every ideal has the form $I = \langle a \rangle$ for some $a \in \mathbb{Z}$.

Every ideal $I$ can be written as an intersection of primary ideals. For example,

$$\langle 6 \rangle = \langle 2 \rangle \cap \langle 3 \rangle, \quad \text{and} \quad \langle 45 \rangle = \langle 9 \rangle \cap \langle 5 \rangle.$$ 

This is called a primary decomposition of the ideal.

Note that there is no way to further break up $\langle 9 \rangle$ into an expression involving $\langle 3 \rangle$.

Ideals of the form $I = \langle p \rangle$ for a prime $p$ are called prime ideals and those of the form $I = \langle p^k \rangle$ are called primary ideals.

These concepts and this construction holds in a much larger class of commutative rings than just $\mathbb{Z}$. 
Primary decomposition

Definition

Let $I$ be an ideal of a commutative ring $R$.

- $I$ is a **prime ideal** if $fg \in I$ implies either $f \in I$ or $g \in I$.
- $I$ is a **primary ideal** if $fg \in I$ implies either $f \in I$ or $g^k \in I$ for some $k \in \mathbb{N}$.

Example

Consider the ring $R = \mathbb{Z}$.

- The **prime ideals** (excluding 0 and $\mathbb{Z}$) are of the form $I = \langle p \rangle$ for some prime $p$.
- The **primary ideals** (excluding 0 and $\mathbb{Z}$) are of the form $I = \langle p^k \rangle$ for $k \in \mathbb{N}$.

The following theorem can be thought of as a way to “factor” ideals in polynomial rings, much like how integers can be factored into primes.

Lasker-Noether Theorem

Every ideal $I$ of $\mathbb{F}[x_1, \ldots, x_n]$ can be written as $I = \bigcap_{i=1}^{r} p_i$, where $p_i$ is a primary ideal. We call this a **primary decomposition** of $I$. The $p_i$ are called **primary components**.

In general, primary decompositions are hard to compute and need not be unique. But for square-free monomial ideals, they have a simple combinatorial description.
Ideals and varieties

Definition

Given an ideal \( I \leq \mathbb{F}[x_1, \ldots, x_n] \), the variety of \( I \) is its set of common zeros:

\[
V(I) := \{x \in \mathbb{F}^n : f(x) = 0 \text{ for all } f \in I\}.
\]

The ideal generated by a variety \( V \subseteq \mathbb{F}^n \) is

\[
I(V) := \{f \in \mathbb{F}[x_1, \ldots, x_n] \mid f(v) = 0, \forall v \in V\}.
\]

Proposition

For any two varieties \( V_1 \) and \( V_2 \) in \( \mathbb{F}^n \),

\[
I(V_1 \cup V_2) = I(V_1) \cap I(V_2).
\]

For any \( \alpha \subseteq [n] \), define \( p^\alpha = \langle x_i : i \in \alpha \rangle \) and \( p^{\bar{\alpha}} = p^{[n] - \alpha} = \langle x_i : i \not\in \alpha \rangle \). Both are prime.

Theorem

Let \( \Delta \) be a simplicial complex over \( [n] \). The Stanley-Reisner ideal of \( \Delta \) in \( R = \mathbb{F}[x_1, \ldots, x_n] \) is

\[
l_\Delta^c = \bigcap_{\alpha \in \Delta} p^{\bar{\alpha}} = \bigcap_{\alpha \in \Delta \text{ maximal}} p^{\bar{\alpha}}.
\]
Example 2 (continued)

Faces: $\Delta = \{\emptyset, x, y, z, xz\}$  \hspace{1cm} (maximal: $y, xz$)
Non-faces: $\Delta^c = \{xy, yz, xyz\}$  \hspace{1cm} (minimal: $xy, yz$)

$I_{\Delta^c} = \langle xy, yz \rangle = \langle x, z \rangle \cap \langle y \rangle$

The primary decomposition of $I_{\Delta^c}$ is generated by the complements of the 5 faces in $\Delta$.

This is not the set complement of $\Delta$, i.e., the 3 non-faces $\Delta^c = \{xy, yz, xyz\}$, but rather,

$$\{\emptyset, \overline{x}, \overline{z}, \overline{y}, \overline{xz}\} = \{xy, yz, xy, xz, y\}.$$

By the previous theorem, the primary decomposition of $I_{\Delta^c}$ is

$$I_{\Delta^c} = \langle xy, yz \rangle = \bigcap_{\alpha \in \Delta} p^{\overline{\alpha}} = p^{\overline{\emptyset}} \cap p^{\overline{x}} \cap p^{\overline{z}} \cap p^{\overline{y}} \cap p^{\overline{xz}}$$

$$= p^{xyz} \cap p^{yz} \cap p^{xy} \cap p^{xz} \cap p^y$$

$$= \langle x, y, z \rangle \cap \langle y, z \rangle \cap \langle x, y \rangle \cap \langle x, z \rangle \cap \langle y \rangle$$

unnecessary

$$= \langle x, z \rangle \cap \langle y \rangle = \bigcap_{\alpha \in \Delta} p^{\overline{\alpha}}.$$
Computing the primary decomposition

Example 1 (continued)

Faces: $\Delta = \{\emptyset, a, b, c, d, e, f, bc, cd, ce, de, cde, df, ef\}$

Maximal faces: $a, bc, cde, df, ef$

Complements of maximal faces: $bcdef, adef, abf, abce, abcd$

Minimal non-faces: $ab, ac, ad, ae, af, bd, be, bf, cf, def$

The Stanley-Reisner ideal $I_{\Delta^c}$ is generated by the (minimal) non-faces.

The primary components correspond to the complement of the maximal faces:

$$I_{\Delta^c} = \langle ab, ac, ad, ae, af, bd, be, bf, cf, def \rangle = \bigcap_{\alpha \in \Delta} p^{\alpha} = \bigcap_{\alpha \in \Delta \text{ maximal}} p^{\alpha}$$

$$= \langle b, c, d, e, f \rangle \cap \langle a, d, e, f \rangle \cap \langle a, b, f \rangle \cap \langle a, b, c, e \rangle \cap \langle a, b, c, d \rangle.$$
The plan from here

Now, we are ready to apply Stanley-Reisner theory to reverse engineering the wiring diagram of a local model.

Here is a summary of the process:

1. Consider every pair of input vectors that give a different output.
2. For each pair, take the monomial $x^\alpha$, where $\alpha \subseteq [n]$ is the set where the entries differ.
3. These generate an ideal. The primary decomposition encodes all minimal wiring diagrams.

Simplification

We can consider each coordinate independently.

This is best seen with an example. Consider the following Boolean local model $f = (f_1, f_2, f_3)$.

$$
\begin{align*}
    f_1 &= x_2 \\
    f_2 &= x_2 \land x_3 \\
    f_3 &= x_1 \lor \overline{x_2}
\end{align*}
$$

Thus, we will consider a function $f : \mathbb{F}^n \rightarrow \mathbb{F}$ with partial data, and attempt to reverse-engineer its wiring diagram.
Let $f : \mathbb{F}^n \rightarrow \mathbb{F}$ be a function, where $\mathbb{F} = \mathbb{F}_p$.

**Definition**

Consider a set

$$D = \{ (s_1, t_1), \ldots , (s_m, t_m) \}, \quad s_i \in \mathbb{F}^n, \quad t_i \in \mathbb{F}$$

of input-output pairs, all $s_i$ are distinct. We call such a set data, and say that $f$ fits the data $D$ if

$$f(s_i) = f(s_{i_1}, \ldots , s_{i_n}) = t_i, \quad \text{for all } i = 1, \ldots , m.$$ 

The model space of $D$ is the set $\text{Mod}(D)$ of all functions that fit the data, i.e.,

$$\text{Mod}(D) = \{ f : \mathbb{F}^n \rightarrow \mathbb{F} \mid f(s_i) = t_i \text{ for all } i = 1, \ldots , m \}.$$

For any $f$ in $\text{Mod}(D)$, the support of $f$, denoted $\text{supp}(f)$, is the set of variables on which $f$ depends.

Under a slight abuse of notation, we can think of the support as a subset of $\{x_1, \ldots , x_n\}$ or as a subset $\alpha \subseteq [n] = \{1, \ldots , n\}$.

Either way, we can write $\text{supp}(f)$ as a string.
Feasible, disposable, and min-sets

Definition

With respect to a set $\mathcal{D}$ of data, a set $\alpha \subseteq [n]$ is:
- **feasible** if there is some $f \in \text{Mod}(\mathcal{D})$ for which $\text{supp}(f) \subseteq \alpha$.
- **disposable** if there is some $f \in \text{Mod}(\mathcal{D})$ for which $\text{supp}(f) \cap \alpha = \emptyset$.

Note that a set $\alpha$ is feasible if and only if its complement $\overline{\alpha} := [n] - \alpha$ is disposable.

Remark

These are *not* opposite concepts; a set can be both feasible and disposable, or neither.

Key point

Let $\mathcal{D}$ be a set of data, and $\alpha, \beta \subseteq [n]$.

(i) If $\alpha$ and $\beta$ are feasible with respect to $\mathcal{D}$, then so is $\alpha \cup \beta$.
(ii) If $\alpha$ and $\beta$ are disposable with respect to $\mathcal{D}$, then so is $\alpha \cap \beta$.

In particular, the disposable sets of $\mathcal{D}$ form a simplicial complex $\Delta_\mathcal{D}$.

Definition

A subset $\alpha \subseteq [n]$ is a **min-set** of $\mathcal{D}$ if its complement $\overline{\alpha} := [n] - \alpha$ is a maximal disposable set of $\mathcal{D}$.
Min-sets and Stanley-Reisner theory applied to min-sets

**Theorem**

There is a bijective correspondence between:
- the simplicial complex $\Delta_D$ of disposable sets,
- the square-free monomial ideal $I_{\Delta_D}^c$ in $\mathbb{F}[x_1, \ldots, x_n]$ of non-disposable sets.

In other words, $\alpha$ is a min-set of $D$ if and only if $\overline{\alpha}$ is a maximal disposable set, and

$$x^\alpha \in I_{\Delta_D}^c \quad \text{if and only if} \quad \alpha \text{ is non-disposable}.$$  

For each pair $(s, t), (s', t') \in D$, define the monomial

$$m(s, s') := \prod_{s_i \neq s'_i} x_i.$$  

By construction, if $t \neq t'$, then $\text{supp}(m(s, s'))$ must be non-disposable.

**Theorem**

The ideal of non-disposable sets is the ideal in $\mathbb{F}_2[x_1, \ldots, x_n]$ defined by

$$I_{\Delta_D}^c = \langle m(s, s') \mid t \neq t' \rangle.$$  

The generators of the primary components of $I_{\Delta_D}^c$ are the min-sets of $D$. 
Example 2 (continued)

Consider a Boolean function $f : \mathbb{F}_2^3 \rightarrow \mathbb{F}_2$ with the following partial data:

<table>
<thead>
<tr>
<th>$xyz$</th>
<th>101</th>
<th>000</th>
<th>110</th>
</tr>
</thead>
<tbody>
<tr>
<td>$f(x, y, z)$</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>

Using our notation, the *data* $\mathcal{D}$, grouped by output value, is

$$\mathcal{D} = \{(s_1, t_1), (s_2, t_2), (s_3, t_3)\} = \{(101, 0), (000, 0), (110, 1)\}.$$ 

Since $t_1 = t_2 \neq t_3$, we compute $m(s_1, s_3) = yz$ and $m(s_2, s_3) = xy$. 

Non-disposable sets $\Delta^c_{\mathcal{D}}$; Monomials in $I_{\Delta^c_{\mathcal{D}}}$

Disposable sets $\Delta_{\mathcal{D}}$

Feasible sets of $\mathcal{D}$

The min-sets are shaded
Example 3

Consider a Boolean function $f: \mathbb{F}_2^3 \rightarrow \mathbb{F}_2$ with the following partial data:

<table>
<thead>
<tr>
<th>$xyz$</th>
<th>111</th>
<th>000</th>
<th>110</th>
</tr>
</thead>
<tbody>
<tr>
<td>$f(x, y, z)$</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>

Using our notation, the data $\mathcal{D}$, grouped by output value, is

$$\mathcal{D} = \{(s_1, t_1), (s_2, t_2), (s_3, t_3)\} = \{(111, 0), (000, 0), (110, 1)\}.$$ 

Since $t_1 = t_2 \neq t_3$, we compute $m(s_1, s_3) = z$ and $m(s_2, s_3) = xy$. 

- Non-disposable sets $\Delta^c_\mathcal{D}$; Monomials in $I_{\Delta^c_\mathcal{D}}$
- Disposable sets $\Delta_\mathcal{D}$
- Feasible sets of $\mathcal{D}$

The min-sets are shaded.
Summary so far

The following table summarizes the correspondence between the combinatorial structures in the Boolean network problem to Stanley-Reisner theory and Alexander duality.

<table>
<thead>
<tr>
<th>Reverse engineering of local models</th>
<th>Stanley-Reisner theory</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disposable sets of $\mathcal{D}$</td>
<td>Faces of the simplicial complex $\Delta_\mathcal{D}$</td>
</tr>
<tr>
<td>Non-disposable sets of $\mathcal{D}$</td>
<td>The non-faces, $\Delta^c_\mathcal{D}$</td>
</tr>
<tr>
<td>The ideal $\langle m(s, s') \mid t \neq t' \rangle$ of non-disposable sets</td>
<td>The Stanley-Reisner ideal $I_{\Delta^c_\mathcal{D}}$</td>
</tr>
<tr>
<td>Feasible sets of $\mathcal{D}$</td>
<td>Complements of faces of $\Delta_\mathcal{D}$</td>
</tr>
<tr>
<td>Min-sets of $\mathcal{D}$</td>
<td>Complements of max’l faces of $\Delta_\mathcal{D}$ ↔ primary components of $I_{\Delta^c_\mathcal{D}}$</td>
</tr>
</tbody>
</table>
Consider a function $f : \mathbb{F}_5^5 \to \mathbb{F}_5$ with the following partial data:

$$
\begin{align*}
(s_1, t_1) &= (01210, 0), & \text{The monomials } m(s_i, s_j) \text{ are:} \\
(s_2, t_2) &= (01211, 0), & m(s_1, s_4) = x_1x_2x_3x_4, \\
(s_3, t_3) &= (01214, 1), & m(s_1, s_5) = m(s_2, s_5) = m(s_3, s_5) = x_1x_3x_5, \\
(s_4, t_4) &= (30000, 3), & m(s_2, s_4) = m(s_3, s_4) = m(s_4, s_5) = x_1x_2x_3x_4x_5, \\
(s_5, t_5) &= (11113, 4). & m(s_1, s_3) = m(s_2, s_3) = x_5.
\end{align*}
$$

The ideal of non-disposable sets in $\mathbb{F}_2[x_1, x_2, x_3, x_4, x_5]$ is

$$I_{\Delta_c^D} = \langle m(s_i, s_j) \mid t_i \neq t_j \rangle = \langle x_1x_2x_3x_4x_5, x_1x_3x_5, x_1x_2x_3x_4, x_5 \rangle = \langle x_1x_2x_3x_4, x_5 \rangle.$$

We can compute the primary decomposition in Macaulay2:

```
R = ZZ/2[x1,x2,x3,x4,x5];
I_nonDisp = ideal(x5, x1*x2*x3*x4);
primaryDecomposition I_nonDisp
```

Output: \{ideal (x1, x5), ideal(x2, x5), ideal(x3, x5), ideal(x4, x5)\}

- Primary decomposition: $I_{\Delta_c^D} = \langle x_1, x_5 \rangle \cap \langle x_2, x_5 \rangle \cap \langle x_3, x_5 \rangle \cap \langle x_4, x_5 \rangle$.
- Unsigned min-sets: \{x1, x5\}, \{x2, x5\}, \{x3, x5\}, \{x4, x5\}. 

E. Dimitrova (Clemson)  
Reverse engineering minimal wiring diagrams  
Algebraic Biology 30 / 40
Finding signed min-sets of local models

Consider a set of data (i.e., input-output pairs) with all \( s_i \) distinct:

\[ D = \{(s_1, t_1), \ldots, (s_m, t_m)\}, \quad s_i \in \mathbb{F}^n, \quad t_i \in \mathbb{F}. \]

Order the data so the output values are non-decreasing, i.e., \( t_1 \leq \cdots \leq t_m \).

**Last time:** For each pair \( (s, t), (s', t') \in D \), define the monomial \( m(s, s') := \prod_{s_i \neq s'_i} x_i \).

That is, for each coordinate \( i \) where \( s \) and \( s' \) differ, include \( x_i \).

**This time:** For each coordinate \( i \) that \( s \) and \( s' \) differ, include:

- \( (x_i - 1) \) if the interaction is positive \( (s_i < s'_i) \),
- \( (x_i + 1) \) if the interaction is negative \( (s_i > s'_i) \).

Then define the pseudomonomial

\[ p(s, s') := \prod_{s_i \neq s'_i} (x_i - \text{sign}(s'_i - s_i)). \]

**Theorem**

The ideal of signed non-disposable sets is the ideal in \( \mathbb{F}_3[x_1, \ldots, x_n] \) defined by

\[ J_{\Delta \Delta D} = \langle p(s_i, s_j) \mid i < j, \ t_i \neq t_j \rangle. \]

The primary components of \( J_{\Delta \Delta D} \) give the signed min-sets.
Example 3

Consider a Boolean function \( f : \mathbb{F}_2^3 \rightarrow \mathbb{F}_2 \) with the following partial data:

<table>
<thead>
<tr>
<th>( \text{xyz} )</th>
<th>111</th>
<th>000</th>
<th>110</th>
</tr>
</thead>
<tbody>
<tr>
<td>( f(x,y,z) )</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>

The data \( \mathcal{D} \) is

\[
\mathcal{D} = \{(s_1, t_1), (s_2, t_2), (s_3, t_3)\} = \{(111, 0), (000, 0), (110, 1)\}.
\]

Note that

\[
p(s_1, s_3) = z - (\text{sign}(s_{33} - s_{13})) = z + 1, \quad p(s_2, s_3) = (x - 1)(y - 1).
\]

The ideal of signed non-disposable sets for \( \mathcal{D} \) is thus

\[
J_{\Delta s}^\mathcal{D} = \langle p(s_1, s_3), p(s_2, s_3) \rangle = \langle z + 1, (x - 1)(y - 1) \rangle.
\]

The following Macaulay2 commands compute the primary decomposition of \( J_{\Delta s}^\mathcal{D} \):

```plaintext
R = ZZ/3[x,y,z];
J_nonDisp = ideal(z+1, (x-1)*(y-1));
primaryDecomposition J_nonDisp
```

Output: \{ideal (z + 1, y - 1), ideal (z + 1, x - 1)\}

- Primary decomposition: \( J_{\Delta s}^\mathcal{D} = \langle x - 1, z + 1 \rangle \cap \langle y - 1, z + 1 \rangle \).
- Signed min-sets: \( \{x, \bar{z}\} \) and \( \{y, \bar{z}\} \).
Signed min-sets over non-Boolean fields

Let's compute the pseudomonomials for our previous example of $f : \mathbb{F}_5^5 \rightarrow \mathbb{F}_5$ with data:

\[(s_1, t_1) = (01210, 0), \quad p(s_1, s_3) = p(s_2, s_3) = x_5 - 1,\]
\[(s_2, t_2) = (01211, 0), \quad p(s_3, s_5) = (x_1 - 1)(x_3 + 1)(x_5 + 1),\]
\[(s_3, t_3) = (01214, 1), \quad p(s_1, s_4) = (x_1 - 1)(x_2 + 1)(x_3 + 1)(x_4 + 1),\]
\[(s_4, t_4) = (30000, 3), \quad p(s_1, s_5) = p(s_2, s_5) = (x_1 - 1)(x_3 + 1)(x_5 - 1),\]
\[(s_5, t_5) = (11113, 4). \quad p(s_4, s_5) = (x_1 + 1)(x_2 - 1)(x_3 - 1)(x_4 - 1)(x_5 - 1),\]
\[p(s_2, s_4) = p(s_3, s_4) = (x_1 - 1)(x_2 + 1)(x_3 + 1)(x_4 + 1)(x_5 + 1).\]

The last three are redundant. The ideal of signed non-disposable sets in $\mathbb{F}_3[x_1, x_2, x_3, x_4, x_5]$ is

\[J_{\Delta_D}^c = \langle p(s_i, s_j) \mid t_i \neq t_j \rangle = \langle x_5 - 1, (x_1 - 1)(x_3 + 1)(x_5 + 1), (x_1 - 1)(x_2 + 1)(x_3 + 1)(x_4 + 1) \rangle.\]

We can compute the primary decomposition in Macaulay2:

```plaintext
R = ZZ/3[x1,x2,x3,x4,x5];
J_nonDisp = ideal(x5-1, (x1-1)*(x3+1)*(x5+1), (x1-1)*(x2+1)*(x3+1)*(x4+1));
primaryDecomposition J_nonDisp
```

Output: \{ideal (x5-1, x3+1), ideal(x5-1, x1-1)\}

- Primary decomposition: $J_{\Delta_D}^c = \langle x_1 - 1, x_5 - 1 \rangle \cap \langle x_3 + 1, x_5 - 1 \rangle$.
- Signed min-sets: $\{x_1, x_5\}, \{x_3, x_5\}$. 
Application to a real gene network

*Caenorhabditis elegans* is a microscopic roundworm and common model organism in biology.

It was the first multicellular organism to have its full genome sequenced, and its nervous system (*connectome*) completely mapped. The latter consists of just 302 neurons and \( \approx 7000 \) synapses.

In 2012, Stigler & Chamberlin studied a network with 20 genes involved in embryonal development of *C. elegans*.

They discretized data from two time series, \( s_1, \ldots, s_{10} \) and \( u_1, \ldots, u_{10} \), to 7 states, i.e., \( s_i, u_i \in \mathbb{F}_7^{20} \).

The \( i^{th} \) input state is \( s_i \) and the \( i^{th} \) output state is \( t_i = f(s_i) = s_{i+1} \), where \( f : \mathbb{F}_7^{20} \to \mathbb{F}_7^{20} \) is the FDS map of an unknown local model over \( \mathbb{F}_7 \). Similarly, \( v_i = f(u_i) = u_{i+1} \).
Note that the 20 points in $\mathbb{F}_7^{20}$ in two time series describe 18 input-output pairs.

|      | $x_1$ | $x_2$ | $x_3$ | $x_4$ | $x_5$ | $x_6$ | $x_7$ | $x_8$ | $x_9$ | $x_{10}$ | $x_{11}$ | $x_{12}$ | $x_{13}$ | $x_{14}$ | $x_{15}$ | $x_{16}$ | $x_{17}$ | $x_{18}$ | $x_{19}$ | $x_{20}$ |
|------|-------|-------|-------|-------|-------|-------|-------|-------|-------|----------|----------|----------|----------|----------|----------|----------|----------|----------|----------|
| $s_1$ | 4     | 6     | 5     | 0     | 3     | 0     | 0     | 0     | 0     | 0        | 1        | 0        | 0        | 0        | 1        | 0        | 0        | 0        | 0        | 0        |
| $s_2 = t_1$ | 3     | 6     | 5     | 0     | 2     | 1     | 1     | 1     | 0     | 0        | 0        | 1        | 1        | 0        | 0        | 0        | 1        | 0        | 0        | 0        |
| $s_3 = t_2$ | 1     | 3     | 1     | 0     | 2     | 1     | 1     | 1     | 1     | 0        | 0        | 1        | 1        | 0        | 1        | 0        | 1        | 0        | 1        | 0        |
| $s_4 = t_3$ | 1     | 3     | 1     | 2     | 2     | 1     | 1     | 1     | 1     | 1        | 0        | 0        | 0        | 1        | 0        | 0        | 1        | 2        | 1        |
| $s_5 = t_4$ | 0     | 1     | 1     | 2     | 2     | 1     | 1     | 1     | 1     | 1        | 0        | 0        | 1        | 1        | 0        | 1        | 0        | 1        | 2        | 1        |
| $s_6 = t_5$ | 0     | 2     | 1     | 4     | 6     | 4     | 1     | 3     | 1     | 1        | 0        | 0        | 1        | 2        | 0        | 1        | 0        | 1        | 1        | 1        |
| $s_7 = t_6$ | 0     | 3     | 1     | 6     | 5     | 5     | 1     | 4     | 2     | 1        | 0        | 0        | 1        | 1        | 1        | 2        | 1        | 1        | 1        | 0        |
| $s_8 = t_7$ | 1     | 3     | 1     | 4     | 2     | 6     | 1     | 4     | 2     | 3        | 1        | 1        | 3        | 2        | 4        | 4        | 0        | 3        | 3        | 0        |
| $s_9 = t_8$ | 1     | 3     | 1     | 6     | 2     | 5     | 1     | 5     | 1     | 5        | 2        | 5        | 6        | 2        | 5        | 5        | 0        | 4        | 4        | 0        |
| $t_9$ | 0     | 2     | 1     | 4     | 2     | 3     | 1     | 3     | 1     | 4        | 1        | 3        | 4        | 2        | 5        | 3        | 1        | 5        | 5        | 5        |

<table>
<thead>
<tr>
<th></th>
<th>$x_1$</th>
<th>$x_2$</th>
<th>$x_3$</th>
<th>$x_4$</th>
<th>$x_5$</th>
<th>$x_6$</th>
<th>$x_7$</th>
<th>$x_8$</th>
<th>$x_9$</th>
<th>$x_{10}$</th>
<th>$x_{11}$</th>
<th>$x_{12}$</th>
<th>$x_{13}$</th>
<th>$x_{14}$</th>
<th>$x_{15}$</th>
<th>$x_{16}$</th>
<th>$x_{17}$</th>
<th>$x_{18}$</th>
<th>$x_{19}$</th>
<th>$x_{20}$</th>
</tr>
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<tbody>
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<td>0</td>
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<td>$u_5 = v_4$</td>
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<tr>
<td>$u_6 = v_5$</td>
<td>2</td>
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<td>1</td>
<td>2</td>
<td>4</td>
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<td>$u_7 = v_6$</td>
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<tr>
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<td>$v_9$</td>
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</tbody>
</table>
Application to a real gene network

Goal

Reconstruct a wiring diagram for the subnetwork of three genes responsible for body wall (mesodermal) tissue development.

<table>
<thead>
<tr>
<th>Gene</th>
<th>Variable</th>
<th>Muscle Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>hlh-1</td>
<td>x_8</td>
<td>skeletal</td>
</tr>
<tr>
<td>hnd-1</td>
<td>x_18</td>
<td>cardiac</td>
</tr>
<tr>
<td>unc-120</td>
<td>x_19</td>
<td>cardiac, smooth, skeletal</td>
</tr>
</tbody>
</table>

These genes are known to be regulated by the maternally controlled \textit{pal-1} genes.

Though all three regulate a single tissue type in \textit{C. elegans}, some vertebrates have homologous transcription factors related to these genes that regulate three different muscle types.

Understanding their regulatory interactions has implications in human muscle development and disease.

For each gene \( j \) of interest \((j = 8, 18, 19)\), we extract a set \( \mathcal{D}_j \) of data. For example, the data for the \textit{hlh-1} gene is

\[
\mathcal{D}_8 = \{(s_1, t_{18}), (s_2, t_{28}), \ldots, (s_9, t_{98}), (u_1, v_{18}), (u_2, v_{28}), \ldots, (u_9, v_{98})\}.
\]

The ideal of non-disposable sets for the \textit{hlh-1} gene is

\[
I_{\mathcal{D}_8} = \langle \{ m(s_i, s_j) \mid t_{i8} \neq t_{j8} \} \cup \{ m(u_i, u_j) \mid v_{i8} \neq v_{j8} \} \cup \{ m(s_i, u_j) \mid t_{i8} \neq v_{j8} \} \rangle.
\]
The ideal of non-disposable sets for the $hlh-1$ gene

$$I_{D_8}^c = \langle x_1 x_2 x_4 x_5 x_6 x_7 x_8 x_9 x_{13} x_{14}, x_2 x_3 x_5 x_9 x_{11} x_{13} x_{14}, x_2 x_4 x_6 x_9 x_{12} x_{13} x_{14}, x_1 x_3 x_9 x_{11} x_{12} x_{13} x_{14},$$

$$x_1 x_2 x_3 x_5 x_7 x_{11} x_{12} x_{13} x_{15}, x_2 x_3 x_5 x_7 x_{11} x_{13} x_{14} x_{15}, x_1 x_2 x_{13} x_{16}, x_1 x_2 x_4 x_6 x_7 x_8 x_9 x_{10} x_{14} x_{15} x_{17},$$

$$x_1 x_4 x_6 x_7 x_8 x_9 x_{10} x_{12} x_{13} x_{14} x_{15} x_{17}, x_1 x_2 x_3 x_4 x_5 x_6 x_7 x_8 x_9 x_{12} x_{13} x_{18}, x_1 x_2 x_3 x_4 x_5 x_6 x_8 x_{12} x_{14} x_{18},$$

$$x_1 x_2 x_3 x_5 x_6 x_7 x_8 x_9 x_{10} x_{11} x_{14} x_{16} x_{18}, x_1 x_2 x_3 x_5 x_6 x_8 x_{10} x_{11} x_{14} x_{15} x_{16} x_{18}, x_1 x_2 x_4 x_9 x_{19},$$

$$x_1 x_4 x_5 x_6 x_7 x_8 x_9 x_{13} x_{19}, x_2 x_4 x_5 x_6 x_8 x_{14} x_{19}, x_1 x_2 x_4 x_6 x_{12} x_{13} x_{14} x_{19}, x_1 x_4 x_5 x_6 x_8 x_{12} x_{13} x_{14} x_{19},$$

$$x_1 x_5 x_6 x_7 x_8 x_9 x_{13} x_{16} x_{19}, x_2 x_4 x_6 x_{12} x_{13} x_{14} x_{16} x_{19}, x_1 x_4 x_5 x_7 x_8 x_9 x_{10} x_{12} x_{14} x_{15} x_{17} x_{19},$$

$$x_1 x_2 x_3 x_4 x_6 x_{12} x_{18} x_{19}, x_1 x_2 x_3 x_4 x_{13} x_{14} x_{18} x_{19}, x_4 x_6 x_8 x_9 x_{10} x_{11} x_{12} x_{13} x_{15} x_{16} x_{18} x_{19},$$

$$x_1 x_3 x_4 x_5 x_6 x_7 x_8 x_9 x_{11} x_{14} x_{15} x_{16} x_{17} x_{18} x_{19}, x_1 x_6 x_7 x_8 x_9 x_{11} x_{12} x_{13} x_{14} x_{15} x_{16} x_{17} x_{18} x_{19},$$

$$x_1 x_4 x_5 x_6 x_{10} x_{11} x_{12} x_{13} x_{14} x_{15} x_{16} x_{17} x_{18} x_{19}, x_1 x_5 x_8 x_9 x_{10} x_{11} x_{12} x_{13} x_{14} x_{15} x_{16} x_{17} x_{18} x_{19},$$

$$x_1 x_4 x_5 x_6 x_7 x_8 x_9 x_{13} x_{15} x_{16} x_{17} x_{20}, x_1 x_2 x_3 x_4 x_5 x_7 x_8 x_{11} x_{12} x_{13} x_{18} x_{20},$$

$$x_1 x_3 x_5 x_6 x_7 x_8 x_{11} x_{14} x_{18} x_{20}, x_1 x_2 x_3 x_4 x_5 x_7 x_8 x_9 x_{13} x_{14} x_{18} x_{20},$$

$$x_1 x_2 x_3 x_5 x_6 x_8 x_{11} x_{14} x_{15} x_{18} x_{20}, x_3 x_4 x_5 x_6 x_7 x_8 x_9 x_{10} x_{13} x_{14} x_{15} x_{17} x_{18} x_{20},$$

$$x_1 x_2 x_3 x_4 x_5 x_6 x_8 x_9 x_{12} x_{15} x_{16} x_{17} x_{18} x_{20}, x_2 x_4 x_5 x_6 x_8 x_9 x_{15} x_{16} x_{17} x_{19} x_{20},$$

$$x_2 x_3 x_5 x_8 x_9 x_{11} x_{12} x_{14} x_{15} x_{19} x_{20}, x_1 x_4 x_5 x_6 x_8 x_9 x_{15} x_{16} x_{17} x_{19} x_{20}, x_2 x_5 x_7 x_8 x_{11} x_{12} x_{14} x_{19} x_{20},$$

$$x_1 x_3 x_4 x_5 x_6 x_7 x_8 x_{11} x_{13} x_{14} x_{16} x_{18} x_{19} x_{20}, x_2 x_4 x_6 x_8 x_9 x_{10} x_{11} x_{13} x_{14} x_{15} x_{16} x_{18} x_{19} x_{20},$$

$$x_4 x_6 x_8 x_{10} x_{11} x_{12} x_{13} x_{14} x_{15} x_{16} x_{18} x_{19} x_{20}, x_1 x_4 x_6 x_7 x_8 x_9 x_{10} x_{11} x_{13} x_{14} x_{15} x_{16} x_{17} x_{18} x_{19} x_{20},$$

$$x_1 x_4 x_5 x_7 x_9 x_{10} x_{12} x_{13} x_{14} x_{15} x_{16} x_{17} x_{18} x_{19} x_{20}, x_1 x_4 x_7 x_8 x_9 x_{10} x_{12} x_{13} x_{14} x_{15} x_{16} x_{17} x_{18} x_{19} x_{20} \rangle.$$
Min-sets of the *hlh-1* gene

The primary decomposition of $I_{D_8^c}$ consists of 483 primary components (min-sets). That is,

$$I_{D_8^c} = \bigcap_{i=1}^{483} p_i.$$ 

However, it is known experimentally that *hlh-1* is controlled by the *pal-1* genes (variables $x_1, x_2, x_3$).

Therefore, we can disregard all min-sets that involve none of these variables.

This happens to be 481 of them, leaving two candidates for min-sets of *hlh-1*:

$$\{x_2, x_3, x_8, x_{18}\} \quad \text{and} \quad \{x_2, x_3, x_8, x_{19}\}.$$ 

There are two possible wiring diagrams at the *hlh-1* gene (variable $x_8$):
Min-sets of the *hnd-1* and *unc-120* genes

Applying a similar process for the other two genes gives:

- 580 min-sets for the *hnd-1* gene,
- 498 min-sets for the *unc-120* gene.

As before, these can be drastically reduced by discarding those that do not contain any of the *pal-1* genes \((x_1, x_2, x_3)\).

Then, they are filtered so that they contain (i) as many of the variables for *hlh-1*, *hnd-1*, *unc-120* \((x_8, x_{18}, x_{19})\) as possible, and (ii) no other variables. The min-sets are:

<table>
<thead>
<tr>
<th>hlh-1 ((x_8))</th>
<th>hnd-1 ((x_{18}))</th>
<th>unc-120 ((x_{19}))</th>
</tr>
</thead>
<tbody>
<tr>
<td>{x_2, x_3, x_8, x_{18}}</td>
<td>{x_2, x_8, x_{18}}</td>
<td>{x_2, x_3, x_8, x_{18}}</td>
</tr>
<tr>
<td>{x_2, x_3, x_8, x_{19}}</td>
<td>{x_2, x_8, x_{19}}</td>
<td>{x_2, x_3, x_8, x_{19}}</td>
</tr>
<tr>
<td></td>
<td>{x_3, x_8, x_{19}}</td>
<td>{x_2, x_8, x_9, x_{19}}</td>
</tr>
<tr>
<td></td>
<td>{x_3, x_8, x_{19}}</td>
<td>{x_2, x_8, x_9, x_{19}}</td>
</tr>
</tbody>
</table>

Collapsing the *pal-1* variables into a single node \(P\) gives the following simplified min-sets:

<table>
<thead>
<tr>
<th>hlh-1 ((x_8))</th>
<th>hnd-1 ((x_{18}))</th>
<th>unc-120 ((x_{19}))</th>
</tr>
</thead>
<tbody>
<tr>
<td>{P, x_8, x_{18}}</td>
<td>{P, x_8, x_{18}}</td>
<td>{P, x_8, x_{18}}</td>
</tr>
<tr>
<td>{P, x_8, x_{19}}</td>
<td>{P, x_8, x_{19}}</td>
<td>{P, x_8, x_{19}}</td>
</tr>
</tbody>
</table>
Minimal wiring diagrams

\[ \text{hlf-1} : \quad \xrightarrow{x_8} x_{18} \quad \text{OR} \quad \xrightarrow{x_8} x_{18} \]

\[ \text{hnd-1} : \quad \xrightarrow{x_8} x_{18} \quad \text{OR} \quad \xrightarrow{x_8} x_{18} \]

\[ \text{unc-120} : \quad \xrightarrow{x_8} x_{18} \quad \text{OR} \quad \xrightarrow{x_8} x_{18} \]