Reverse engineering minimal wiring diagrams

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Algebraic Biology

Broad goals

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

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

In other words, its truth table looks like

$x_1x_2x_3$	111	110	101	100	011	010	001	000
$f_i(x)$	0	1	?	?	?	?	?	0

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:

$$f_j = x_i \wedge x_k$$

$$x_i \longrightarrow x_j$$

"x_i activates x_j"

$$f_j = \overline{x_i} \wedge x_k$$

$$x_i \dashv x_j$$

"x_i inhibits x_j"

$$f_j = x_i + x_k$$

$$\begin{tikzcd} x_i \arrow[r, bend left] \arrow[r, bend right, -|] & x_j \end{tikzcd}$$

"x_i affects x_j positively & negatively"

Unate functions

Consider the following unknown Boolean function:

$x_1x_2x_3$	111	110	101	100	011	010	001	000
$f_i(x)$	0	1	?	?	?	?	?	0

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 $f\colon \mathbb{F}_2^n \to \mathbb{F}_2$ is unate if no variable x_i and its negation $\overline{x_i}$ both appear.

Examples

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

Fact

Most functions that appear in biological networks are unate.

Min-sets

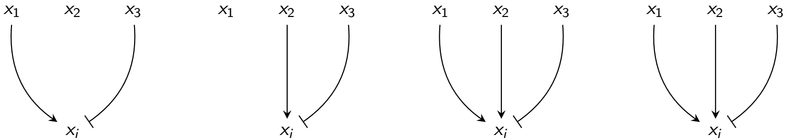
Recall the following unknown Boolean function:

$x_1x_2x_3$	111	110	101	100	011	010	001	000
$f_i(x)$	0	1	?	?	?	?	?	0

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

$$x_1 \wedge \overline{x_3}, \qquad x_2 \wedge \overline{x_3}, \qquad x_1 \wedge x_2 \wedge \overline{x_3}, \qquad (x_1 \vee x_2) \wedge \overline{x_3}.$$

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



$(1, 0, -1)$ $\quad$ $(0, 1, -1)$ $\quad$ $(1, 1, -1)$ $\quad$ $(1, 1, -1)$

$\{x_1, \overline{x_3}\}$ $\quad$ $\{x_2, \overline{x_3}\}$ $\quad$ $\{x_1, x_2, \overline{x_3}\}$ $\quad$ $\{x_1, x_2, \overline{x_3}\}$

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

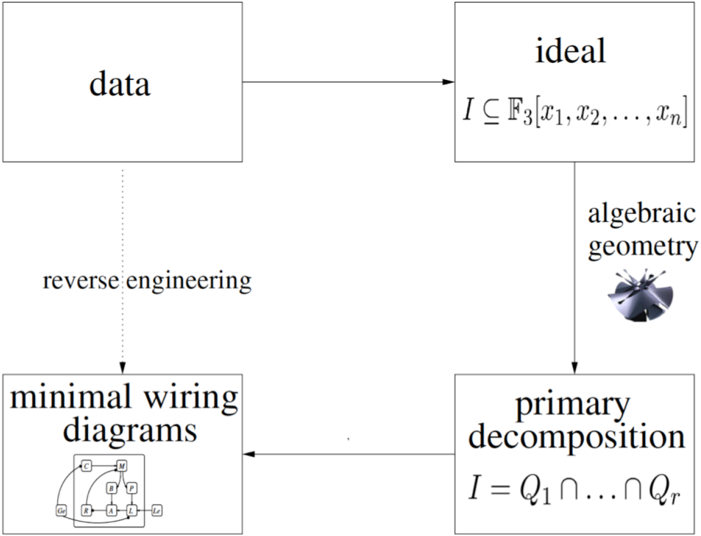


Figure : Image courtesy of Alan Veliz-Cuba.

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 combinatoral 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^{α}, where $x^{\alpha} := x_1^{\alpha_1} \cdots x_n^{\alpha_n}$ and $\alpha = (\alpha_1, \ldots, \alpha_n) \in \mathbb{Z}^n_{\geq 0}$.

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

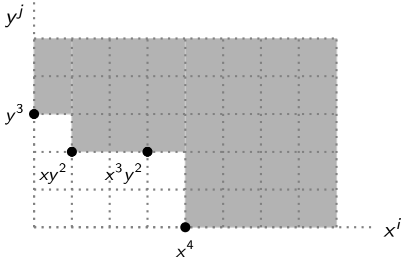
Definition

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^α canonically determines a subset of $[n] = \{1, \ldots, n\}$.

Notations

- Given x^α, we may speak of α 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

$$x^\alpha \in I \quad \text{and} \quad x^\beta \in I \quad \Longrightarrow \quad x^{\alpha\cup\beta} \in I,$$

$$x^\alpha \notin I \quad \text{and} \quad x^\beta \notin I \quad \Longrightarrow \quad x^{\alpha\cap\beta} \notin I.$$

Simplicial complexes

Definition

A simplicial complex over a finite set X is a collection Δ of subsets of X, closed under taking subsets. That is,

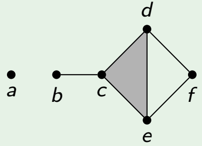
$$\beta \in \Delta \quad \text{and} \quad \alpha \subset \beta \quad \Longrightarrow \quad \alpha \in \Delta.$$

Elements in Δ 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 a:

- 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 Δ be a simplicial complex.

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

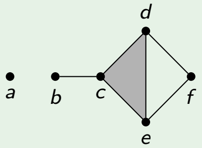
(ii) Non-faces of Δ are closed under unions: $\alpha, \beta \in \Delta^c \Rightarrow \alpha \cup \beta \in \Delta^c$.

Remark

- Δ is determined by its maximal faces.
- Δ^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 Δ^c.
- Maximal faces: a, bc, cde, df, ef.
- Minimal non-faces: ab, ac, ad, ae, af, bd, be, bf, cf, def.

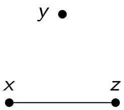


Example 2

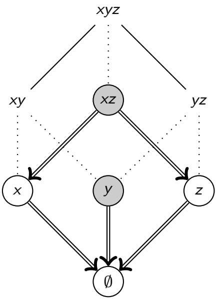
Consider the following simplicial complex Δ over $X = \{x, y, z\}$.

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

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

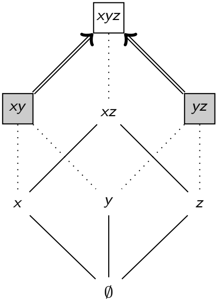


The faces Δ and non-faces Δ^c form a down-set and a up-set on the Boolean lattice.



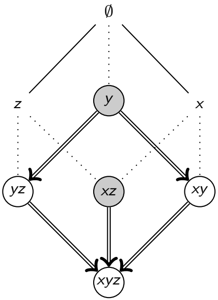
Faces in Δ

Facets are shaded



Non-faces in Δ^c

Minimal non-faces are shaded



Complements of faces in Δ

Maximal complements are shaded

An interplay between algebra and combinatorics (Example 1)

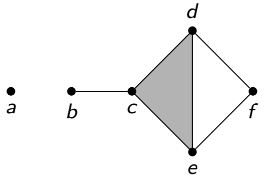
Consider the following square-free monomial ideal I in $\mathbb{F}[a,b,c,d,e,f]$:

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

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 Δ_{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, Δ_{I^c}.
- Every simplicial complex Δ defines a canonical square-free monomial ideal I_{Δ^c}.

This process is bijective, and is called Alexander duality.

An interplay between algebra and combinatorics (Example 2)

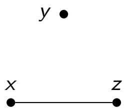
Let's see another example, this time the square-free monomial ideal I in $\mathbb{F}[x, y, z]$:

$$I = \langle xy, yz \rangle.$$

The monomials *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 Δ_{I^c} is determined by its maximal faces: y, xz.

The unique minimal generating set of I are the minimal non-faces: xy, xz.

Also, note that

$$I = \langle xy, yz \rangle = \Big\{ \underbrace{xy \cdot h_1(x,y,z) + yz \cdot h_2(x,y,z)}_{y\left(x \cdot h_1(x,y,z) + z \cdot h_2(x,y,z)\right) \in \langle y \rangle \cap \langle x, z \rangle} : h_1, h_2 \in R \Big\} = \langle y \rangle \cap \langle x, z \rangle.$$

This is called the primary decomposition of $I = \langle xy, yz \rangle$. The ideals $\langle y \rangle$ and $\langle x, z \rangle$ are called the primary components.

Let's see that last example again

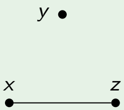
But this time we'll start with the simplicial complex Δ.

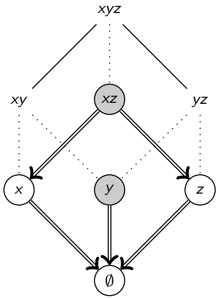
Example 2

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

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

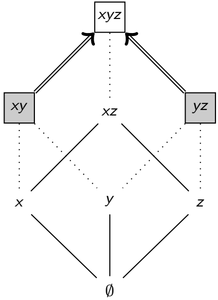
$I_{\Delta^c} = \langle xy, yz \rangle = \langle y \rangle \cap \langle x, z \rangle$





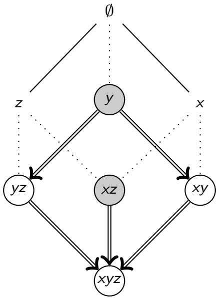
Faces in Δ

Facets are shaded



Monomials in I_{Δ^c}

Minimal generators are shaded



Complements of faces in Δ

Primary components of I_{Δ^c} shaded

Now let's see those examples together

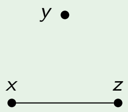
Example 2 (continued)

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

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



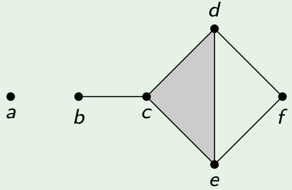
Example 1 (continued)

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

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 α 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 $x^\beta \notin I$, then $x^\alpha \notin I$.

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^α not in I;
- *combinatorially*: the faces α of a simplicial complex, that we will denote by Δ_{I^c}.

Alexander duality

Definition

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

$$\Delta_{I^c} := \{\alpha \mid x^\alpha \notin I\}.$$

Given a simplicial complex Δ, define a square-free monomial ideal

$$I_{\Delta^c} := \langle x^\alpha \mid \alpha \notin \Delta \rangle.$$

This is called the Stanley-Reisner ideal of Δ.

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

Defintion

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 $R = \mathbb{Z}$. Recall that all ideals I are principal, i.e. $I = \langle a \rangle$ for some $a \in \mathbb{Z}$.

- 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 $\mathbb{F}[x_1, \dots, x_n]$ can be written as $I = \bigcap_{i=1}^{r} \mathfrak{p}_i$, where $\mathfrak{p}_i$ is a primary ideal. We call this a primary decomposition of I. The $\mathfrak{p}_i$ 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 $\mathbf{p}^{\alpha} = \langle x_i : i \in \alpha \rangle$ and $\mathbf{p}^{\overline{\alpha}} = \mathbf{p}^{[n]-\alpha} = \langle x_i : i \notin \alpha \rangle$. Both are prime.

Theorem

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

$$I_{\Delta^c} = \bigcap_{\alpha \in \Delta} \mathbf{p}^{\overline{\alpha}} = \bigcap_{\substack{\alpha \in \Delta \\ \text{maximal}}} \mathbf{p}^{\overline{\alpha}}.$$

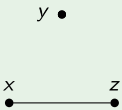
Computing the primary decomposition

Example 2 (continued)

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

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

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



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

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

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

By the previous theorem, the primary decomposition of I_{Δ^c} is

$$\begin{aligned} I_{\Delta^c} = \langle xy, yz \rangle = \bigcap_{\alpha \in \Delta} \mathbf{p}^{\overline{\alpha}} &= \mathbf{p}^{\overline{\emptyset}} \cap \mathbf{p}^{\overline{x}} \cap \mathbf{p}^{\overline{z}} \cap \mathbf{p}^{\overline{y}} \cap \mathbf{p}^{\overline{xz}} \\ &= \mathbf{p}^{xyz} \cap \mathbf{p}^{yz} \cap \mathbf{p}^{xy} \cap \mathbf{p}^{xz} \cap \mathbf{p}^{y} \\ &= \underbrace{\langle x, y, z \rangle \cap \langle y, z \rangle \cap \langle x, y \rangle}_{\text{unnecessary}} \cap \langle x, z \rangle \cap \langle y \rangle \\ &= \langle x, z \rangle \cap \langle y \rangle = \bigcap_{\substack{\alpha \in \Delta \\ \text{maximal}}} \mathbf{p}^{\overline{\alpha}}. \end{aligned}$$

Computing the primary decomposition

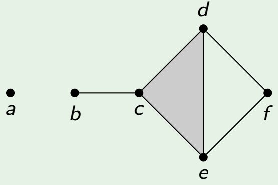
Example 1 (continued)

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_{Δ^c} is generated by the (minimal) non-faces.

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

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

$$= \langle b, c, d, e, f\rangle \cap \langle a, d, e, f\rangle \cap \langle a, b, f\rangle \cap \langle a, b, c, e\rangle \cap \langle a, b, c, d\rangle.$$

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:

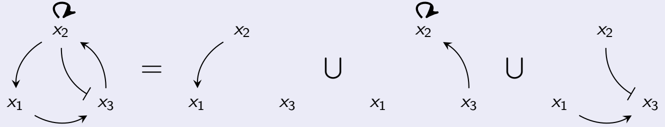
1. Consider every pair of input vectors that give a different output.
2. For each pair, take the monomial x^α, where $\alpha \subseteq [n]$ is the set where the entries differ.
3. These generate an ideal. The primary decomposition encodes all minimal wiring diagrams.

Simplification

We can consider each coordinate independently.

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

$$\begin{cases} f_1 = x_2 \\ f_2 = x_2 \wedge x_3 \\ f_3 = x_1 \vee \overline{x_2} \end{cases}$$



Thus, we will consider a function $f \colon \mathbb{F}^n \to \mathbb{F}$ with partial data, and attempt to reverse-engineer its wiring diagram.

Data and model spaces

Let $f\colon \mathbb{F}^n \to \mathbb{F}$ be a function, where $\mathbb{F} = \mathbb{F}_p$.

Definition

Consider a set

$$\mathcal{D} = \{(\mathbf{s}_1, t_1), \dots, (\mathbf{s}_m, t_m)\}, \qquad \mathbf{s}_i \in \mathbb{F}^n, \quad t_i \in \mathbb{F}$$

of input-output pairs, all $\mathbf{s}_i$ are distinct. We call such a set data, and say that f fits the data $\mathcal{D}$ if

$$f(\mathbf{s}_i) = f(s_{i1}, \dots, s_{in}) = t_i, \qquad \text{for all } i = 1, \dots, m.$$

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

$$\text{Mod}(\mathcal{D}) = \{f\colon \mathbb{F}^n \to \mathbb{F} \mid f(\mathbf{s}_i) = t_i \text{ for all } i = 1, \dots, m\}.$$

For any f in $\text{Mod}(\mathcal{D})$, 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 $\{x_1, \dots, x_n\}$ or as a subset $\alpha \subseteq [n] = \{1, \dots, n\}$.

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 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 α 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 α and β are feasible with respect to $\mathcal{D}$, then so is $\alpha \cup \beta$.

(ii) If α and β 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 $\Delta_{\mathcal{D}}$ of disposable sets,
- the square-free monomial ideal $I_{\Delta^c_{\mathcal{D}}}$ in $\mathbb{F}[x_1, \ldots, x_n]$ of non-disposable sets.

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

$$x^\alpha \in I_{\Delta^c_{\mathcal{D}}} \quad \text{if and only if } \alpha \text{ is non-disposable.}$$

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

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

By construction, if $t \neq t'$, then $\mathrm{supp}(m(\mathbf{s}, \mathbf{s}'))$ *must* be non-disposible.

Theorem

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

$$I_{\Delta^c_{\mathcal{D}}} = \big\langle m(\mathbf{s}, \mathbf{s}') \mid t \neq t' \big\rangle.$$

The generators of the primary components of $I_{\Delta^c_{D}}$ are the min-sets of $\mathcal{D}$.

Example 2 (continued)

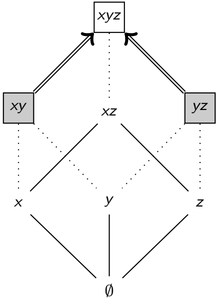
Consider a Boolean function $f\colon \mathbb{F}_2^3 \to \mathbb{F}_2$ with the following partial data:

xyz	101	000	110
$f(x,y,z)$	0	0	1

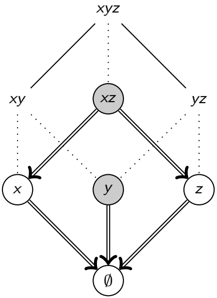
Using our notation, the *data* $\mathcal{D}$, grouped by output value, is

$$\mathcal{D} = \big\{(\mathbf{s}_1, t_1), (\mathbf{s}_2, t_2), (\mathbf{s}_3, t_3)\big\} = \big\{(101, 0), (000, 0), (110, 1)\big\}.$$

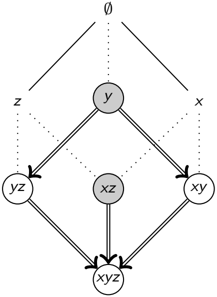
Since $t_1 = t_2 \neq t_3$, we compute $m(\mathbf{s}_1, \mathbf{s}_3) = yz$ and $m(\mathbf{s}_2, \mathbf{s}_3) = xy$.



Non-disposable sets $\Delta_{\mathcal{D}}^c$; Monomials in $I_{\Delta_{\mathcal{D}}^c}$



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



Feasible sets of $\mathcal{D}$

The min-sets are shaded

Example 3

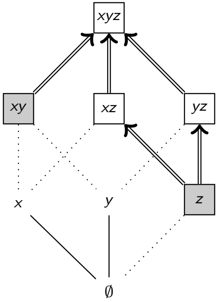
Consider a Boolean function $f\colon \mathbb{F}_2^3 \to \mathbb{F}_2$ with the following partial data:

xyz	111	000	110
$f(x,y,z)$	0	0	1

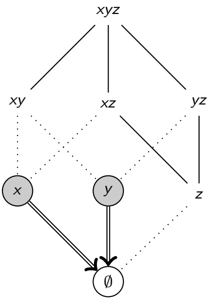
Using our notation, the *data* $\mathcal{D}$, grouped by output value, is

$$\mathcal{D} = \big\{(\mathbf{s}_1, t_1), (\mathbf{s}_2, t_2), (\mathbf{s}_3, t_3)\big\} = \big\{(111, 0), (000, 0), (110, 1)\big\}.$$

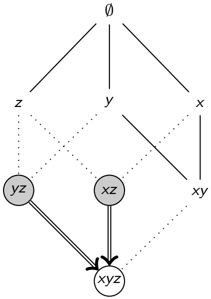
Since $t_1 = t_2 \neq t_3$, we compute $m(\mathbf{s}_1, \mathbf{s}_3) = z$ and $m(\mathbf{s}_2, \mathbf{s}_3) = xy$.



Non-disposable sets $\Delta_{\mathcal{D}}^c$; Monomials in $I_{\Delta_{\mathcal{D}}^c}$



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.

Reverse engineering of local models	Stanley-Reisner theory
Disposable sets of $\mathcal{D}$	Faces of the simplicial complex $\Delta_{\mathcal{D}}$
Non-disposable sets of $\mathcal{D}$	The non-faces, $\Delta_{\mathcal{D}}^c$
The ideal $\langle m(\mathbf{s},\mathbf{s}') \mid t \neq t' \rangle$ of non-disposable sets	The Stanley-Reisner ideal $I_{\Delta_{\mathcal{D}}^c}$
Feasible sets of $\mathcal{D}$	Complements of faces of $\Delta_{\mathcal{D}}$
Min-sets of $\mathcal{D}$	Complements of max'l faces of $\Delta_{\mathcal{D}}$ $\leftrightarrow$ primary components of $I_{\Delta_{\mathcal{D}}^c}$

Min-sets over non-Boolean fields

Consider a function $f\colon \mathbb{F}_5^5 \to \mathbb{F}_5$ with the following partial data:

$$(\mathbf{s}_1, t_1) = (01210, 0),$$
$$(\mathbf{s}_2, t_2) = (01211, 0),$$
$$(\mathbf{s}_3, t_3) = (01214, 1),$$
$$(\mathbf{s}_4, t_4) = (30000, 3),$$
$$(\mathbf{s}_5, t_5) = (11113, 4).$$

The monomials $m(\mathbf{s}_i, \mathbf{s}_j)$ are:

$$m(\mathbf{s}_1, \mathbf{s}_4) = x_1x_2x_3x_4,$$
$$m(\mathbf{s}_1, \mathbf{s}_5) = m(\mathbf{s}_2, \mathbf{s}_5) = m(\mathbf{s}_3, \mathbf{s}_5) = x_1x_3x_5,$$
$$m(\mathbf{s}_2, \mathbf{s}_4) = m(\mathbf{s}_3, \mathbf{s}_4) = m(\mathbf{s}_4, \mathbf{s}_5) = x_1x_2x_3x_4x_5,$$
$$m(\mathbf{s}_1, \mathbf{s}_3) = m(\mathbf{s}_2, \mathbf{s}_3) = x_5.$$

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

$$I_{\Delta^c_{\mathcal{D}}} = \langle m(\mathbf{s}_i, \mathbf{s}_j) \mid t_i \neq t_j \rangle = \langle x_1x_2x_3x_4x_5,\ x_1x_3x_5,\ x_1x_2x_3x_4,\ x_5 \rangle = \langle x_1x_2x_3x_4,\ x_5 \rangle.$$

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: $I_{\Delta^c_{\mathcal{D}}} = \langle x_1, x_5 \rangle \cap \langle x_2, x_5 \rangle \cap \langle x_3, x_5 \rangle \cap \langle x_4, x_5 \rangle.$
- Unsigned min-sets: $\{x_1, x_5\}$, $\{x_2, x_5\}$, $\{x_3, x_5\}$, $\{x_4, x_5\}$.

Finding signed min-sets of local models

Consider a set of data (i.e., input-output pairs) with all $\mathbf{s}_i$ distinct:

$$\mathcal{D} = \big\{(\mathbf{s}_1, t_1), \dots, (\mathbf{s}_m, t_m)\big\}, \qquad \mathbf{s}_i \in \mathbb{F}^n, \quad t_i \in \mathbb{F}.$$

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

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

That is, for each coordinate i where $\mathbf{s}$ and $\mathbf{s}'$ differ, include x_i.

This time: For each coordinate i that $\mathbf{s}$ and $\mathbf{s}'$ 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

$$p(\mathbf{s}, \mathbf{s}') := \prod_{s_i \neq s_i'} \big(x_i - \operatorname{sign}(s_i' - s_i)\big).$$

Theorem

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

$$J_{\Delta^c_{\mathcal{D}}} = \big\langle p(\mathbf{s}_i, \mathbf{s}_j) \mid i < j,\ t_i \neq t_j \big\rangle.$$

The primary components of $J_{\Delta^c_{\mathcal{D}}}$ give the signed min-sets.

Example 3

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

xyz	111	000	110
$f(x,y,z)$	0	0	1

The *data* $\mathcal{D}$ is

$$\mathcal{D} = \big\{(\mathbf{s}_1, t_1), (\mathbf{s}_2, t_2), (\mathbf{s}_3, t_3)\big\} = \big\{(111, 0), (000, 0), (110, 1)\big\}.$$

Note that

$$p(\mathbf{s}_1, \mathbf{s}_3) = z - (\operatorname{sign}(s_{33} - s_{13})) = z + 1, \qquad p(\mathbf{s}_2, \mathbf{s}_3) = (x-1)(y-1).$$

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

$$J_{\Delta^c_{\mathcal{D}}} = \big\langle p(\mathbf{s}_1, \mathbf{s}_3),\ p(\mathbf{s}_2, \mathbf{s}_3)\big\rangle = \big\langle z+1,\ (x-1)(y-1)\big\rangle.$$

The following Macaulay2 commands compute the primary decomposition of $J_{\Delta^c_{\mathcal{D}}}$:

```
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: $J_{\Delta^c_{\mathcal{D}}} = \big\langle x-1, z+1\big\rangle \cap \langle y-1, z+1\rangle$.
- Signed min-sets: $\{x, \overline{z}\}$ and $\{y, \overline{z}\}$.

Signed min-sets over non-Boolean fields

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

$$\begin{aligned}
(\mathbf{s}_1, t_1) &= (01210, 0), & p(\mathbf{s}_1,\mathbf{s}_3) &= p(\mathbf{s}_2,\mathbf{s}_3) = x_5 - 1,\\
(\mathbf{s}_2, t_2) &= (01211, 0), & p(\mathbf{s}_3,\mathbf{s}_5) &= (x_1-1)(x_3+1)(x_5+1),\\
(\mathbf{s}_3, t_3) &= (01214, 1), & p(\mathbf{s}_1,\mathbf{s}_4) &= (x_1-1)(x_2+1)(x_3+1)(x_4+1),\\
(\mathbf{s}_4, t_4) &= (30000, 3), & p(\mathbf{s}_1,\mathbf{s}_5) &= p(\mathbf{s}_2,\mathbf{s}_5) = (x_1-1)(x_3+1)(x_5-1),\\
(\mathbf{s}_5, t_5) &= (11113, 4). & p(\mathbf{s}_4,\mathbf{s}_5) &= (x_1+1)(x_2-1)(x_3-1)(x_4-1)(x_5-1),\\
& & p(\mathbf{s}_2,\mathbf{s}_4) &= p(\mathbf{s}_3,\mathbf{s}_4) = (x_1-1)(x_2+1)(x_3+1)(x_4+1)(x_5+1).
\end{aligned}$$

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

$$J_{\Delta^c_{\mathcal{D}}} = \langle p(\mathbf{s}_i,\mathbf{s}_j) \mid t_i \neq t_j \rangle = \langle x_5 - 1,\ (x_1-1)(x_3+1)(x_5+1),\ (x_1-1)(x_2+1)(x_3+1)(x_4+1) \rangle.$$

We can compute the primary decomposition in Macaulay2:

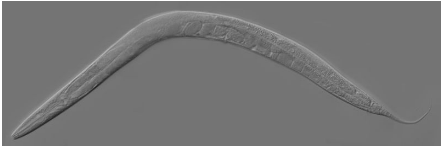
```
R = ZZ/3[x1,x2,x3,x4,x5];
J_nonDisp = ideal(x5-1, (x1-1)*(x3+1)*(x5+1), (x1-1)*(x2+1)*(x3+1)*(x4+1));
primaryDecomposition J_nonDisp
```

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

- Primary decomposition: $J_{\Delta^c_{\mathcal{D}}} = \langle x_1 - 1, x_5 - 1 \rangle \cap \langle x_3 + 1, x_5 - 1 \rangle$.
- Signed min-sets: $\{x_1, x_5\}$, $\{\overline{x_3}, x_5\}$.

Application to a real gene network

Caenorhabditis elegans is a microscopic roundworm and common 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 ≈ 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, $\mathbf{s}_1, \dots, \mathbf{s}_{10}$ and $\mathbf{u}_1, \dots, \mathbf{u}_{10}$, to 7 states, i.e., $\mathbf{s}_i, \mathbf{u}_i \in \mathbb{F}_7^{20}$.

The i^{th} input state is $\mathbf{s}_i$ and the i^{th} output state is $\mathbf{t}_i = f(\mathbf{s}_i) = \mathbf{s}_{i+1}$, where $f \colon \mathbb{F}_7^{20} \to \mathbb{F}_7^{20}$ is the FDS map of an unknown local model over $\mathbb{F}_7$. Similarly, $\mathbf{v}_i = f(\mathbf{u}_i) = \mathbf{u}_{i+1}$.

Time-series data

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}
$\mathbf{s}_1$	4	6	5	0	3	0	0	0	0	1	0	0	0	1	0	1	0	0	0	0
$\mathbf{s}_2 = \mathbf{t}_1$	3	6	5	0	2	1	1	1	0	0	0	0	1	1	0	0	0	1	0	0
$\mathbf{s}_3 = \mathbf{t}_2$	1	3	1	0	2	1	1	1	0	1	0	0	1	1	0	1	0	1	0	1
$\mathbf{s}_4 = \mathbf{t}_3$	1	3	1	2	2	1	1	1	1	1	0	0	0	1	0	0	0	1	2	1
$\mathbf{s}_5 = \mathbf{t}_4$	0	1	1	2	2	1	1	1	1	1	0	0	1	1	0	1	0	1	2	1
$\mathbf{s}_6 = \mathbf{t}_5$	0	2	1	4	6	4	1	3	1	1	0	0	1	2	0	1	0	1	1	1
$\mathbf{s}_7 = \mathbf{t}_6$	0	3	1	6	5	5	1	4	2	1	0	0	1	1	1	2	1	1	1	0
$\mathbf{s}_8 = \mathbf{t}_7$	1	3	1	4	2	6	1	4	2	3	1	1	3	2	4	4	0	3	3	0
$\mathbf{s}_9 = \mathbf{t}_8$	1	3	1	6	2	5	1	5	1	5	2	5	6	2	5	5	0	4	4	0
$\mathbf{t}_9$	0	2	1	4	2	3	1	3	1	4	1	3	4	2	5	3	1	5	5	2

	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}
$\mathbf{u}_1$	4	3	3	0	1	0	0	0	1	1	1	0	1	0	0	1	0	0	0	0
$\mathbf{u}_2 = \mathbf{v}_1$	4	0	0	0	0	0	1	0	0	1	1	0	1	2	1	1	0	0	0	0
$\mathbf{u}_3 = \mathbf{v}_2$	5	3	2	0	1	0	0	0	0	1	0	1	0	2	0	1	0	0	0	0
$\mathbf{u}_4 = \mathbf{v}_3$	4	4	3	0	2	0	1	1	1	1	0	1	1	1	0	1	0	0	1	1
$\mathbf{u}_5 = \mathbf{v}_4$	1	2	1	1	2	0	1	1	1	1	0	1	2	0	0	1	0	1	0	1
$\mathbf{u}_6 = \mathbf{v}_5$	2	3	1	2	4	2	2	2	3	1	0	0	2	1	0	1	0	1	1	1
$\mathbf{u}_7 = \mathbf{v}_6$	5	3	1	3	2	2	3	3	5	2	0	1	2	3	1	1	1	1	0	1
$\mathbf{u}_8 = \mathbf{v}_7$	6	5	6	5	4	5	6	4	6	1	0	4	2	2	3	2	1	2	2	0
$\mathbf{u}_9 = \mathbf{v}_8$	3	3	1	4	2	2	4	2	4	3	0	4	5	0	3	2	2	2	4	0
$\mathbf{v}_9$	4	5	4	6	2	3	5	6	2	6	2	6	5	2	6	6	1	6	6	3

Application to a real gene network

Goal

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

Gene	Variable	Muscle Type
hlh-1	x_8	skeletal
hnd-1	x_{18}	cardiac
unc-120	x_{19}	cardiac, smooth, skeletal

These genes are known to be regulated by the maternally controlled *pal-1* genes.

Though all three regulate a single tissue type in *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 *hlh-1* gene is

$$\mathcal{D}_8 = \{(\mathbf{s}_1, t_{18}), (\mathbf{s}_2, t_{28}), \dots, (\mathbf{s}_9, t_{98}), (\mathbf{u}_1, v_{18}), (\mathbf{u}_2, v_{28}), \dots, (\mathbf{u}_9, v_{98})\}.$$

The ideal of non-disposable sets for the *hlh-1* gene is

$$I_{\mathcal{D}_8^c} = \langle \{m(\mathbf{s}_i, \mathbf{s}_j) \mid t_{i8} \neq t_{j8}\} \cup \{m(\mathbf{u}_i, \mathbf{u}_j) \mid v_{i8} \neq v_{j8}\} \cup \{m(\mathbf{s}_i, \mathbf{u}_j) \mid t_{i8} \neq v_{j8}\}\rangle.$$

The ideal of non-disposable sets for the *hlh-1* gene

$$
\begin{aligned}
I_{\mathcal{D}_8^c} = \langle & x_1x_2x_4x_5x_6x_7x_8x_9x_{13}x_{14},\ x_2x_3x_5x_9x_{11}x_{13}x_{14},\ x_2x_4x_6x_9x_{12}x_{13}x_{14},\ x_1x_3x_9x_{11}x_{12}x_{13}x_{14},\\
& x_1x_2x_3x_5x_7x_{11}x_{12}x_{13}x_{15},\ x_2x_3x_5x_7x_{11}x_{13}x_{14}x_{15},\ x_1x_2x_{13}x_{16},\ x_1x_2x_4x_6x_7x_8x_9x_{10}x_{14}x_{15}x_{17},\\
& x_1x_4x_6x_7x_8x_9x_{10}x_{12}x_{13}x_{14}x_{15}x_{17},\ x_1x_2x_3x_4x_5x_6x_7x_8x_9x_{12}x_{13}x_{18},\ x_1x_2x_3x_4x_5x_6x_8x_{12}x_{14}x_{18},\\
& x_1x_2x_3x_5x_6x_7x_8x_9x_{10}x_{11}x_{14}x_{16}x_{18},\ x_1x_2x_3x_5x_6x_8x_{10}x_{11}x_{14}x_{15}x_{16}x_{18},\ x_1x_2x_4x_9x_{19},\\
& x_1x_4x_5x_6x_7x_8x_9x_{13}x_{19},\ x_2x_4x_5x_6x_8x_{14}x_{19},\ x_1x_2x_4x_6x_{12}x_{13}x_{14}x_{19},\ x_1x_4x_5x_6x_8x_{12}x_{13}x_{14}x_{19},\\
& x_1x_5x_6x_7x_8x_9x_{13}x_{16}x_{19},\ x_2x_4x_6x_{12}x_{13}x_{14}x_{16}x_{19},\ x_1x_4x_5x_7x_8x_9x_{10}x_{12}x_{14}x_{15}x_{17}x_{19},\\
& x_1x_2x_3x_4x_6x_{12}x_{18}x_{19},\ x_1x_2x_3x_4x_{13}x_{14}x_{18}x_{19},\ x_4x_6x_8x_9x_{10}x_{11}x_{12}x_{13}x_{15}x_{16}x_{18}x_{19},\\
& x_1x_3x_4x_5x_6x_7x_8x_9x_{11}x_{14}x_{15}x_{16}x_{17}x_{18}x_{19},\ x_1x_6x_7x_8x_9x_{11}x_{12}x_{13}x_{14}x_{15}x_{16}x_{17}x_{18}x_{19},\\
& x_1x_4x_5x_6x_{10}x_{11}x_{12}x_{13}x_{14}x_{15}x_{16}x_{17}x_{18}x_{19},\ x_1x_5x_8x_9x_{10}x_{11}x_{12}x_{13}x_{14}x_{15}x_{16}x_{17}x_{18}x_{19},\\
& x_1x_4x_5x_6x_7x_8x_9x_{13}x_{15}x_{16}x_{17}x_{20},\ x_1x_2x_3x_4x_5x_7x_8x_{11}x_{12}x_{13}x_{18}x_{20},\\
& x_1x_3x_5x_6x_7x_8x_9x_{11}x_{14}x_{18}x_{20},\ x_1x_2x_3x_4x_5x_7x_8x_9x_{13}x_{14}x_{18}x_{20},\\
& x_1x_2x_3x_5x_6x_8x_{11}x_{14}x_{15}x_{18}x_{20},\ x_3x_4x_5x_6x_7x_8x_9x_{10}x_{13}x_{14}x_{15}x_{17}x_{18}x_{20},\\
& x_1x_2x_3x_4x_5x_6x_8x_9x_{12}x_{15}x_{16}x_{17}x_{18}x_{20},\ x_2x_4x_5x_6x_8x_9x_{15}x_{16}x_{17}x_{19}x_{20},\\
& x_2x_3x_5x_8x_9x_{11}x_{12}x_{14}x_{15}x_{19}x_{20},\ x_1x_4x_5x_6x_8x_9x_{15}x_{16}x_{17}x_{19}x_{20},\ x_2x_5x_7x_8x_{11}x_{12}x_{14}x_{19}x_{20},\\
& x_1x_3x_4x_5x_6x_7x_8x_{11}x_{13}x_{14}x_{16}x_{18}x_{19}x_{20},\ x_2x_4x_6x_8x_9x_{10}x_{11}x_{13}x_{14}x_{15}x_{16}x_{18}x_{19}x_{20},\\
& x_4x_6x_8x_{10}x_{11}x_{12}x_{13}x_{14}x_{15}x_{16}x_{18}x_{19}x_{20},\ x_1x_4x_6x_7x_8x_9x_{10}x_{11}x_{13}x_{14}x_{15}x_{16}x_{17}x_{18}x_{19}x_{20},\\
& x_1x_4x_5x_7x_9x_{10}x_{12}x_{13}x_{14}x_{15}x_{16}x_{17}x_{18}x_{19}x_{20},\ x_1x_4x_7x_8x_9x_{10}x_{12}x_{13}x_{14}x_{15}x_{16}x_{17}x_{18}x_{19}x_{20}\rangle.
\end{aligned}
$$

Min-sets of the *hlh-1* gene

The primary decomposition of $I_{\mathcal{D}_8^c}$ consists of 483 primary components (min-sets). That is,

$$I_{\mathcal{D}_8^c} = \bigcap_{i=1}^{483} \mathfrak{p}_i.$$

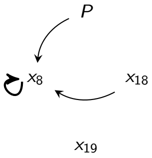
However, it is known experimentally that *hlh-1* is controlled by the *pal-1* genes (variables x_1, x_2, x_3).

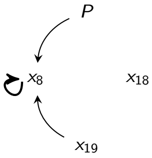
Therefore, we can disregard all min-sets that involve none of these variables.

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

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

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:

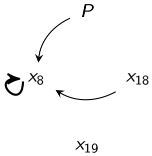
hlh-1 (x_8)	*hnd-1* (x_{18})	*unc-120* (x_{19})
$\{x_2, x_3, x_8, x_{18}\}$	$\{x_2, x_8, x_{18}\}$	$\{x_2, x_3, x_8, x_{18}\}$
$\{x_2, x_3, x_8, x_{19}\}$	$\{x_2, x_8, x_{19}\}$	$\{x_2, x_3, x_8, x_{19}\}$
	$\{x_3, x_8, x_{19}\}$	$\{x_2, x_8, x_9, x_{19}\}$
	$\{x_3, x_8, x_9, x_{18}\}$	

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

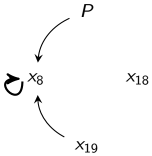
hlh-1 (x_8)	*hnd-1* (x_{18})	*unc-120* (x_{19})
$\{P, x_8, x_{18}\}$	$\{P, x_8, x_{18}\}$	$\{P, x_8, x_{18}\}$
$\{P, x_8, x_{19}\}$	$\{P, x_8, x_{19}\}$	$\{P, x_8, x_{19}\}$

Minimal wiring diagrams

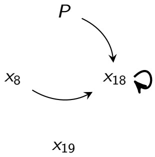
hlh-1 :



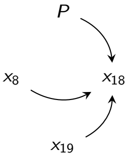
OR



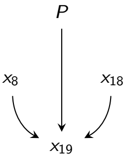
hnd-1 :



OR



unc-120 :



OR