Boolean network models

Goal: Design a basic dynamic model that reflects its biological behavior.

Bare minimum: lactose absent \(\Rightarrow\) operon off
lactose present, glucose absent \(\Rightarrow\) operon on.

Need
- **Model variables**: Represent dynamic elts. of the system
- **Parameters**: Outside elements (constant)

Lac operon: Model variables

- \(M\): mRNA
- \(L\): internal lactose

From Lac Z

\[ E: \text{Lac Z polypeptide} \]
\[ \beta: \beta\text{-galactosidase} \]

From Lac Y \(\rightarrow\) P: lac permease
- \(A\): allolactose

Simplifications:

- \(\beta\text{-gal}\) made up of \(4\) identical Lac Z polypeptides \(\Rightarrow\) \(B = E/4\)
- Lac Y \& Lac Z translated at same rate \(\Rightarrow\) \(P = E\)
- Concentration of internal lactose \& allolactose proportional \(\Rightarrow\) \(A = kL\)
Thus, we can ignore B, P, c, A in the Boolean framework.  

Note: This is just one, of many possible models!

Wiring diagram:

Boolean operations

<table>
<thead>
<tr>
<th>Operation</th>
<th>Logical</th>
<th>Polynomial</th>
</tr>
</thead>
<tbody>
<tr>
<td>AND</td>
<td>( z = x \land y )</td>
<td>( z = xy )</td>
</tr>
<tr>
<td>OR</td>
<td>( z = x \lor y )</td>
<td>( z = x + y + xy )</td>
</tr>
<tr>
<td>NOT</td>
<td>( z = \overline{y} )</td>
<td>( z = 1 + y )</td>
</tr>
</tbody>
</table>

Only 2 states allowed: 0, 1: on/off, present/absent, above/below certain threshold, etc.

Framework:

Wiring diagram consists of \( n \) nodes: \( X_1, X_2, \ldots, X_n \)

Each takes a value of 0 or 1

The set of global states is \( V = \{ 0, 1 \}^n = \{ (x_1, \ldots, x_n) : x_i \in \{0, 1\} \} \)

Each \( X_i(t) \) is a function \( \mathbb{N} \to \{ 0, 1 \} \).
\[ X_i(t+1) = f_{X_i}(X_1(t), X_2(t), ..., X_n(t)) \]  

"transition functions"

"update rules" or "rules"

Use a **synchronous** update:

\[ X = (X_1, X_2, ..., X_n) \]

\[ f(x) = (f_{X_1}(x), f_{X_2}(x), ..., f_{X_n}(x)) \]

\[ \uparrow \]

recall: these are Functions of \( t \)

**State space** (or "phase space"): Directed graph \((V, T)\),

where \( T = \{(x, f(x)) : x \in V\} \).

**Ex:**

\[ X_1(t+1) = f_{X_1}(X_1(t), X_2(t), X_3(t)) = X_2(t) \]

write as:

\[ \begin{align*}
X_1 &= f(x_1, x_2, x_3) = x_2 \\
X_2 &= f_{X_2}(x_1, x_2, x_3) = x_1 \lor x_3 \\
X_3 &= f_{X_3}(x_1, x_2, x_3) = (x_1 \land x_2) \lor x_3
\end{align*} \]

**Suppose the initial condition** is \( X(0) = (x_1, x_2, x_3) = (0, 0, 1) \).

\[ \begin{align*}
X_1(1) &= f_{X_1}(0, 0, 1) = 0 \\
X_2(1) &= f_{X_2}(0, 0, 1) = 0 \lor 1 = 1 \\
X_3(1) &= f_{X_3}(0, 0, 1) = (0 \land 0) \lor 1 = 1 \\
\end{align*} \implies X(1) = (0, 1, 1) \]

\[ \begin{align*}
X_1(2) &= f_{X_1}(0, 1, 1) = 1 \\
X_2(2) &= f_{X_2}(0, 1, 1) = 1 \implies X(2) = (1, 1, 1). \\
X_3(2) &= f_{X_3}(0, 1, 1) = 1
\end{align*} \]
\[\begin{align*}
X_1(3) &= f(x_1(1,1,1)) = 1, \\
X_2(3) &= f(x_2(1,1,1)) = 1 & \Rightarrow & X(3) = (1,1,1) & \Rightarrow & X(4) = X(5) = \ldots = (1,1,1), \\
X_3(3) &= f(x_3(1,1,1)) = 1.
\end{align*}\]

The trajectory of \((0,0,1)\) is \((0,0,1) \rightarrow (0,1,1) \rightarrow (1,1,1)\).

The state \((1,1,1)\) is a fixed point.

The entire state space looks like:

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(Use dud.vbi.vt.edu to plot)
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Sometimes we use capital letters instead:

**Ex:** \textit{lac operon}

\[\begin{align*}
X_1 &= M, & X_2 &= E, & X_3 &= L, \\
F_{x_1} &= f_M, & F_{x_2} &= f_E, & F_{x_3} &= f_L.
\end{align*}\]

**Next step:** Choose functions.

**Model assumptions** "everything takes 1 time-step"

- Transcription \& translation require 1 unit time.
- Degradation of mRNA \& proteins occurs in 1 time step.
- If \(\beta\)-gal is present, lactose metabolism takes 1 time step.

If lactose \& \(\beta\)-gal available at \(t\), but new lactose can't be brought in, then at \(t+1\), all lactose converted to glucose \& galactose.
Update Functions

**mRNA**: $F_M$

For mRNA to be present at time $t+1$ ($F_M(t) = 1$)

- no external glucose present at time $t$: ($G_e(t) = 1$)

and

- either internal or external lactose should be present:

Propose: $X_M(t+1) = F_M(t+1) = \overline{G_e} \land (L(t) \lor L_e)$.

Ask: Does this make sense when: $G_e(t) = 1$?

**LacZ polypeptide**: $F_E$

If mRNA is available at time $t$ ($M(t) = 1$), LacZ polypeptide is produced if available at $t+1$ ($M(t+1) = 1$).

Propose: $X_E(t+1) = F_E(t+1) = \overline{M(t)}$.

**Lactose (internal)**: $F_L$

- External glucose available ($G_e = 1$) $\Rightarrow$ no lactose brought into cell $\Rightarrow L(t+1) = 0$.

- External glucose absent ($G_e = 0$):

  Internal lactose will be available if either of these is satisfied:

(i) External lactose and lac permease ($P=E$) are present: $E(t) \land L_e = 1$

(ii) Internal lactose is present but no $\beta$-gal ($P=E/4$) to metabolize it:

Propose: $X_L(t+1) = F_L(t+1) = \overline{G_e} \land [(E(t) \land L_e) \lor (L(t) \land \overline{E(t)})]$. 