

Read: Chapter 6 of Robeva: *Steady state analysis of Boolean models: a dimension reduction approach*. By D. Murrugarra and A. Veliz-Cuba, pages 121–139.

Do:

1. Draw the wiring diagram of the Boolean network

$$f = (f_1, f_2, f_3, f_4, f_5, f_6) = (x_6, x_1, x_2, \overline{x_3}, x_4, \overline{x_5})$$

and then reduce it by eliminating the variables in the order x_6, x_5, \dots . At each step along the way, write out the functions and draw the wiring diagram.

2. Suppose we want to reduce a Boolean network by removing a vertex x_i with no self-loop (equivalently, f_{x_i} doesn't depend on x_i). First, for every vertex y such that $x_i \longrightarrow y$, substitute f_{x_i} into x_i :

$$f_y(x_1, \dots, \underbrace{\dots x_i \dots}_{\text{pos. } y}, \dots, x_n) \quad \text{becomes} \quad f_y((x_1, \dots, \underbrace{\dots f_{x_i} \dots}_{\text{pos. } y}, \dots, x_n).$$

Next, each pair of edges $v \longrightarrow x_i \longrightarrow y$ in the wiring diagram must be replaced with the single edge $v \longrightarrow y$. The situation is similar for the other three possibilities:

- (a) $v \longrightarrow x_i \longrightarrow \neg y$
- (b) $v \longrightarrow \neg x_i \longrightarrow y$
- (c) $v \longrightarrow \neg x_i \longrightarrow \neg y$

For each of these pairs of edges, determine what to replace them with in the wiring diagram of the new network. This would allow one to characterize algorithmically how to construct the wiring diagram of a reduced Boolean network.

3. Consider the following Boolean network model of the *lac* operon:

$x_1 = \textit{lac}$ mRNA (M)	$f_1 = x_4 \wedge \overline{x_5}$
$x_2 = \textit{lac}$ permease (P)	$f_2 = x_1$
$x_3 = \beta$ -galactosidase (B)	$f_3 = x_1$
$x_4 = \textit{catabolite}$ activator protein (C)	$f_4 = \overline{x_{11}}$
$x_5 = \textit{repressor}$ protein (R)	$f_5 = \overline{x_6} \wedge \overline{x_7}$
$x_6 = \textit{high allolactose}$ (A)	$f_6 = x_3 \wedge x_8$
$x_7 = \textit{medium allolactose}$ (A_m)	$f_7 = x_6 \vee x_8 \vee x_9$
$x_8 = \textit{high intracellular lactose}$ (L)	$f_8 = x_2 \wedge x_{10} \wedge \overline{x_{11}}$
$x_9 = \textit{medium intracellular lactose}$ (L_m)	$f_9 = (x_8 \vee x_{10}) \wedge \overline{x_{11}}$
$x_{10} = \textit{extracellular lactose}$ (L_e)	$f_{10} = x_{10}$
$x_{11} = \textit{extracellular glucose}$ (G_e)	$f_{11} = x_{11}$

- (a) Reduce this Boolean network starting from the last variable. It is strongly recommended that you use Macaulay2 in Sage or at web.macaulay2.com.
- (b) Draw the wiring diagram of the reduced network. Find its fixed points and use these to determine the fixed points of the original network.
- (c) Repeat Part (a) but using a completely different variable order.