Chapter 6

Solutions to Exercises

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Exercise 6.1. Check that $x = 000100$ and $x = 111011$ are in fact steady states; that is, check that $f(x) = x$.
   Solution. Consider $x = (M, P, B, R, A, L) = (0, 0, 0, 1, 0, 0)$. Using the regulatory functions we obtain

$f_M = \neg R = 0,$
$f_P = M = 0,$
$f_B = M = 0,$
$f_R = \neg A = 1,$
$f_A = L \wedge B = 0,$
$f_L = P = 0.$

Thus, $f(x) = (f_M, f_P, f_B, f_R, f_A, f_L) = (0, 0, 0, 1, 0, 0) = x$. Similarly one can check that $x = 111011$ is a steady state. $\square$

   Exercise 6.2. Consider $x^0 = 000000$ and compute $x^{t+1} := f(x^t)$ for $t = 0, \ldots, 10$. Repeat the process for $x^0 = 111111$.
   Solution. For $x^0 = 000000$, we have

$$x^1 := f(x^0) = (1, 0, 0, 1, 0, 0)$$
$$x^2 := f(x^1) = (0, 1, 1, 1, 0, 0)$$
$$x^3 := f(x^2) = (0, 0, 0, 1, 0, 1)$$
$$x^4 := f(x^3) = (0, 0, 0, 1, 0, 0)$$
$$x^5 := f(x^4) = (0, 0, 0, 1, 0, 0)$$
$$x^6 := f(x^5) = (0, 0, 0, 1, 0, 0)$$
$$x^7 := f(x^6) = (0, 0, 0, 1, 0, 0)$$
$$x^8 := f(x^7) = (0, 0, 0, 1, 0, 0)$$
$$x^9 := f(x^8) = (0, 0, 0, 1, 0, 0)$$
$$x^{10} := f(x^9) = (0, 0, 0, 1, 0, 0)$$
$$x^{11} := f(x^{10}) = (0, 0, 0, 1, 0, 0)$$

For $x^0 = 111111$, we have

$$x^1 := f(x^0) = (0, 1, 1, 0, 1, 1)$$
$$x^2 := f(x^1) = (1, 0, 0, 0, 1, 1)$$

$$x^3 := f(x^2) = (1, 1, 1, 0, 0, 0)$$
$$x^4 := f(x^3) = (1, 1, 1, 1, 0, 1)$$
$$x^5 := f(x^4) = (0, 1, 1, 1, 1, 1)$$
$$x^6 := f(x^5) = (0, 0, 0, 0, 1, 1)$$
$$x^7 := f(x^6) = (1, 0, 0, 0, 0, 0)$$
$$x^8 := f(x^7) = (1, 1, 1, 1, 0, 0)$$
$$x^9 := f(x^8) = (0, 1, 1, 1, 0, 1)$$
$$x^{10} := f(x^9) = (0, 0, 0, 1, 1, 1)$$
$$x^{11} := f(x^{10}) = (0, 0, 0, 0, 0, 0) \qquad \square$$

Exercise 6.3. By exhaustive enumeration, find all steady states of $f(M, R, A, L) = (\neg R, \neg A, L \wedge M, M)$.
Solution. The only steady states of f are $(0, 1, 0, 0)$ and $(1, 0, 1, 1)$. $\qquad \square$

Exercise 6.4. By an exhaustive enumeration, find all steady states of $f(M, R, L) = (\neg R, \neg L \vee \neg M, M)$ by exhaustive enumeration and compare with Exercise 6.3.
Solution. The only steady states of f are $(0, 1, 0)$ and $(1, 0, 1)$. $\qquad \square$

Exercise 6.5. Consider $f_1 = f_1(x_1, x_2, x_3) = x_2 \wedge x_3$, $f_2 = f_2(x_1, x_2, x_3) = x_1 \vee \neg x_3$, $f_3 = f_3(x_1, x_2, x_3) = x_1 \vee x_2$. Compute $f_1(x_1, x_2, f_3)$ and $f_2(x_2, x_2, f_3)$.
Solution.

$$f_1(x_1, x_2, f_3) = x_2 \wedge x_3 = x_2 \wedge (x_1 \vee x_2) = x_2 \wedge (x_2 \vee x_1)$$
$$= x_2 \,(\text{absorption law})$$
$$f_2(x_1, x_2, f_3) = x_1 \vee \neg x_3 = x_1 \vee \neg(x_1 \vee x_2)$$
$$= x_1 \vee (\neg x_1 \wedge \neg x_2) = (x_1 \vee \neg x_1) \wedge (x_1 \vee \neg x_2)$$
$$= 1 \wedge (x_1 \vee \neg x_2) = x_1 \vee \neg x_2 \qquad \square$$

Exercise 6.6. Reduce the following Boolean expressions using Boolean algebra or truth tables.

1. $x_1 \wedge \neg x_1$,   2. $(x_1 \vee x_2) \wedge \neg x_1$,
3. $(x_1 \vee x_2) \wedge x_1$,   4. $(x_1 \wedge x_2) \vee x_1$,
5. $(x_1 \vee x_2) \wedge x_2$,   6. $(x_1 \vee \neg x_2) \wedge (x_1 \vee x_2)$,
7. $(x_1 \vee x_2) \wedge x_1 \wedge x_2$,   8. $x_1 \wedge x_2 \wedge x_3 \wedge \neg x_1$.

Solution.
1. $x_1 \wedge \neg x_1 = 0$,
2. $(x_1 \vee x_2) \wedge \neg x_1 = (x_1 \wedge \neg x_1) \vee (x_2 \wedge \neg x_1) = 0 \vee (x_2 \wedge \neg x_1) = x_2 \wedge \neg x_1$.,
3. $(x_1 \vee x_2) \wedge x_1 = x_1$,
4. $(x_1 \wedge x_2) \vee x_1 = x_1$,
5. $(x_1 \vee x_2) \wedge x_2 = x_2$,
6. $(x_1 \vee \neg x_2) \wedge (x_1 \vee x_2) = x_1 \vee (\neg x_2 \wedge x_2) = x_1 \vee 0 = x_1$,
7. $(x_1 \vee x_2) \wedge x_1 \wedge x_2 = x_1 \wedge x_2$,
8. $x_1 \wedge x_2 \wedge x_3 \wedge \neg x_1 = 0$. $\qquad \square$

Exercise 6.7. Consider $f_1 = f_1(x_1, x_2, x_3) = x_1 \wedge x_2 \wedge \neg x_3$, $f_2 = f_2(x_1, x_2, x_3) = \neg x_3$, $f_3 = f_3(x_1, x_2, x_3) = x_1 \vee x_2$. Compute and simplify $f_1(x_1, x_2, f_3)$ and $f_2(x_2, x_2, f_3)$.

Solution.

$$f_1(x_1, x_2, f_3) = x_1 \wedge x_2 \wedge \neg x_3 = x_1 \wedge x_2 \wedge \neg(x_1 \vee x_2) = x_1 \wedge x_2 \wedge \neg x_1 \wedge \neg x_2 = 0.$$
$$f_2(x_1, x_2, f_3) = \neg x_3 = \neg(x_1 \vee x_2) = \neg x_1 \wedge \neg x_2.$$ □

Exercise 6.8. Find the steady states of f and h, if any.
Solution. $(0,0)$ is the only steady state of h and $(0,0,0)$ is the only steady state of f.   □

Exercise 6.9. Consider the Boolean network $f(x) = (x_2, (x_1 \wedge x_3) \vee x_2, \neg x_1)$. Reduce the network by removing variable x_3 (make sure you simplify the Boolean expressions in the reduced system). Find the steady states of the original and reduced networks, and compare their first and second coordinates. Also, using the steady states of the reduced network, compute f_3.
Solution.

$$h_1(x_1, x_2) = f_1(x_1, x_2, f_3) = f_1(x_1, x_2, \neg x_1) = x_2,$$
$$h_2(x_1, x_2) = f_2(x_1, x_2, f_3) = f_2(x_1, x_2, \neg x_1) = (x_1 \wedge \neg x_1) \vee x_2 = x_2.$$

$(0,0)$ and $(1,1)$ are the only steady states of h and, since $f_3 = \neg x_1$, $(0,0,1)$ and $(1,1,0)$ are the only steady states of f.   □

Exercise 6.10. Consider the Boolean network $f(x) = (x_2, (x_1 \wedge x_3) \wedge x_2, \neg x_1)$. Reduce the network by removing variable x_3 (make sure you simplify the Boolean expressions in the reduced system). Find the steady states of the original and reduced networks, and compare their first and second coordinates. Also, using the steady states of the reduced network, compute f_3.
Solution.

$$h_1(x_1, x_2) = f_1(x_1, x_2, f_3) = f_1(x_1, x_2, \neg x_1) = x_2,$$
$$h_2(x_1, x_2) = f_2(x_1, x_2, f_3) = f_2(x_1, x_2, \neg x_1) = (x_1 \wedge \neg x_1) \wedge x_2 = 0.$$

$(0,0)$ is the only steady state of h and, because $f_3 = \neg x_1$, $(0,0,1)$ is the only steady state of f.   □

Exercise 6.11. Find the steady states of the Boolean network $h(x_1, x_2) = (x_1 \vee \neg x_2, \neg x_1 \wedge x_2)$. Also, draw the wiring diagram of h.
Solution. $(0,1)$ and $(1,0)$ are the only steady states of h.   □

Exercise 6.12. Consider the Boolean network $f = f(x_1, x_2, x_3, x_4, x_5) = (x_5 \vee \neg x_2 \vee x_4, \neg x_1 \wedge \neg x_3, \neg x_2, \neg x_2, x_1 \vee x_4)$ from Example 6.2 , and reduce the network by removing variables x_3, x_4, and x_5. Compare this reduced network with the reduced network from Example 6.2. Are the reduced networks equal? Are the equations for x_3, x_4, x_5 the same? Use the reduced network and the equations for x_3, x_4, x_5 to find the steady states of f. Compare your answers with the steady states found in Example 6.2.
Solution. First remove $x_3 = \neg x_2$ and get

$$h_1(x_1, x_2, x_4, x_5) = x_5 \vee \neg x_2 \vee x_4,$$
$$h_2(x_1, x_2, x_4, x_5) = \neg x_1 \wedge \neg x_3 = \neg x_1 \wedge x_2,$$
$$h_4(x_1, x_2, x_4, x_5) = \neg x_2,$$
$$h_5(x_1, x_2, x_4, x_5) = x_1 \vee x_4$$

Then remove $x_4 = \neg x_2$ and get

$$h_1(x_1, x_2, x_5) = x_5 \vee \neg x_2 \vee x_4 = x_5 \vee \neg x_2 \vee \neg x_2 = x_5 \vee \neg x_2,$$
$$h_2(x_1, x_2, x_5) = \neg x_1 \wedge x_2,$$
$$h_5(x_1, x_2, x_4, x_5) = x_1 \vee x_4$$

Finally remove $x_5 = x_1 \vee x_4 = x_1 \vee \neg x_2$ and get

$$h_1(x_1, x_2) = x_5 \vee \neg x_2 = x_1 \vee \neg x_2 \vee \neg x_2 = x_1 \vee \neg x_2,$$
$$h_2(x_1, x_2) = \neg x_1 \wedge x_2. \qquad \square$$

Exercise 6.13. Consider the Boolean network $f = f(x_1, x_2, x_3, x_4, x_5) = (x_5 \vee \neg x_2 \vee x_4, \neg x_1 \wedge \neg x_3, \neg x_2, \neg x_2, x_1 \vee x_4)$ from Example 6.2 and reduce the network by removing variables x_1, x_3, and x_4. Compare this reduced network with the reduced network from Example 6.2. Are the reduced networks equal? Are the equations for x_1, x_3, x_4 the same? Use the reduced network and the equations for x_1, x_3, x_4 to find the steady states of f. Compare your answers with the steady states found in Example 6.2.

Solution. First remove $x_1 = x_5 \vee \neg x_2 \vee x_4$ and get

$$h_2(x_2, x_3, x_4, x_5) = \neg x_1 \wedge \neg x_3 = \neg x_5 \wedge x_2 \wedge \neg x_4 \wedge \neg x_3,$$
$$h_3(x_2, x_3, x_4, x_5) = \neg x_2,$$
$$h_4(x_2, x_3, x_4, x_5) = \neg x_2,$$
$$h_5(x_2, x_3, x_4, x_5) = x_1 \vee x_4 = x_5 \vee \neg x_2 \vee x_4 \vee x_4 = x_5 \vee \neg x_2 \vee x_4$$

Then remove $x_3 = \neg x_2$ and get

$$h_2(x_3, x_4, x_5) = \neg x_5 \wedge x_2 \wedge \neg x_4 \wedge \neg x_3 = \neg x_5 \wedge x_2 \wedge \neg x_4 \wedge x_2 = \neg x_5 \wedge \neg x_4 \wedge x_2,$$
$$h_4(x_3, x_4, x_5) = \neg x_2,$$
$$h_5(x_3, x_4, x_5) = x_5 \vee \neg x_2 \vee x_4$$

Finally remove $x_4 = \neg x_2$ and get

$$h_2(x_2, x_5) = \neg x_5 \wedge \neg x_4 \wedge x_2 = \neg x_5 \wedge x_2 \wedge x_2 = \neg x_5 \wedge x_2,$$
$$h_5(x_2, x_5) = x_5 \vee \neg x_2 \vee x_4 = x_5 \vee \neg x_2 \vee \neg x_2 = x_5 \vee \neg x_2. \qquad \square$$

Exercise 6.14. Consider the Boolean network $f = f(x_1, x_2, x_3, x_4, x_5) = (x_5 \vee \neg x_2 \vee x_4, \neg x_1 \wedge \neg x_3, \neg x_2, \neg x_2, x_1 \vee x_4)$ from Example 6.2 and reduce the network by removing variables x_5, x_2, and x_4. Compare this reduced network with the reduced network from Example 6.2. Are the reduced networks equal? Are the equations for x_5, x_2, x_4 the same? Use the reduced network and the equations for x_5, x_2, x_4 to find the steady states of f. Compare your answers with the steady states found in Example 6.2.

Solution. First remove $x_5 = x_1 \vee x_4$ and get

$$h_1(x_1, x_2, x_3, x_4) = x_5 \vee \neg x_2 \vee x_4 = (x_1 \vee x_4) \vee \neg x_2 \vee x_4 = x_1 \vee \neg x_2 \vee x_4,$$
$$h_2(x_1, x_2, x_3, x_4) = \neg x_1 \wedge \neg x_3,$$
$$h_3(x_1, x_2, x_3, x_4) = \neg x_2,$$
$$h_4(x_1, x_2, x_3, x_4) = \neg x_2$$

Then remove $x_2 = \neg x_1 \wedge \neg x_3$ and get

$$h_1(x_1, x_3, x_4) = x_1 \vee \neg x_2 \vee x_4 = x_1 \vee x_1 \vee x_3 \vee x_4 = \vee x_1 \vee x_3 \vee x_4,$$
$$h_3(x_1, x_3, x_4) = x_1 \vee x_3,$$
$$h_4(x_1, x_3, x_4) = x_1 \vee x_3$$

Finally remove $x_4 = \neg x_2 = x_1 \vee x_3$ and get

$$h_1(x_1, x_3) = x_1 \vee x_3 \vee x_4 = x_1 \vee x_3 \vee x_1 \vee x_3 = x_1 \vee x_3,$$
$$h_3(x_1, x_3) = x_1 \vee x_3. \qquad \square$$

Exercise 6.15. Reduce the network $f = (x_3, x_1 \vee x_3, x_1 \vee x_2)$ using all possible orders (remember that variables with self-loops cannot be removed), and draw the wiring diagrams of the reduced networks (and the intermediate wiring diagrams). Do all reduced networks have the same size? Compute the steady states of the reduced networks, and use them to find the steady states of the original network.

   Solution. There are six possible orders given by the permutations of $\{x_1, x_2, x_3\}$. Here we show the reduction for the orders 1-2-3 and 3-2-1.

1. For the canonical order x_1, x_2, x_3, first reduce $x_1 = x_3$ and get

$$h_2(x_2, x_3) = x_1 \vee x_3 = x_3,$$
$$h_3(x_2, x_3) = x_1 \vee x_2 = x_3 \vee x_2.$$

   Then remove $x_2 = x_1 \vee x_3 = x_3$ and get

$$h_3(x_3) = x_3 \vee x_3 = x_3.$$

2. For the order x_3, x_2, x_1, first reduce $x_3 = x_1 \vee x_2$ and get

$$h_1(x_2, x_3) = x_3 = x_1 \vee x_2,$$
$$h_2(x_2, x_3) = x_3 = x_1 \vee x_2.$$

□

   Because both variables have self-loops, we cannot remove either one.

Exercise 6.16. Reduce the network $f = (x_4, x_4, x_4, (x_1 \wedge x_2) \vee x_3)$ using all possible orders (remember that variables with self-loops cannot be removed), and draw the wiring diagrams of the reduced networks (and the intermediate wiring diagrams). Do all reduced networks have the same size? Compute the steady states of the reduced networks, and use them to find the steady states of the original network.

   Solution. There are 24 possible orders given by the permutations of $\{x_1, x_2, x_3, x_4\}$. Here we show the reduction for the orders 1-2-3-4 and 4-3-2-1.

1. For the canonical order x_1, x_2, x_3, x_4, first reduce $x_1 = x_4$ and get

$$h_2(x_2, x_3) = x_4,$$
$$h_3(x_2, x_3) = x_4.$$
$$h_4(x_2, x_3) = (x_1 \wedge x_2) \vee x_3 = (x_4 \wedge x_2) \vee x_3.$$

   Then remove $x_2 = x_4$ and get

$$h_3(x_3, x_4) = x_4.$$
$$h_4(x_3, x_4) = (x_1 \wedge x_2) \vee x_3 = (x_4 \wedge x_2) \vee x_3 = (x_4 \wedge x_4) \vee x_3 = x_4 \vee x_3.$$

   Then remove $x_3 = x_4$ and get

$$h_4(x_4) = x_4 \vee x_3 = x_4 \vee x_4 = x_4.$$

2. For the order x_4, x_3, x_2, x_1, first reduce $x_4 = (x_1 \wedge x_2) \vee x_3$ and get

$$h_1(x_1, x_2, x_3) = x_4 = (x_1 \wedge x_2) \vee x_3,$$
$$h_2(x_1, x_2, x_3) = x_4 = (x_1 \wedge x_2) \vee x_3.$$
$$h_3(x_1, x_2, x_3) = x_4 = (x_1 \wedge x_2) \vee x_3.$$

□

   Because all three variables have self-loops, we cannot remove either one.

Exercise 6.17. Repeat Exercises 6.12–6.14 using the Mathematica code and compare with your answers.
Solution.

```
X={"x1","x2","x3","x4","x5"};
F={" (x5 || !x2) || x4 ","!x1 && !x3","!x2","!x2","x1 || x4"};
{Xr,Fr} = {X,F};
{Xr,Fr}=REMOVEVERTEX[{Xr,Fr},"x3"];
{Xr,Fr}=REMOVEVERTEX[{Xr,Fr},"x4"];
{Xr,Fr}=REMOVEVERTEX[{Xr,Fr},"x5"];
Print[Xr]
Print[Fr]
{x1,x2}
{x1 || !x2,!x1 && x2}

X={"x1","x2","x3","x4","x5"};
F={" (x5 || !x2) || x4 ","!x1 && !x3","!x2","!x2","x1 || x4"};
{Xr,Fr} = {X,F};
{Xr,Fr}=REMOVEVERTEX[{Xr,Fr},"x1"];
{Xr,Fr}=REMOVEVERTEX[{Xr,Fr},"x3"];
{Xr,Fr}=REMOVEVERTEX[{Xr,Fr},"x4"];
Print[Xr]
Print[Fr]
{x2,x5}
{x2 && !x5,!x2 || x5}

X={"x1","x2","x3","x4","x5"};
F={" (x5 || !x2) || x4 ","!x1 && !x3","!x2","!x2","x1 || x4"};
{Xr,Fr} = {X,F};
{Xr,Fr}=REMOVEVERTEX[{Xr,Fr},"x5"];
{Xr,Fr}=REMOVEVERTEX[{Xr,Fr},"x2"];
{Xr,Fr}=REMOVEVERTEX[{Xr,Fr},"x4"];
Print[Xr]
Print[Fr]
{x1,x3}
{x1 || x3,x1 || x3}
```
                                                                                    □

Exercise 6.18. Reduce the network $f = (x_5 \vee \neg x_2 \vee x_4, \neg x_1 \wedge \neg x_3, \neg x_2, \neg x_2, x_1 \vee x_4)$ using all possible orders (preferably writing a piece of code that goes over all possible reductions). Do all reduced networks have the same size? Is there a variable that always appears in the reduced networks? Is there a variable that never appears in the reduced networks?
Solution.

```
X = {"x1", "x2", "x3", "x4", "x5"};
F = {" (x5 || !x2) || x4 ", "!x1 && !x3","!x2", "!x2", "x1 || x4"};
XX = Permutations[{1, 2, 3, 4, 5}];
TotalXr = {}; TotalFr = {};
For[i = 1, i <= 5!, i++, per = XX[[i]];
   k1 = per[[1]]; k2 = per[[2]]; k3 = per[[3]];k4 = per[[4]];
   k5 = per[[5]];
   Xr = {X[[k1]], X[[k2]], X[[k3]], X[[k4]],X[[k5]]};
   Fr = {F[[k1]], F[[k2]], F[[k3]], F[[k4]],F[[k5]]};
   {Xr, Fr} = REDUCEALLF[{Xr, Fr}];
   AppendTo[TotalXr, Xr]; AppendTo[TotalFr,Fr];];
Print[TotalXr]
Print[TotalFr]
```

- All reduced networks have the same size.
- There is no variable that appears in all the reduced networks.
- Variable x_4 does not appear in any reduced network. □

Exercise 6.19. Reduce the network $f = (x_6, x_6, x_6, x_6, x_6, x_1 \lor (x_2 \land x_3) \lor (x_4 \land x_5))$ using REDUCEALLF and REDUCEALLB. Do the reduced networks have the same size?

Solution. For REDUCEALLF type in a Mathematica cell the following,

```
X = {"x1", "x2", "x3", "x4", "x5", "x6"};
F = {" x6 ", " x6 ", " x6 ", " x6 ", " x6 ",
    "x1 || (x2 && x3)|| (x4 && x5)"};
{Xr, Fr} = REDUCEALLF[{X, F}];
Print[Xr]
Print[Fr]
{x6}
{x6}
```

and for REDUCEALLB type

```
X={"x1","x2","x3","x4","x5","x6"};
F={" x6 "," x6 "," x6 "," x6 "," x6 ","x1|| (x2 && x3)|| (x4 && x5)"};
{Xr,Fr}=REDUCEALLB[{X,F}];
Print[Xr]
Print[Fr]
{x1,x2,x3,x4,x5}
{x1 || (x2 && x3) || (x4 && x5),x1|| (x2 && x3) || (x4 && x5),
 x1 || (x2 && x3) || (x4 && x5),x1|| (x2 && x3) || (x4 && x5),
 x1 || (x2 && x3) || (x4 && x5)}
```

The reduced networks have very different sizes. □

Exercise 6.20. Create examples of networks such that REDUCEALLF and REDUCEALLB give reduced networks of very different sizes.

Solution. The network at Exercise 6.19 is one example. □

Exercise 6.21. Use formulas from Eq. (6.1) to find the polynomial representation of the following Boolean functions:

1. $x_1 \land \neg x_1$, 2. $(x_1 \lor x_2) \land x_1$,
3. $(x_1 \lor x_2) \land \neg x_1$, 4. $(x_1 \land x_2) \lor x_1$,
5. $(x_1 \lor x_2) \land x_2$, 6. $(x_1 \lor \neg x_2) \land (x_1 \lor x_2)$,
7. $(x_1 \lor x_2) \land x_1 \land x_2$, 8. $x_1 \land x_2 \land x_3 \land \neg x_1$.

Solution.
1. $x_1 \land \neg x_1 = x_1(1 + x_1) = x_1 + x_1^2 = x_1 + x_1 = 2x_1 = 0$
2. $(x_1 \lor x_2) \land x_1 = (x_1 + x_2 + x_1 x_2)x_1 = x_1^2 + x_1 x_2 + x_1^2 x_2 = x_1 + x_1 x_2 + x_1 x_2 = x_1$
3. $(x_1 \lor x_2) \land \neg x_1 = (x_1 + x_2 + x_1 x_2)(1 + x_1) = x_1 + x_2 + x_1 x_2 + x_1^2 + x_1 x_2 + x_1^2 x_2 = x_2 + x_1 x_2$
4. $(x_1 \land x_2) \lor x_1 = x_1 x_2 + x_1 + x_1^2 x_2 = x_1$
5. $(x_1 \lor x_2) \land x_2 = (x_1 + x_2 + x_1 x_2)x_2 = x_1 x_2 + x_2^2 + x_1 x_2^2 = x_2$ □

Exercise 6.22. Consider $f_1 = x_1 \land x_2 \land \neg x_3, f_2 = \neg x_3, f_3 = x_1 \lor x_2$. Compute and simplify $f_1(x_1, x_2, f_3)$ and $f_2(x_1, x_2, f_3)$ using polynomial algebra.

Solution. Note $f_1 = x_1x_2 + x_1x_2x_3, f_2 = 1 + x_3$, and $f_3 = x_1 + x_2 + x_1x_2$. Then,

$$f_1(x_1,x_2,f_3) = x_1x_2 + x_1x_2(x_1 + x_2 + x_1x_2)$$
$$= x_1x_2 + x_1^2x_2 + x_1x_2^2 + x_1^2x_2^2$$
$$= x_1x_2 + x_1x_2 + x_1x_2 + x_1x_2 = 0$$
$$f_2(x_1,x_2,f_3) = 1 + x_1 + x_2 + x_1x_2. \qquad \square$$

Exercise 6.23. Compute the polynomial representation of the reduced network from Example 6.2, and verify that it is equal to the reduced network from Example 6.5.

Solution. The reduced network from Example 6.2 is $(x_1 \vee \neg x_2, \neg x_1 \wedge x_2)$ with polynomial form $(1 + x_2 + x_1x_2, x_2 + x_1x_2)$, which coincides with our answer in Example 6.5. $\qquad \square$

Exercise 6.24. Use computational algebra to reduce the Boolean network from Example 6.5 using the order x_3, x_4, x_5.

Solution. We proceed as in Example 6.5 up to the definition of the network (step i8). Then, for Exercise 6.24, the Macaulay2 code is

```
S={x3=>f3}; f1=sub(f1,S); f2=sub(f2,S); f4=sub(f4,S); f5=sub(f5,S);
S={x4=>f4}; f1=sub(f1,S); f2=sub(f2,S); f5=sub(f5,S);
S={x5=>f5}; f1=sub(f1,S); f2=sub(f2,S); (f1,f2)
```

which returns `(x1*x2 + x2 + 1, x1*x2 + x2)`. Thus, the reduced network with this order coincides with the reduced network from Example 6.5. $\qquad \square$

Exercise 6.25. Use computational algebra to reduce the Boolean network from Example 6.5 using the order x_1, x_3, x_4.

Solution. We obtain the reduced network `(x2*x5 + x2, x2*x5 + x2 + 1)`. $\qquad \square$

Exercise 6.26. Use computational algebra to reduce the Boolean network from Example 6.5 using the order x_5, x_2, x_4.

Solution. We obtain the reduced network `(x1*x3 + x1 + x3, x1*x3 + x1 + x3)`. $\qquad \square$

Exercise 6.27. Use computational algebra to reduce the network defined by $f = (x_6, x_6, x_6, x_6, x_6, x_1 \vee (x_2 \wedge x_3) \vee (x_4 \wedge x_5))$. First start with x_1 (then x_2, and so on); then repeat the reduction staring with x_6 (then x_5, and so on). Before removing a variable x_i, make sure that f_i does not depend on x_i; if it does, then continue with the next variable.

Solution. Using the order $x_1, x_2, \ldots$ we can remove x_1, x_2, x_3, x_4, x_5:

```
R=ZZ/2[x1,x2,x3,x4,x5,x6]/ideal(x1^2-x1,x2^2-x2,x3^2-x3,x4^2-x4,x5^2-x5,x6^2-x6);
RingElement | RingElement :=(x,y)->x+y+x*y;
RingElement & RingElement :=(x,y)->x*y;
f1=x6; f2=x6; f3=x6; f4=x6; f5=x6; f6= x1|(x2&x3)|(x4&x5)
S={x1=>f1}; f2=sub(f2,S);f3=sub(f3,S);f4=sub(f4,S);f5=sub(f5,S);f6=sub(f6,S);
S={x2=>f2}; f3=sub(f3,S);f4=sub(f4,S);f5=sub(f5,S);f6=sub(f6,S);
S={x3=>f3}; f4=sub(f4,S);f5=sub(f5,S);f6=sub(f6,S);
S={x4=>f4}; f5=sub(f5,S);f6=sub(f6,S);
S={x5=>f5}; f6=sub(f6,S);
```

We obtain the reduced network $f_6(x_6) = x_6$. Using the order $x_6, x_5, \ldots$ we can only remove x_6:

```
R=ZZ/2[x1,x2,x3,x4,x5,x6]/ideal(x1^2-x1,x2^2-x2,x3^2-x3,x4^2-x4,x5^2-x5,x6^2-x6);
RingElement | RingElement :=(x,y)->x+y+x*y;
```

```
RingElement & RingElement :=(x,y)->x*y;
f1=x6; f2=x6; f3=x6; f4=x6; f5=x6; f6= x1|(x2&x3)|(x4&x5)
S={x6=>f6}; f1=sub(f1,S);f2=sub(f2,S);f3=sub(f3,S);f4=sub(f4,S);f5=sub(f5,S);
```

We obtain the reduced network

$$f_1 = x_1x_2x_3x_4x_5 + x_2x_3x_4x_5 + x_1x_2x_3 + x_1x_4x_5 + x_2x_3 + x_4x_5 + x_1,$$
$$f_2 = x_1x_2x_3x_4x_5 + x_2x_3x_4x_5 + x_1x_2x_3 + x_1x_4x_5 + x_2x_3 + x_4x_5 + x_1,$$
$$f_3 = x_1x_2x_3x_4x_5 + x_2x_3x_4x_5 + x_1x_2x_3 + x_1x_4x_5 + x_2x_3 + x_4x_5 + x_1,$$
$$f_4 = x_1x_2x_3x_4x_5 + x_2x_3x_4x_5 + x_1x_2x_3 + x_1x_4x_5 + x_2x_3 + x_4x_5 + x_1,$$
$$f_5 = x_1x_2x_3x_4x_5 + x_2x_3x_4x_5 + x_1x_2x_3 + x_1x_4x_5 + x_2x_3 + x_4x_5 + x_1,$$

which cannot be further reduced due to self-loops. □

Exercise 6.28. By hand or using software, reduce the model of the *lac* operon starting from the last variable.
Solution. We use the Mathematica code:

```
VV = {"M", "P", "B", "Ca", "R", "Rm", "A","Am", "L", "Lm"};
FF = {"!Rm && !R &&Ca", "M", "M", "!Ge","!A&&!Am", "R||(!A&&!Am)", "L&&B",
    "L||Lm", "!Ge&&P&&Le","!Ge&&(Le||(Lem&&P))"};
{VR, FR} = REDUCEALLB[{VV, FF}];
```

This returns `{(!Ge && Le) || (!Ge && Lem && M)}`. □

Exercise 6.29. Analyze $h(x_1) = ((x_1 \wedge x_{12}) \vee x_{11}) \wedge \neg x_{13}$ for low extracellular lactose ($x_{11} = 0$, $x_{12} = 0$) and low extracellular glucose ($x_{13} = 0$). How many steady states does the reduced network have? How many steady states does the original network have?
Solution. The network simplifies to $h(x_1) = 0$, then there is only one steady state, $x_1 = 0$. Therefore, the original network has one steady state. □

Exercise 6.30. Analyze $h(x_1) = ((x_1 \wedge x_{12}) \vee x_{11}) \wedge \neg x_{13}$ for low extracellular lactose ($x_{11} = 0$, $x_{12} = 0$) and high extracellular glucose ($x_{13} = 1$). How many steady states does the reduced network have? How many steady states does the original network have?
Solution. The network simplifies to $h(x_1) = 0$, then there is only one steady state, $x_1 = 0$. Therefore, the original network has one steady state. □

Exercise 6.31. Analyze $h(x_1) = ((x_1 \wedge x_{12}) \vee x_{11}) \wedge \neg x_{13}$ for high extracellular lactose ($x_{11} = 1$, $x_{12} = 1$) and low extracellular glucose ($x_{13} = 0$). How many steady states does the reduced network have? How many steady states does the original network have?
Solution. The network simplifies to $h(x_1) = 1$, then there is only one steady state, $x_1 = 1$. Therefore, the original network has one steady state. □

Exercise 6.32. By hand or using a software package, reduce the model of Th-cell differentiation starting from the last variable.
Solution. We use the Mathematica code:

```
VV = {"x1", "x2", "x3", "x4", "x5", "x6", "x7","x8", "x9", "x10", "x11", "x12", "x13",
    "x14", "x15", "x16", "x17", "x18", "x19","x20", "x21", "x22", "x23"};
FF = {"(x1 || x21) && !x22", "0", "x2","(x14||x16||x20||x22) && !x19", "x4", "x1",
    "x6", "0", "x8&&!x21", "0", "x10&&!x21","x1&&!x18", "x12&&!x17", "x11","x5&&!x17",
    "x23", "x18||x22", "x3||x15","x7", "x9&&!x1", "x13","(x18||x22)&&!x1", "0"};
{VR, FR} = REDUCEALLB[{VV, FF}];
```

This returns `{x1 && !x22,!x1 && x22}`. □

Exercise 6.33. Find the steady states of the reduced Boolean network $h_1 = x_1x_{12} + x_1$, $h_{22} = x_1x_{22} + x_{22}$.

Solution. We need to solve the system of equations $x_1 = x_1x_1x_{22} + x_1$, $x_{22} = x_1x_{22} + x_{22}$; that is, $0 = x_1x_{22}$. The only solutions are $(x_1, x_{22}) = 00, 01, 10$. □

Exercise 6.34. Find the wiring diagram of the following Boolean networks.
1. $f(x) = (x_2x_3, x_1x_2x_6, x_2, x_1x_5, x_5x_6, x_1x_5x_6)$
2. $f(x) = (x_2, x_3, x_4, x_1)$
3. $f(x) = (x_4, x_1, x_2, x_3)$
4. $f(x) = (x_6, x_6, x_6, x_6, x_6, x_1x_2x_3x_4x_5)$
5. $f(x) = (x_2x_3, x_1x_3, x_1x_2)$
6. $f(x) = (x_2, x_1, x_4, x_5, x_1x_3)$

Solution. See Figure S6.1. □

Exercise 6.35. Find the AND networks associated to the wiring diagrams shown in Figure 6.8.

Solution.
1. $f(x) = (x_2, x_3, x_1x_2, x_1x_5, x_3x_4)$
2. $f(x) = (x_2x_4, x_3, x_1x_2, x_1x_5, x_3x_4)$
3. $f(x) = (x_2, x_3, x_1, x_1x_5, x_3x_4)$
4. $f(x) = (x_4, x_3, x_1x_2x_5, x_1x_5, x_4)$
5. $f(x) = (x_1, x_3, x_1x_2, x_1x_5, x_3x_4)$
6. $f(x) = (x_1x_2, x_3, x_1x_2, x_1x_5, x_3x_4)$ □

Exercise 6.36. Find the strongly connected components of the wiring diagrams in Figure 6.8.

Solution. The scc are indicated as ellipses in Figure S6.2. □

Exercise 6.37. Find all steady states of the AND networks corresponding to the wiring diagrams in Figure 6.8.

Solution. The calculations are simpler if we consider cases. For example, for the first wiring diagram we have $f(x) = (x_2, x_3, x_1x_2, x_1x_5, x_3x_4)$, so we need to solve:

$$x_1 = x_2$$

$$x_2 = x_3$$

$$x_3 = x_1x_2$$
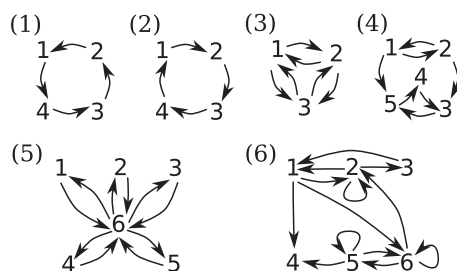
$$x_4 = x_1x_5$$

$$x_5 = x_3x_4$$

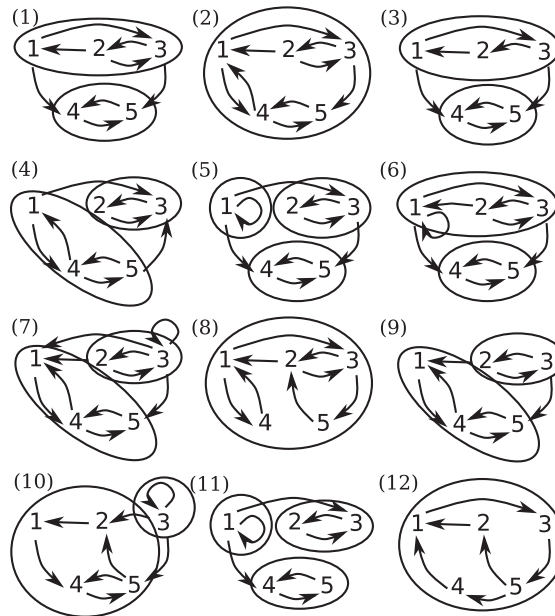**FIGURE S6.1** Solution for Exercise 6.34.

FIGURE S6.2 Strongly connected components of the wiring diagrams in Exercise 6.36.
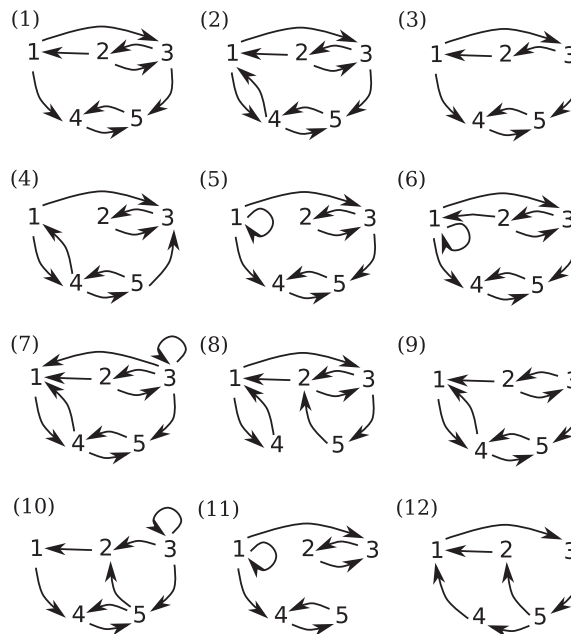

FIGURE 6.8 Wiring diagrams for 6.35, 6.36, and 6.38.

Case $x_1 = 0$. Here we obtain $x_2 = x_3 = x_4 = x_5 = 0$. Thus, one steady state is 00000.
Case $x_1 = 1$. Here we obtain $x_2 = x_3 = 1$ and the equations $x_4 = x_5$. Thus, we have two steady states 11100 and 11111. □

Exercise 6.38. Find all steady states of the AND networks corresponding to the wiring diagrams in Figure 6.8 using reduction of AND networks.

Solution. Analysis for wiring diagrams 1 and 5.

1. Based on the scc, the reduced AND network is $h(x_1, x_4) = (x_1, x_1 x_4)$, which has steady states 00, 10, and 11. Then, the steady states of the original AND network are 00000, 11100, and 11111.

5. Based on the scc, the reduced AND network is $h(x_1, x_2, x_4) = (x_1, x_1 x_2, x_1 x_4)$, which has steady states 000, 100, and 110, 101, and 111. Then, the steady states of the original AND network are 00000, 10000, 11100, 10011, and 11111.

$\square$

Exercise 6.39. Use reduction of AND networks to find the steady states of the following Boolean networks.

1.	2.	3.	4.	5.	6.
$f_1 = x_4 x_5$	$f_1 = x_4 x_5$	$f_1 = x_4 x_5$	$f_1 = x_4 x_5$	$f_1 = x_4 x_5$	$f_1 = x_4 x_5$
$f_2 = x_3 x_5$	$f_2 = x_3 x_5$	$f_2 = x_3$	$f_2 = x_3 x_9$	$f_2 = x_3$	$f_2 = x_3$
$f_3 = x_2 x_1 x_6$	$f_3 = x_2 x_1 x_6$	$f_3 = x_2 x_6$	$f_3 = x_2 x_9 x_6$	$f_3 = x_2 x_8$	$f_3 = x_2 x_9$
$f_4 = x_5$	$f_4 = x_5$	$f_4 = x_5$	$f_4 = x_5$	$f_4 = x_5$	$f_4 = x_5$
$f_5 = x_1 x_8$	$f_5 = x_1$	$f_5 = x_1$	$f_5 = x_1 x_2$	$f_5 = x_1$	$f_5 = x_1$
$f_6 = x_9 x_5 x_3$	$f_6 = x_9 x_3 x_7$	$f_6 = x_9 x_3 x_7$	$f_6 = x_9 x_7$	$f_6 = x_9 x_7$	$f_6 = x_9 x_3$
$f_7 = x_8 x_1$	$f_7 = x_8 x_1$	$f_7 = x_8 x_1$	$f_7 = x_8 x_1$	$f_7 = x_8 x_1 x_2$	$f_7 = x_8 x_1 x_2$
$f_8 = x_7 x_4$	$f_8 = x_7 x_4$	$f_8 = x_7 x_4$	$f_8 = x_7 x_4$	$f_8 = x_7 x_4 x_3$	$f_8 = x_7 x_4 x_3$
$f_9 = x_6 x_4$	$f_9 = x_6 x_3 x_8$	$f_9 = x_6 x_3 x_8$	$f_9 = x_6 x_8$	$f_9 = x_6 x_8$	$f_9 = x_6 x_3$

Solution. For each network:

- Find the wiring diagram.
- Find the scc of the wiring diagram.
- Find the reduced AND network.
- Compute the steady states of the reduced AND network (use exhaustive search or proceed by cases).
- Use the steady states of the reduced AND network and the scc to compute the steady states of the original AND network.

$\square$

Exercise 6.40. Find all steady states of the AND networks corresponding to the wiring diagrams in Figure 6.12 using reduction of AND networks.
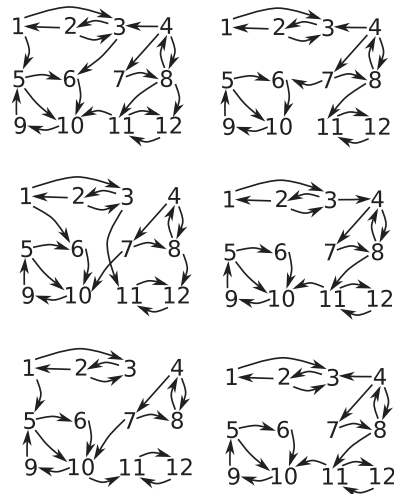

FIGURE 6.12 Wiring diagrams for Exercise 6.40.

Solution. For each network:

– Find the scc of the wiring diagram.
– Find the reduced AND network.
– Compute the steady states of the reduced AND network (use exhaustive search or proceed by cases).
– Use the steady states of the reduced AND network and the scc to compute the steady states of the original AND network.   □