Bioinformatics III

Sixth Assignment

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Exercise 6.1: Boolean Networks

All the listings are at the end of the exercise.

(a) **Weighted Interactions**

Table 1: Propagation Matrix

	F	E	D	C	B	A
F	0	0	1	0	0	0
E	1	0	0	0	0	0
D	-3	-3	0	0	-3	0
C	0	1	0	0	1	0
B	0	0	0	1	0	0
A	0	0	0	0	1	1

(b) **Implementation**

When does it make sense to stop the propagation and why?

We stop the propagation once we meet an already visited state. If we continue, we will just loop over and over again.

Which sequences do you get when you start from states 1, 4, 21, and 33?

Sequence with starting state 1: [1, 3, 7, 23, 55, 63, 13, 1]
Sequence with starting state 4: [4, 18, 36, 26, 4]
Sequence with starting state 21: [21, 51, 47, 13, 1, 3, 7, 23, 55, 63, 13]
Sequence with starting state 33: [33, 11, 5, 19, 39, 31, 5]

(c) **Periodic Orbits**
(1) List these orbits with their respective lengths and basins of attraction

To make things clearer let's recall the different definition. "If the attractor has only a single state it is called a point attractor, and if the attractor consists of more than one state it is called a cycle attractor. The set of states that lead to an attractor is called the basin of the attractor. States which occur only at the beginning of trajectories (no trajectories lead to them), are called garden-of-Eden states" [1]

[1] https://en.wikipedia.org/wiki/Boolean_network#Attractors

Table 2: List of states, orbith length, Cycle attractor and relative coverage of the basin of attraction. The basin of attraction's coverage includes the steps before the cycle attractor.

Start State	**Period**	**Basin**	**Attractor**	**Basin Coverage**
0	1	[]	[0]	1.5625%
1	7	[]	[1, 3, 7, 23, 55, 63, 13]	10.9375%
2	4	[2]	[4, 18, 36, 26]	7.8125%
3	7	[]	[3, 7, 23, 55, 63, 13, 1]	10.9375%
4	4	[]	[4, 18, 36, 26]	6.25%
5	4	[]	[5, 19, 39, 31]	6.25%
6	1	[6, 22, 54, 62, 12]	[0]	9.375%
7	7	[]	[7, 23, 55, 63, 13, 1, 3]	10.9375%
8	1	[8]	[0]	3.125%
9	7	[9]	[1, 3, 7, 23, 55, 63, 13]	12.5%
10	4	[10]	[4, 18, 36, 26]	7.8125%
11	4	[11]	[5, 19, 39, 31]	7.8125%
12	1	[12]	[0]	3.125%
13	7	[]	[13, 1, 3, 7, 23, 55, 63]	10.9375%
14	4	[14]	[4, 18, 36, 26]	7.8125%
15	4	[15]	[5, 19, 39, 31]	7.8125%
16	1	[16, 32, 8]	[0]	6.25%
17	4	[17, 35, 15]	[5, 19, 39, 31]	10.9375%
18	4	[]	[18, 36, 26, 4]	6.25%
19	4	[]	[19, 39, 31, 5]	6.25%
20	1	[20, 50, 44, 8]	[0]	7.8125%
21	7	[21, 51, 47]	[13, 1, 3, 7, 23, 55, 63]	15.625%
22	1	[22, 54, 62, 12]	[0]	7.8125%
23	7	[]	[23, 55, 63, 13, 1, 3, 7]	10.9375%
24	1	[24]	[0]	3.125%
25	7	[25]	[1, 3, 7, 23, 55, 63, 13]	12.5%
26	4	[]	[26, 4, 18, 36]	6.25%
27	4	[27]	[5, 19, 39, 31]	7.8125%
28	1	[28]	[0]	3.125%
29	7	[29]	[1, 3, 7, 23, 55, 63, 13]	12.5%
30	4	[30]	[4, 18, 36, 26]	7.8125%
31	4	[]	[31, 5, 19, 39]	6.25%
32	1	[32, 8]	[0]	4.6875%
33	4	[33, 11]	[5, 19, 39, 31]	9.375%
34	1	[34, 12]	[0]	4.6875%
35	4	[35, 15]	[5, 19, 39, 31]	9.375%
36	4	[]	[36, 26, 4, 18]	6.25%
37	4	[37, 27]	[5, 19, 39, 31]	9.375%
38	4	[38, 30]	[4, 18, 36, 26]	9.375%
39	4	[]	[39, 31, 5, 19]	6.25%
40	1	[40, 8]	[0]	4.6875%

Start State	Period	Basin	Attractor	Basin Coverage
41	7	[41, 9]	[1, 3, 7, 23, 55, 63, 13]	14.0625%
42	1	[42, 12]	[0]	4.6875%
43	7	[43]	[13, 1, 3, 7, 23, 55, 63]	12.5%
44	1	[44, 8]	[0]	4.6875%
45	7	[45, 9]	[1, 3, 7, 23, 55, 63, 13]	14.0625%
46	1	[46, 12]	[0]	4.6875%
47	7	[47]	[13, 1, 3, 7, 23, 55, 63]	12.5%
48	1	[48, 40, 8]	[0]	6.25%
49	7	[49, 43]	[13, 1, 3, 7, 23, 55, 63]	14.0625%
50	1	[50, 44, 8]	[0]	6.25%
51	7	[51, 47]	[13, 1, 3, 7, 23, 55, 63]	14.0625%
52	1	[52, 58, 12]	[0]	6.25%
53	7	[53, 59]	[13, 1, 3, 7, 23, 55, 63]	14.0625%
54	1	[54, 62, 12]	[0]	6.25%
55	7	[]	[55, 63, 13, 1, 3, 7, 23]	10.9375%
56	1	[56, 8]	[0]	4.6875%
57	7	[57, 9]	[1, 3, 7, 23, 55, 63, 13]	14.0625%
58	1	[58, 12]	[0]	4.6875%
59	7	[59]	[13, 1, 3, 7, 23, 55, 63]	12.5%
60	1	[60, 8]	[0]	4.6875%
61	7	[61, 9]	[1, 3, 7, 23, 55, 63, 13]	14.0625%
62	1	[62, 12]	[0]	4.6875%
63	7	[]	[63, 13, 1, 3, 7, 23, 55]	10.9375%

(2) Give the relative coverages of the state space by the basins of attraction.
The coverages for each separate basins of attraction are given in the table 2. In table 3 we give the coverage of each attractor.

Table 3: Relative coverage of the cycle attractors (order not taken in account here)

[0] :	23	:	35.9375 %
[1, 3, 7, 13, 55, 23, 63] :	21	:	32.8125 %
[18, 26, 4, 36] :	9	:	14.0625 %
[39, 19, 5, 31] :	11	:	17.1875 %

(d) **Interpretation**

(1) Give the attractors in terms of active genes and characterize them with a few words

In the listing 1 the binary transitions are presented for each attractors.

Attractor [0] : No gene are activated in this attractor and there is only one period. We can see that the states leading to this attractor are the one when **D** is activated and shuts down genes **B**, **E** and **F** even if **C** is activated, in those case it does not get activated again by **B** as in attractor [4, 18, 36, 26]. Here **A** is not activated and there is no cycle between **B** and **C**.

Attractor [1, 3, 7, 23, 55, 63, 13] : Here gene **A** is activated and keeps activating **B**. Thus, whenever **D** is activated and shuts down genes **B**, **E** and **F**, **B** is reactivated again by **A**.

Attractor [4, 18, 36, 26] : This cycle happens when gene **B** and **C** are not active at the same time and keep activating each other one step after another.

Attractor [5, 19, 39, 31] : This attractor is the opposite of attractor [1, 3, 7, 23, 55, 63, 13] for gene **B**, **C** and **D**. Gene **A** is also always activated but the fact that **C** is activated in the first place, shifts the activation of **D** earlier and avoids the total activation before **D** inhibits genes **B**, **E** and **F**.

Listing 1: Output - Binary evolution in the orbits and percentages

```
Current orbit:  [0]
Binary evolution:
[0, 0, 0, 0, 0, 0]
Average occupancy:
 [0.0, 0.0, 0.0, 0.0, 0.0, 0.0]

Current orbit:  [1, 3, 7, 23, 55, 63, 13]
Binary evolution:
[0, 0, 0, 0, 0, 1]
[0, 0, 0, 0, 1, 1]
[0, 0, 0, 1, 1, 1]
[0, 1, 0, 1, 1, 1]
[1, 1, 0, 1, 1, 1]
[1, 1, 1, 1, 1, 1]
[0, 0, 1, 1, 0, 1]
Average occupancy:
 [0.2857142857142857, 0.42857142857142855, 0.2857142857142857,
    0.7142857142857143, 0.7142857142857143, 1.0]

Current orbit:  [4, 18, 36, 26]
Binary evolution:
[0, 0, 0, 1, 0, 0]
[0, 1, 0, 0, 1, 0]
[1, 0, 0, 1, 0, 0]
[0, 1, 1, 0, 1, 0]
Average occupancy:
 [0.25, 0.5, 0.25, 0.5, 0.5, 0.0]

Current orbit:  [5, 19, 39, 31]
Binary evolution:
[0, 0, 0, 1, 0, 1]
[0, 1, 0, 0, 1, 1]
[1, 0, 0, 1, 1, 1]
[0, 1, 1, 1, 1, 1]
Average occupancy:
 [0.25, 0.5, 0.25, 0.75, 0.75, 1.0]
```

(2) Which are the special genes and what are their respective effects on the behavior of the network? For this, explain what is determining the period of the orbits. Further, compare the two shorter orbits which each other. Which gene is responsible for the difference?

Without genes **A** and **C**, the network shuts down. **A** is particular as it is not inhibited by **D** like the others and because it activates itself. As **A** cannot be activated by any other gene, it leads to or odd states, where **A** is active or even states where it is not. It cannot be activated in the middle of a sequence.

D is particular because it deactivates **B**, **E** and **F** what has a big effect on the network. **B** and **C** can propagate the activation to the network but they have to be synchronized correctly. If for instance **C** and **D** are activated, the network will be shut down.

Exercise 6.2: Differential Expression Analysis

(a) **A**

(b) **B**