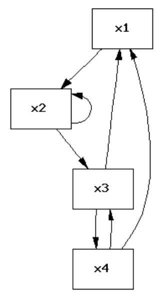
Supporting Information

1. Motivational Example.

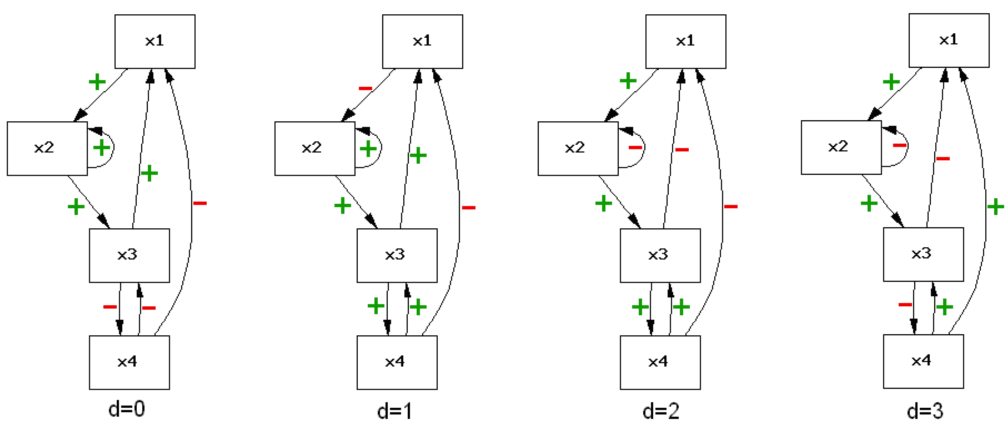
Consider the directed graph G in Figure 1, it is not hard to check that its maximal PF-distance is 3. At random, choose ten Boolean networks such that all have the same dependency graph G. For example, consider the Boolean network $f(x_1,x_2,x_3,x_4)=(x_3 \vee x_4, x_1 \wedge x_2, x_2 \wedge x_4, x_3)$.



G

Figure 1. A directed graph on 4 nodes.

Let G_0, G_1, G_2, G_3 be signed graphs of G of distance 0,1,2,3, respectively, as in Figure 2. Let $S=\{G_0,G_1,G_2, G_3\}$. For each $G_{d,}$ by replacing x_i by $\sim x_i$ wherever it appears for some i, modify f into f' such that G_d is the dependency graph of f', see Figure 2. Similarly, we modify each of the other 9 networks.



d=0	d=1	d=2	d=3
$f_1 = x_3 \vee (\sim x_4)$	$f_1 = x_3 \vee (\sim x_4)$	$f_1 = (\sim x_3) \vee (\sim x_4)$	$f_1 = (\sim x_3) \vee x_4$
$f_2 = x_1 \wedge x_2$	$f_2 = (\sim x_1) \wedge x_2$	$f_2 = x_1 \wedge (\sim x_2)$	$f_2 = x_1 \wedge (\sim x_2)$
$f_3 = x_2 \wedge (\sim x_4)$	$f_3 = x_2 \wedge x_4$	$f_3 = x_2 \wedge x_4$	$f_3 = x_2 \wedge x_4$
$f_4 = \sim x_3$	$f_4 = x_3$	$f_4 = x_3$	$f_4 = \sim x_3$

Figure 2. Possible sign assignments of the graph G and the corresponding modified network of f for each signed graph. For example, for d=1, since the are negative edges from x_4 to x_1 and x_1 to x_2, we write $\sim x_4$ in f_1 and $\sim x_1$ in f_2

For each d, we find the phase spaces of the 10 Boolean networks that have G_d as their signed dependency graph.

Compute the average number as well as average length of limit cycles. We summarize this in Table 1.

d	0	1	2	3
Average number of cycles	3.50	2.80	2.50	1.20
Average Length of cycles	1.23	1.25	1.52	3.50

Table 1. The average number and average length of limit cycles with respect to d. For example, for networks with PF distance 0, the average number of cycles is 3.50 and their average length is 1.23.

We plot the average as a function of d and compute the slope of the best fit line. In our example, the slope of the best fit line of the numbers is -0.72 and the slope of the best fit line of the lengths is 0.71.

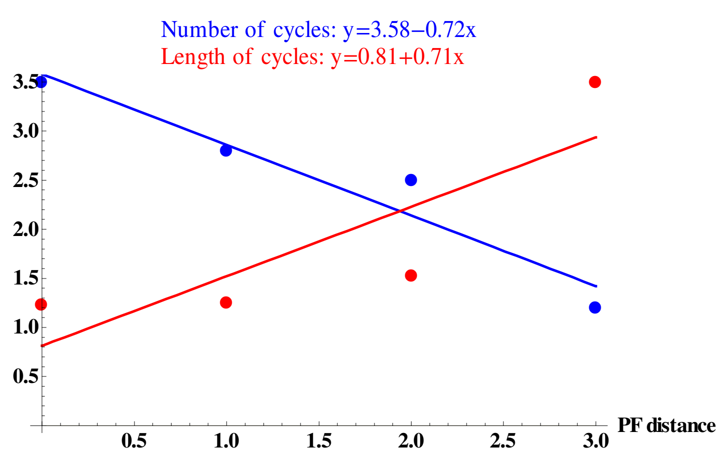


Figure 3. The best fit-line of the average of number (resp. length) of limit cycles is in blue (resp. red).

2. Networks on 5 nodes

We performed 4000 experiments using 5-node networks. We varied the PF-distance from d=0 to D=25%, 50%, 75%, 100% of the maximum distance of the network (Figure 4 and Table 2). We show the histograms for the slopes for the average number and length of limit cycles, and the median number and length of limit cycles.

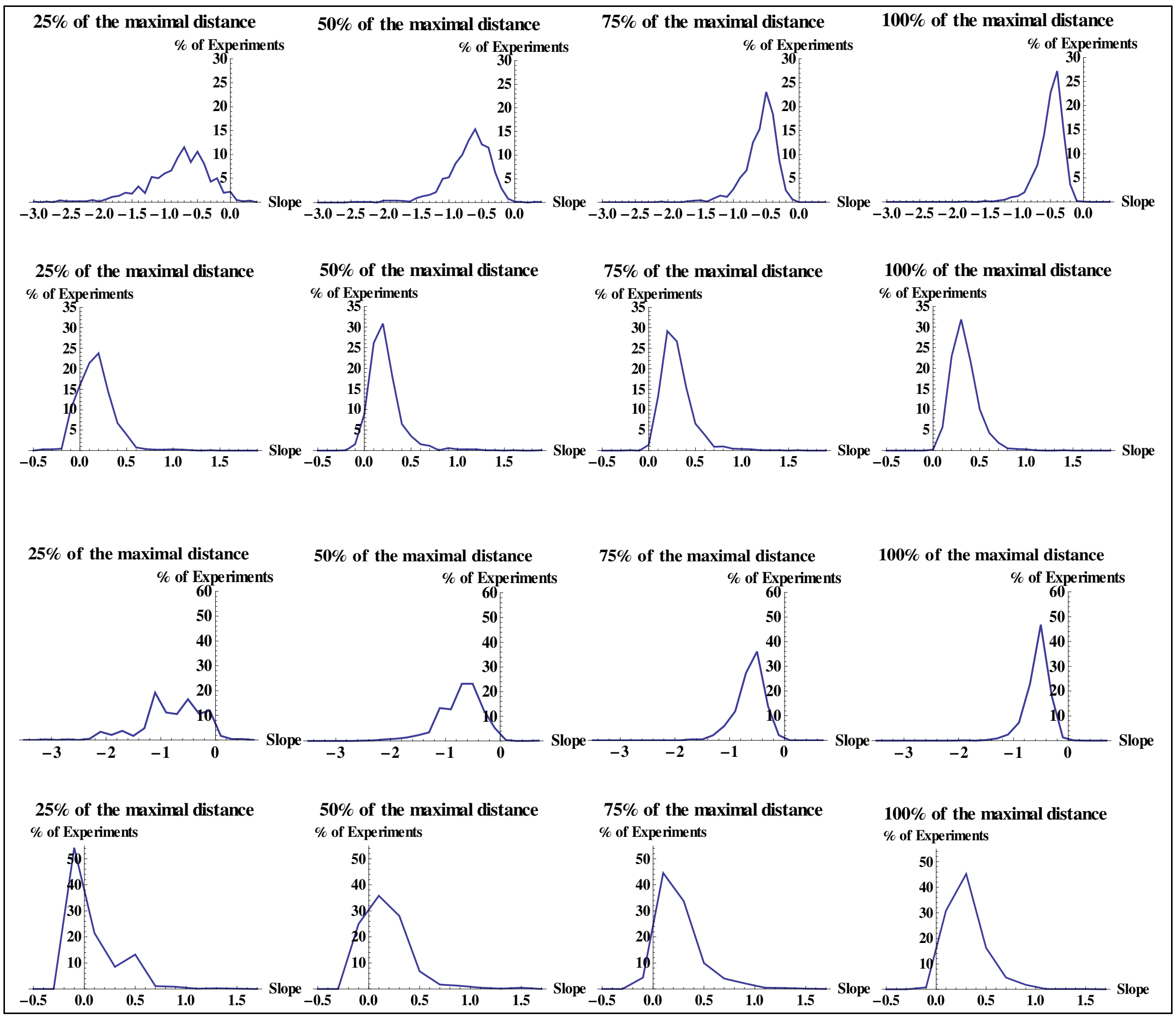


Figure 4. (**5-node networks**) Histograms for the average number/length of cycles (first/second row) and the median number/length of cycles (third/fourth row). The distance d varies from 0 up to D=25, 50, 75, 100% of the maximum distance in the first, second, third, fourth column, respectively.

D	Num. of Exp.	Av. Num.	Av. Len.	Med. Num.	Med. Len.
25%	1000	26	114	29	542
50%	1000	4	16	18	59
75%	1000	0	1	6	3
100%	1000	1	0	2	0

Table 2

We also performed 40000 experiments using 5-node networks, where we varied the PF-distance from d=0 to D = D*+the number of self loops, where D*=2, 3, 5, Maximum distance, respectively (Figure 5 and Table 3). We show the histograms for the slopes for the average number and length of limit cycles, and the median number and length of limit cycles.

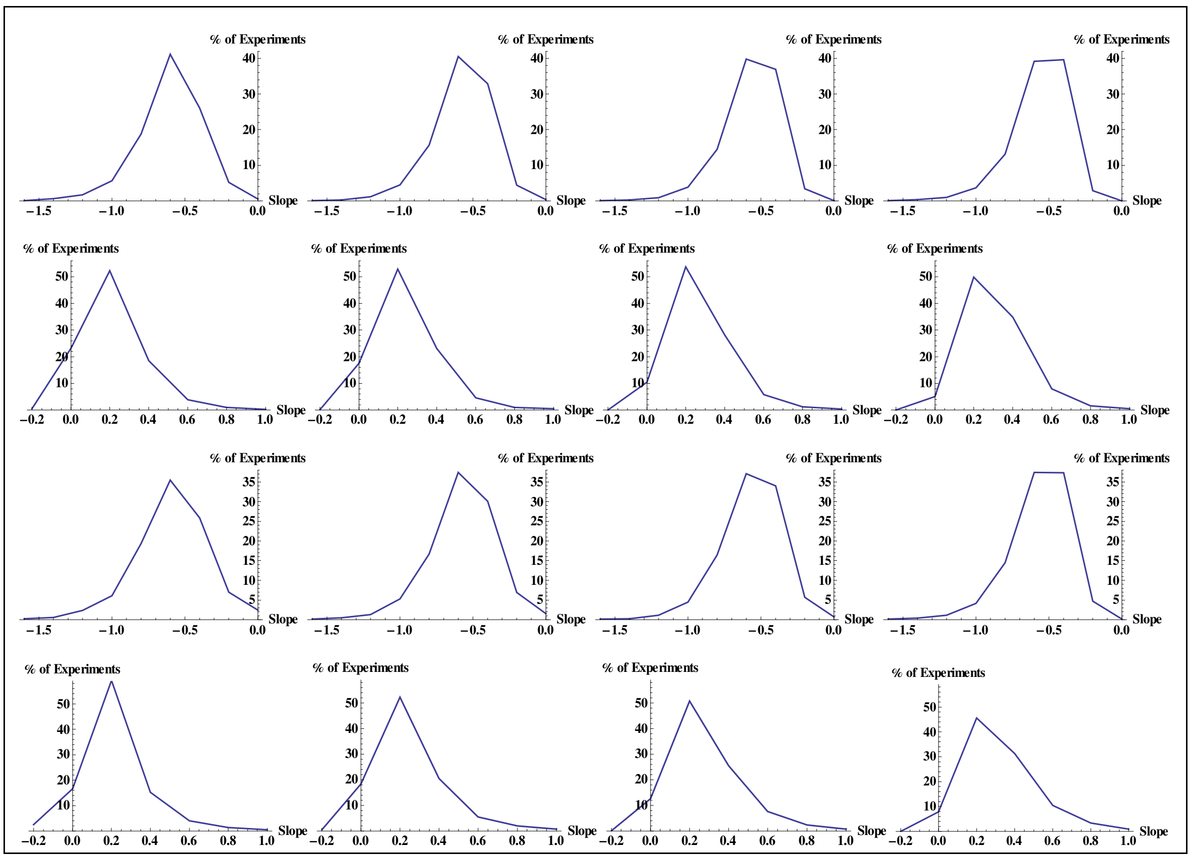


Figure 5. (**5-node networks**) Histograms for the average number/length of cycles (first/second row) and the median number/length of cycles (third/fourth row). The PF-distance varies from 0 to D*+the number of self loops, where D*=2, 3, 5, Maximum distance, respectively of the network without self loops.

D*	Num. of Exp.	Av. Num.	Av. Len.	Med. Num.	Med. Len.
2	10000	63	53	221	258
3	10000	33	19	153	44
5	10000	9	6	65	7
Max. Dis.	10000	6	5	54	7

Table 3

3. Networks of size n=7, 10

The computationally expensive part of the analysis made for 5-node networks is the computation of the maximal PF-distance of a given directed graph. Hence, we performed experiments using networks of n=7, n=10 where we considered the distance to vary from 0 to a fraction of the number of nodes. The results are shown in Table 4, 5, respectively. We show the histograms for the slopes for the average number and length of limit cycles, and the median number and length of limit cycles (Figures 6, 7).

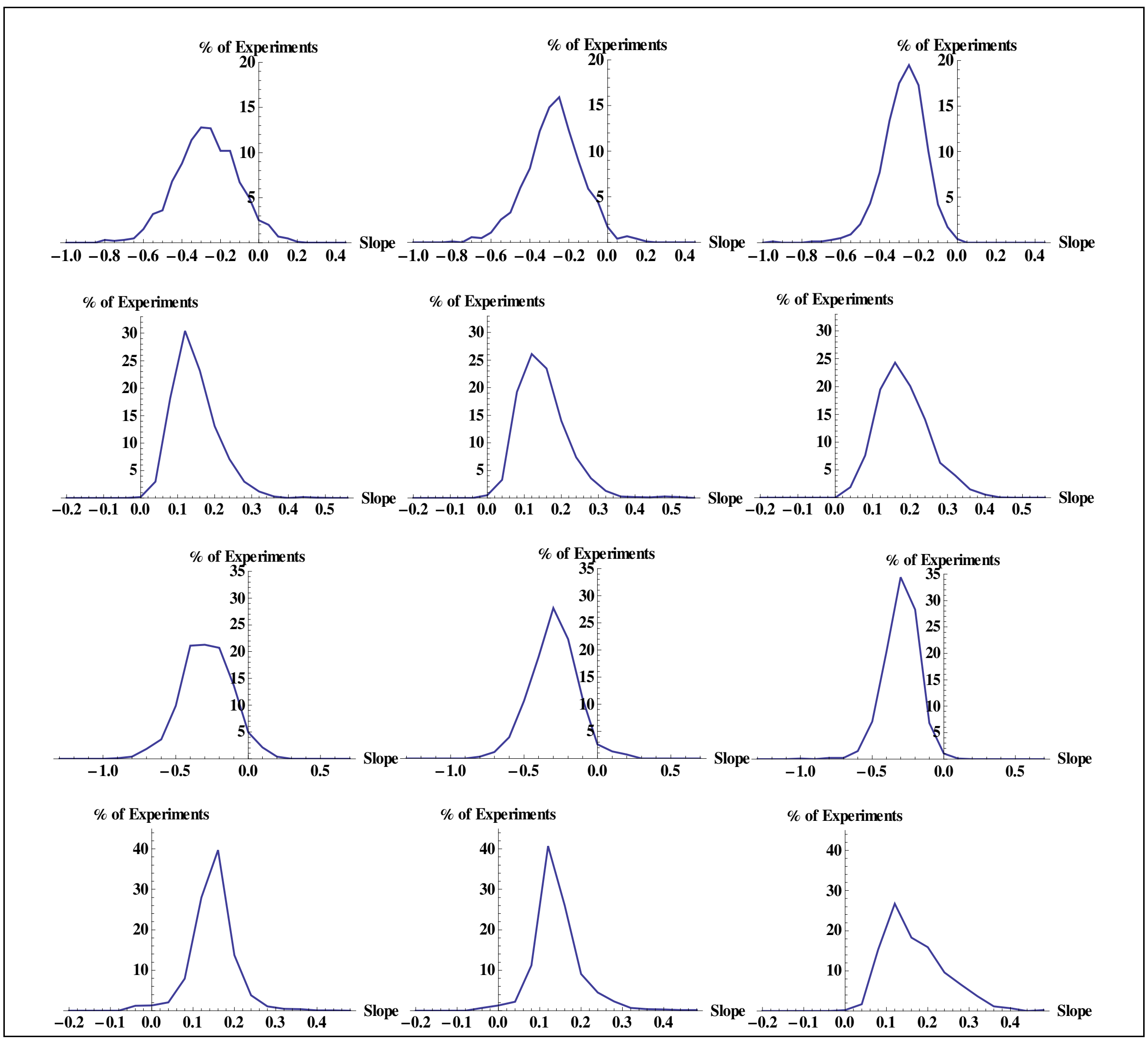


Figure 6. (**7-node networks**) Histograms for the average number/length of cycles (first/second row) and the median number/length of cycles (third/fourth row). The PF-distance varies from 0 to D*+the number of self loops where D*=3,4,7, respectively.

D*	Num. of Exp.	Av. Num.	Av. Len.	Med. Num.	Med. Len.
3	1000	58	0	72	12
4	1000	33	0	44	8
7	1000	4	0	10	0

Table 4

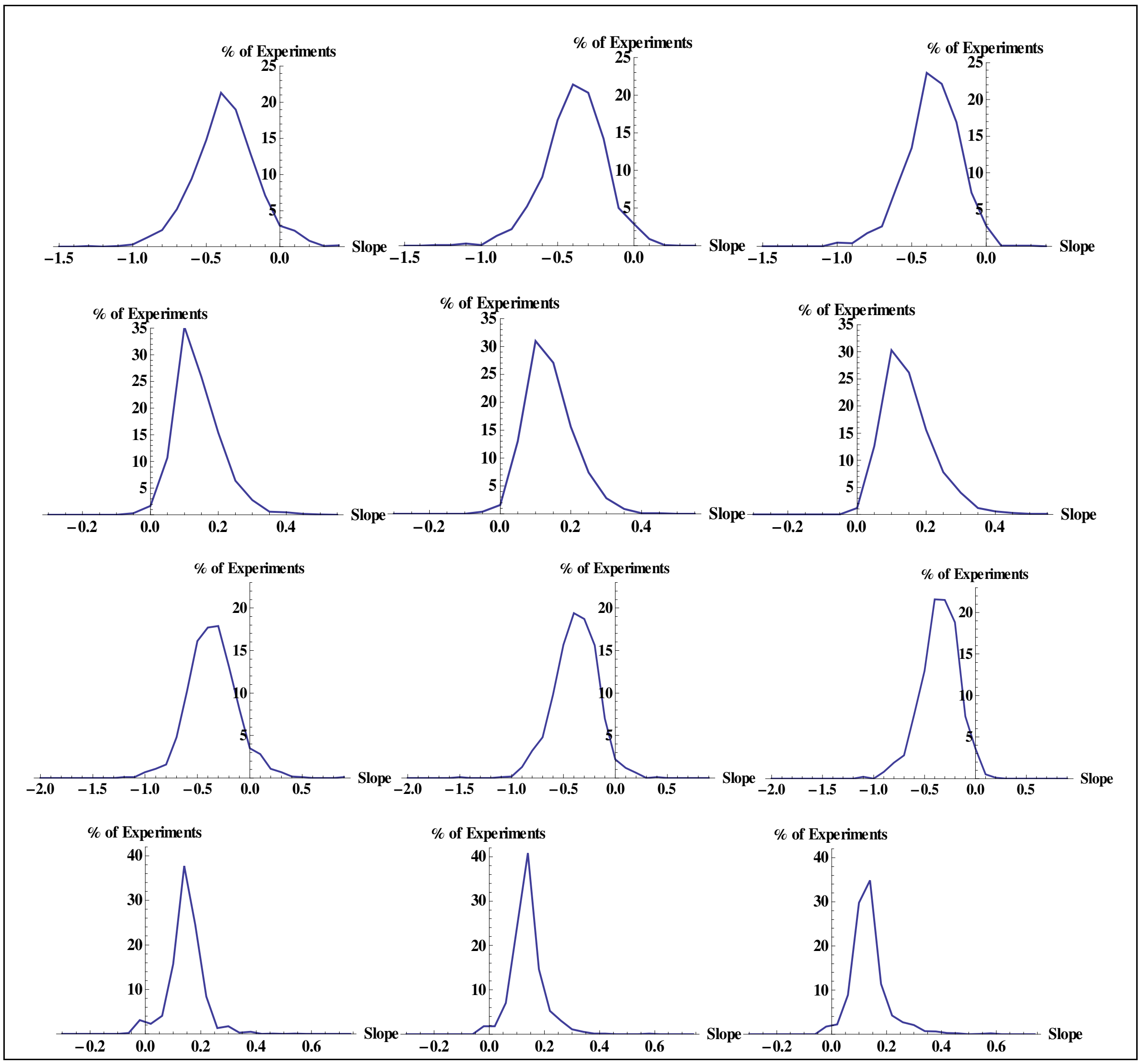


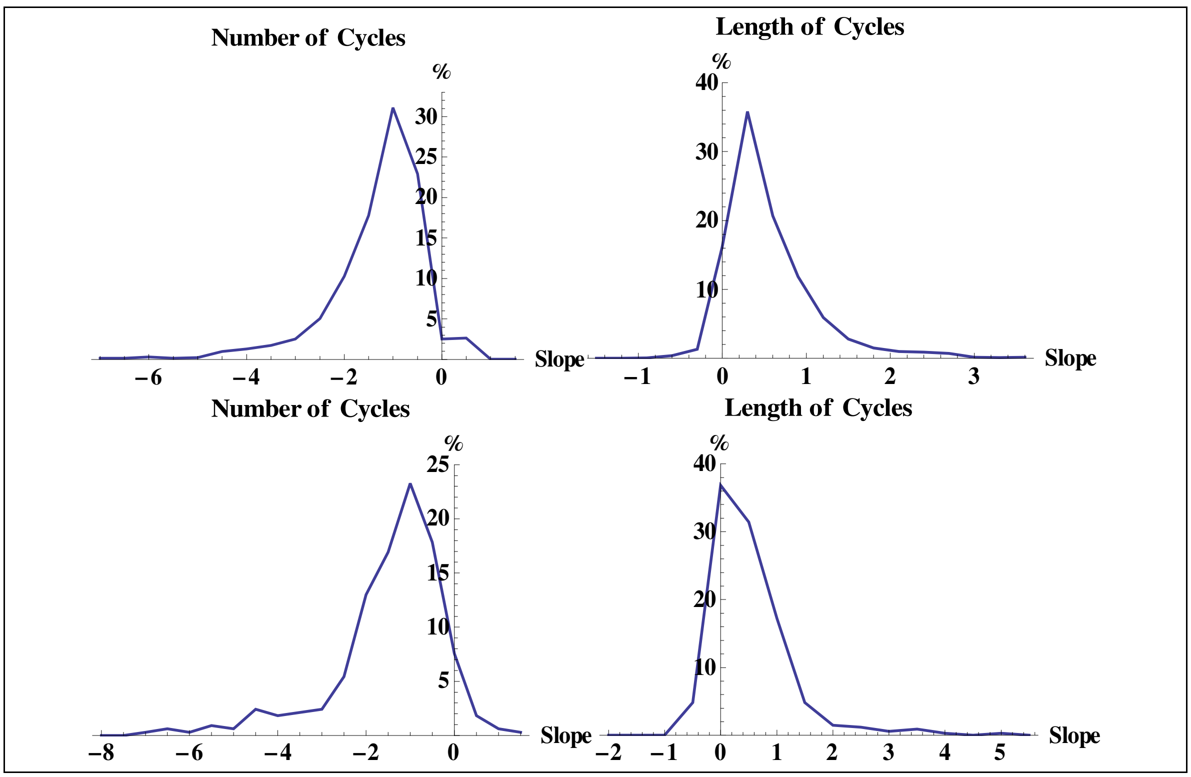
Figure 7. (**10-node networks**) Histograms for the average number/length of cycles (first/second row) and the median number/length of cycles (third/fourth row). The PF-distance varies from 0 to D*+the number of negative self loops where D*=3,4,5, respectively.

D*	Num. of Exp.	Av. Num.	Av. Len.	Med. Num.	Med. Len.
3	1000	61	3	80	17
4	1000	40	4	40	13
5	1000	31	0	39	13

Table 5

4. Networks of n=15, n=20, n=100 nodes

We performed experiments with networks of n=15, 20, 100 nodes. The results are shown in Figure 8 and Table 6. The dynamics of Boolean networks on 100 nodes were computed using 10000 random initializations.



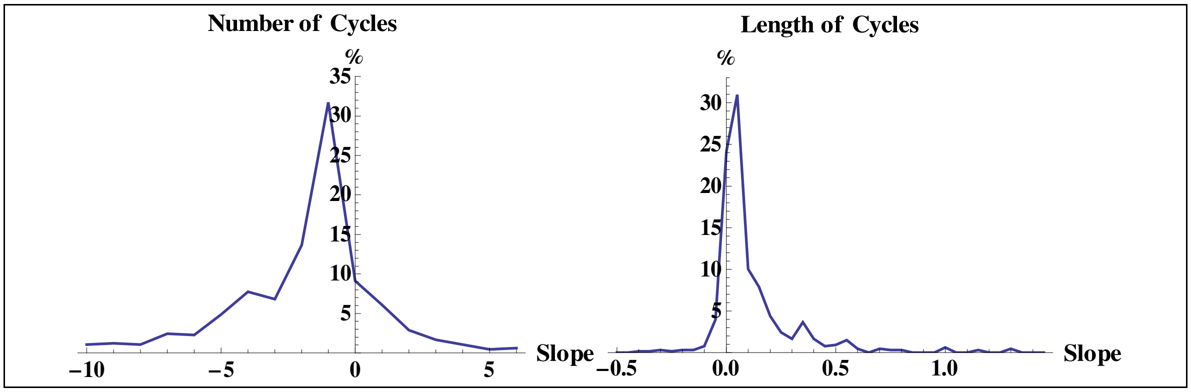


Figure 8. (**15, 20, 100-node networks**) Histograms for the average number and length of cycles for 15-node networks (first row), 20-node networks (second row) and 100-node networks (third row).

n	Num. of Exp.	Av. Num.	Av. Len.
15	2921	95.72	98.25
20	331	90.03	94.86
100	659	77.39	93.93

Table 6

5. An Algorithm for computing the maximal PF distance.

As we noted in body of the article, the distance of any graph is the sum of the distances of its strongly connected components. Furthermore, it is easy to see that each self loop with a negative sign increased the distance by 1. Therefore, without loss of generality, we assume the graph is strongly connected without self loops.

Input: The adjacency matrix $A=(a_{ij})$ of a strongly connected directed graph G on n nodes with m edges.
Output: The maximal distance D of G and a sign assignment S with exactly D negative signs and PF-distance D.

1. Let $B=\left\lfloor \sum_{i=1}^{n} \left\lfloor \sum_{j=1}^{n} (a_{ij}+a_{ji})/2 \right\rfloor /2 \right\rfloor$,
2. For D=B to 1, do
   a. For i=1 to $\binom{m}{D}$ (there are $\binom{m}{D}$ sign assignments having d negative signs)
      - Let S be the i-th sign assignment of A
      - If the PF-distance of S equal to D, then RETURN (D,S)

This algorithm is guaranteed to return the maximal distance and a sign assignment of A with D negative signs and distance D because of the following Lemmas.

Lemma A. The PF-distance of S is less than or equal to

$$\left\lfloor \sum_{i=1}^{n} \left\lfloor \sum_{j=1}^{n} \left(a_{ij} + a_{ji}\right)/2 \right\rfloor /2 \right\rfloor$$

Proof. It follows from the fact that for any given vertex we can flip the sign of the incoming outgoing edges without changing the PF distance. Then we can obtain more positive than negative edges around every vertex (the dynamics of the Boolean network associated to the directed graph does not change either).

Lemma B. If PF-distance of S is d, then there exists a sequence of vertices, v_1, v_2,…,v_t such that the sign assignment R obtained by changing the sign around those vertices has distance d with exactly d negative signs.

Proof. (By induction on d.) Recall that flipping the signs of the (in and out) edges of a given vertex in S does not change its PF-distance [24]. For d=0, the network is monotone and hence, by definition, the statement follows.

6. An Algorithm to check if a network is a PF network.

The following algorithm checks whether a network is positive feedback, which is equivalent to check if there are no negative feedback loops. Again, without loss of generality, we assume the graph is strongly connected without self loops.

Input: The adjacency matrix A=(a_{ij}) of a signed, strongly connected, directed graph G that has no self loop.

Output: TRUE if the G is a PF network and FALSE if G is not.

1. Let P and N be (0,1)-matrices such that A=P-N.
2. Let P'=P, N'=N.
3. For i=1 to n, DO

   If N' has a nonzero diagonal entry,

   RETURN FALSE

   Else, let P'=P'P+N'N and N'=N'P+P'N
4. RETURN TRUE

At each step i, P' keeps track of the number of positive paths and N' keeps track of the number of negative paths of length i. Then, the diagonal entries of N' correspond to the number of negative closed paths (any negative feedback loop will appear as a nonzero diagonal element of N').