

## ПРОЕКТИРОВАНИЕ И ДИАГНОСТИКА ВЫЧИСЛИТЕЛЬНЫХ СИСТЕМ

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### REVERSIBLE STATES OF THE FUNCTIONING OF REGULATORY CIRCUITS DISCRETE MODELS OF GENE NETWORKS<sup>1</sup>

The paper describes reversible states of the functional graphs identified by the discrete models of the gene network regulatory circuits with special functions at its vertices. The recurrent formula of the reversible states number as well as its asymptotic behavior is found.

**Keywords:** *gene network, discrete model, regulatory circuit, reversible state.*

We consider one of the methods for description and modeling of gene networks in terms of discrete models of the regulatory circuits functioning, which are an extension of random models of genetic regulatory networks [1,2]. The regulatory circuit is represented as a connected digraph  $G(V,D)$ , where  $V \in 1, n$  is the set of vertices, identified with the products of genetic elements (RNA, proteins, etc.), and  $D$  is the set of edges associated with the regulatory relations. Circulant digraphs  $G_{n,k}$ , where  $(k-1)$  is the number of incoming (and outgoing) edges,  $k \leq n$ , are considered. Variables taking integer values with the threshold  $p$  are corresponded to all vertices. Each value indicates the weight of a given vertex in a given moment of time and represents a concentration of the product, identified with the vertex. The regulatory circuit functioning is characterized by the stepwise changing of states –  $n$ -vectors in the alphabet  $\langle 0, \dots, (p-1) \rangle$ . The paper describes reversible states that means vectors with incoming edges in the functional graphs of the regulatory circuits, and reports their number estimation depending on values of the parameters  $n, k$  and  $p$ . It is not our goal to provide an overview of various approaches to the modeling of gene networks. We only note that [3] include the sections devoted to the discrete approach to modeling of biochemical networks and the extensive bibliography concerning results of analysis of the networks functioning.

#### 1. The problem of characterization of reversible states of the functional graphs

Gene networks have an important role in the living systems functioning. They are the basis for modeling the processes occurring in cells. A characteristic feature of its organization is their ability to regulate itself through the regulatory circuits with positive and negative feedbacks. These two types of circuits make it possible to maintain a certain functional state or switch to another state of a gene network including the switch under the influence of environmental factors [4].

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The regulatory circuit is determined by specifying of a circulant digraph  $G_{n,k}(V, D)$  with the vertex set  $V$  and the edge set  $D$ , where  $V = \{v_i | i \in \overline{1, n}\}$ ,  $D = \{(v_i, v_{i+j(\text{mod}n)}) | i \in \overline{1, n}, j \in \overline{1, k-1}\}$ ,  $k \in \overline{2, n}$ .

Expect  $v_0 = v_n$  by the condition of cyclicity and denote  $B_p = \{0, \dots, p-1\}$  and  $B_p^n = \{(x_1, \dots, x_n) | x_i \in B_p, i \in \overline{1, n}\}$ .

Define the functions  $f_{v_i} : B_p^{k-1} \rightarrow B_p$  in every vertex  $v_i \in V$ ,  $i \in \overline{1, n}$ . Let values of these functions are calculated for variables  $x_j$ ,  $j \in \overline{i-k+1(\text{mod}n), i-1(\text{mod}n)}$ , assigned to the vertices with edges incoming into  $v_i$ .

The gene network functioning is characterized by the changing of substance concentrations, i.e. changing of  $n$ -vectors (states) in  $B_p^n$ , corresponding to the values of  $f_{v_i}$  in  $n$  graph vertices at every moment of time [5]. Thus, dynamics of state changes for each initial state is determined by the following mapping  $A(f_{v_1}, \dots, f_{v_n}, p) : B_p^n \rightarrow B_p^n$ .

Let the same function  $f : B_p^{k-1} \rightarrow B_p$  is defined for all graph vertices. We will use the notation  $A(X) = Y$  for the vector  $X$  of variables and the vector  $Y$  of values assuming that the mapping  $A$  is defined for the function  $f$  and the threshold  $p$ .

**Definition 1.1.** The sequence of states  $X^1, \dots, X^r \in B_p^n$  is called a *cycle of the length*  $r$  of the mapping  $A : B_p^n \rightarrow B_p^n$ , if

$$\begin{cases} A(X^i) = X^{i+1}, & i \in \overline{1, r}, \\ X^{r+1} = X^1. \end{cases}$$

When  $r = 1$ , we have  $A(X^1) = X^1$  and  $X^1$  is called a *fixed point* of the mapping  $A : B_p^n \rightarrow B_p^n$ .

**Definition 1.2.** The directed graph is called a *functional graph* of the regulatory circuit if its vertices correspond to the elements of  $B_p^n$  and the edge from a state  $X \in B_p^n$  goes to a state  $Y \in B_p^n$  if and only if  $A(X) = Y$ .

**Definition 1.3.** The state  $Y \in B_p^n$  is *reversible* for the mapping  $A : B_p^n \rightarrow B_p^n$  if there exists the state  $X \in B_p^n$  for which  $A(X) = Y$ . This corresponds to the edge  $(X, Y)$  from  $X$  to  $Y$  in the functional graph.

Let  $X = (x_1, \dots, x_n) \in B_p^n$ . The *weight* of  $X$  is a value  $\|X\| = \sum_{i=1}^n x_i$ . Note that in the case  $p = 2$ ,

$$\|X \oplus Y\| = \|X\| + \|Y\| - 2 \langle X, Y \rangle$$

for all  $X, Y \in B_p^n$ , where  $\langle X, Y \rangle$  is the scalar product of vectors  $X$  and  $Y$ .

Suppose  $\delta : B_p^n \rightarrow B_p^n$  is the operator of a sequence cyclic shift. Let  $\delta_+$  is the *right shift operator*, that means  $\delta_+(X) = Y$  for states  $X, Y \in B_p^n$  if and only if  $y_{i+1(\text{mod}n)} = x_i$  for all  $i \in \overline{1, n}$ , and  $\delta_-$  is the *left shift operator*, that means  $\delta_-(X) = Y$  if and only if

$y_i = x_{i+1(\text{mod } n)}$ . Define the function  $f$  compared to the vertices of  $G_{n,k}$  for arbitrary values of the parameters  $n, k$  and  $p$  by the following way

$$f(x_{i-k+1(\text{mod } n)}, \dots, x_{i-1(\text{mod } n)}) = \begin{cases} x_i + 1, & \text{if } \sum_{j \in D_i} x_j = 0 \text{ and } x_i < p - 1, & (1.1) \\ x_i - 1, & \text{if } \sum_{j \in D_i} x_j > 0 \text{ and } x_i > 0, & (1.2) \\ x_i, & \text{otherwise,} & (1.3) \end{cases}$$

where  $D_i = \{i - j(\text{mod } n) \mid j \in \overline{1, k-1}\}$  represents the number of vertices with edges incoming into  $v_i$ . Therefore, we specified the discrete model of the gene network regulatory circuits with the functions.

## 2. Necessary and sufficient conditions for invertibility of functional graph reversible states

This section describes the reversible states of the mapping  $A: B_p^n \rightarrow B_p^n$ . At the beginning we consider the case  $p = 2$  and then the case of an arbitrary  $p$ . We establish that a state is reversible if and only if it does not contain occurrences of the certain kind subvectors. We call such subvectors by *prohibitions*.

### 2.1. Reversible states for $p=2$

**Statement 2.1.** When  $k = 2$ , all states of the functional graph of the mapping  $A: B_2^n \rightarrow B_2^n$  are reversible.

**Proof.** Let  $Y = (y_1, \dots, y_n)$  is an arbitrary state. According to the definition of the mapping  $A: B_2^n \rightarrow B_2^n$  with  $k = 2$ , we have  $A(X) = Y$  for some state  $X$  if and only

$$\text{if } y_i = \begin{cases} x_i + 1, & \text{if } x_{i-1} = 0 \text{ and } x_i = 0, \\ x_i - 1, & \text{if } x_{i-1} = 1 \text{ and } x_i = 1, \\ x_i, & \text{else.} \end{cases}$$

Since  $p = 2$ , then  $x_i + 1 = x_i - 1 = \bar{x}_i = \bar{x}_{i-1}$ . So, it is necessary that  $y_i = \bar{x}_{i-1}$ . Thus,  $A(X) = Y$  for the state  $X = (\bar{y}_2, \dots, \bar{y}_n, \bar{y}_1)$  whose coordinates are obtained by the cyclic shift and negation of  $Y$  coordinates. That means the state  $Y$  is reversible for the mapping  $A: B_2^n \rightarrow B_2^n$ .

**Theorem 2.1.** When  $k \geq 3$  the state  $Y = (y_1, \dots, y_n)$  is reversible for the mapping  $A: B_2^n \rightarrow B_2^n$  if and only if  $Y$  does not contain the prohibitions  $Y_r = (1, 0^r, 1)$  for all  $r \in \overline{1, k-2}$ .

**Proof. Necessity.** Let the state  $Y$  contains a prohibition  $Y_r$  for some  $r \in \overline{1, k-2}$ . Without loss of generality we may assume that the occurrence of this prohibition begins with the first coordinate of  $Y$ , i.e.  $Y = (Y_r, *, \dots, *)$ , where  $* \in \{0, 1\}$  and  $x_1 = x_{r+2} - 1 = 1$ . Because  $Y$  is the reversible state of the mapping  $A$ , there exists the state  $X$  such that  $A(X) = Y$ . Since  $y_1 = 1$ , then according to (1.1) – (1.3) we obtain

$$X = (*, \dots, *, 0^{k-1}). \quad (2.1)$$

Since  $y_{r+2} = 1$ , then similar

$$X = (0^{r+1}, *, \dots, *, 0^{k-r-2}). \quad (2.2)$$

From (2.1) and (2.2) we derive

$$X = (0^{r+1}, *, \dots, *, 0^{k-1}). \quad (2.3)$$

So, we have a contradiction with (2.3) because  $1^{r+2} \neq Y_r$  for  $r > 0$ ,  $A(X) = (1^{r+2}, *, \dots, *) \neq Y$ . Necessity is proved.

*Sufficiency.* Let the state  $Y$  does not contain the prohibitions  $Y_r$  for all  $r \in \overline{1, k-2}$ . Noticing that  $Y = (1, \dots, 1)$  is the state of the cycle  $(0, \dots, 0) \leftrightarrow (1, \dots, 1)$  and, therefore, a reversible state, consider the case when  $Y$  contains zero coordinates. In this case it can be represented as  $Y = (1^{s_1}, 0^{r_1}, 1^{s_2}, 0^{r_2}, \dots, 1^{s_m}, 0^{r_m})$  for some  $m \geq 1$ , where  $\sum_{i=1}^m (r_i + s_i) = n$  and  $r_i \geq k-1$ ,  $s_i \geq 1$ . Form the state

$$X = (0^{s_1-1}, 1^{r_1-k+2}, 0^{s_2+k-2}, \dots, 1^{r_{m-1}-k+2}, 0^{s_m+k-2}, 1^{r_m-k+2}, 0^{k-1}).$$

It is implied from (1.1) – (1.3) that  $A(X) = Y$  and  $Y$  is a reversible state. Sufficiency is proved.

**Corollary 2.1.** The state  $Y \in B_2^n$  is reversible for the mapping  $A: B_2^n \rightarrow B_2^n$  if and only if every block of units in  $Y$  is preceded by no less than  $(k-1)$  zeros.

## 2.2. Reversible states for $p \geq 3$

**Theorem 2.2.** The state  $Y = (y_1, \dots, y_n)$  is reversible for the mapping  $A: B_p^n \rightarrow B_p^n$  if and only if  $Y$  does not contain the prohibitions (2.4) – (2.8).

$$1. (a, 0^r, p-1), \text{ where } a \in \overline{1, p-1}, r \in \overline{1, k-2}, \quad (2.4)$$

$$2. (b, p-1), \text{ where } b \in \overline{2, p-1}, \quad (2.5)$$

$$3. (a, 0^r, 1^s, p-1), \text{ where } a \in \overline{1, p-1}, r \in \overline{1, k-2}, s \in \overline{1, n-k}, \quad (2.6)$$

$$4. (b, 1^s, p-1), \text{ where } b \in \overline{2, p-1}, s \in \overline{1, n-k}, \quad (2.7)$$

$$5. (1^{n-k+1}, p-1). \quad (2.8)$$

*Proof. Necessity.* Let the state  $Y = (y_1, \dots, y_n)$  is reversible for the mapping  $A: B_p^n \rightarrow B_p^n$ , i.e. there exist the state  $X$  for which  $A(X) = Y$ . We will carry out the proof by contradiction, considering all the prohibitions in order. It can be assumed that an occurrence of a prohibition in  $Y$  begins with the first coordinate.

1.  $Y = (a, 0^r, p-1, *, \dots, *)$ , where  $a \in \overline{1, p-1}$  and  $r \in \overline{1, k-2}$ . Here and below  $* \in \overline{0, p-1}$ . According to (1.1), (1.3) and the condition  $y_{r+2} = p-1$  we have  $X = (0^{r+1}, x_{r+2}, *, \dots, *, 0^{k-r-2})$ , where  $x_{r+2} = p-2$  or  $x_{r+2} = p-1$ . At the same time  $x_1 = 0$  and  $y_1 = a > 0$ . So, it is necessary from (1.1) that  $X = (0^{r+1}, x_{r+2}, *, \dots, *, 0^{k-1})$  and  $a = 1$ . Therefore,  $A(X) = (1^{r+1}, p-1, *, \dots, *) \neq Y$ , and we obtain the contradiction. That means  $Y$  does not contain prohibition (2.4).

2.  $Y = (b, p-1, *, \dots, *)$ , where  $b \in \overline{2, p-1}$ . Since  $y_1 = b \geq 2$  and the mapping  $A$  applied to any states does not change coordinates of this state by more than one, then  $x_1 \geq 1$ . From (1.2) we have the contradiction with the condition  $y_2 = p-1$ . So,  $Y$  does not contain prohibition (2.5).

3.  $Y = (a, 0^r, 1^s, p-1, *, \dots, *)$ , where  $a \in \overline{1, p-1}$ ,  $r \in \overline{1, k-2}$  and  $s \in \overline{1, n-k}$ . Arguing as in the first item we derive  $X = (0^{s+r+1}, x_{s+r+2}, *, \dots, *)$ , where  $x_{r+s+2} \in \overline{p-1, p-2}$  and  $s+r \leq n-k-1$ . So, we obtain the contradiction because  $A(X) \neq Y$ . Thus,  $Y$  does not contain prohibition (2.6).

4.  $Y = (b, 1^s, p-1, *, \dots, *)$ , where  $b \in \overline{2, p-1}$  and  $s \in \overline{1, n-k}$ . The condition  $y_1 = b \geq 2$  according to (1.2) implies the expressions  $x_1 \geq 1$  and  $x_2 = \dots = x_{s+1} = 2$ . Then (1.2) leads to the inequality  $y_{s+2} < p-1$ . We have the contradiction. That means  $Y$  does not contain prohibition (2.7).

5.  $Y = (1^{n-k+1}, p-1, *, \dots, *)$ . Since  $y_1 = 1$  and  $\sum_{j=n-k+2}^n y_j \geq y_{n-k+2} = p-1$ , then  $x_1 = 2$ . Similar  $x_2 = \dots = x_{n-k+1} = 2$ . We conclude the contradiction as in the item 4. Therefore,  $Y$  does not contain prohibition (2.8).

Necessity is proved.

*Sufficiency.* Let the state  $Y = (y_1, \dots, y_n)$  does not contain prohibitions (2.4) – (2.8). Show that  $A(X) = Y$  for some state  $X$ . Let  $m$  is the number of  $Y$  coordinates which are equal to  $p-1$ . We have  $m \leq \lfloor \frac{n}{k} \rfloor$ , hence, the following cases are considered below:  $m =$

0,  $m = 1$  and  $2 \leq m \leq \lfloor \frac{n}{k} \rfloor$ .

1.  $m = 0$ . The condition  $y_i \leq p-2$  implies that  $x_i \leq p-1$ . So, it is correctly to form the state  $X$  by the following way  $X = (x_1, \dots, x_n) = (y_1 + 1, \dots, y_n + 1)$ . Further  $A(X) = Y$  from (1.2) because  $x_i \geq 1$  for all  $i \in \overline{1, n}$ .

2.  $m = 1$ . Without loss of generality it can be assumed that  $i = n$ , i.e.  $y_n = p-1$ . So far as  $Y$  does not contain prohibition (2.5), we conclude that  $y_{n-1} \in \{0, 1\}$ .

When  $y_{n-1} = 0$ , prohibition (2.4) implies  $y_{n-k+1} = y_{n-k+2} = \dots = y_{n-1} = 0$ , i.e.  $X = (y_1, \dots, y_{n-k}, 0^{k-1}, p-1)$ , where  $y_1, \dots, y_{n-k} \in \overline{0, p-2}$ . Since  $y_i \leq p-2$  for all  $i \in \overline{1, n-k}$ , then it is correctly to form the state  $X = (y_1 + 1, \dots, y_{n-k} + 1, 0^{k-1}, p-1)$ . Thus,  $A(X) = Y$  from conditions (1.2) – (1.3).

Consider the case  $y_{n-1} = 1$ . Let  $l$  is the index of the rightmost but not the last coordinate of  $Y$ , which is not equal to 1. From prohibition (2.8) we have  $l \geq k-1$  and further (2.7) implies  $y_l = 0$ . So, according to (2.6)  $y_{l-k+2} = \dots = y_l = 0$  and, therefore,  $Y = (y_1, \dots, y_{l-k+1}, 0^{k-1}, 1^{n-l-1}, p-1)$ , where  $y_j \in \overline{0, p-2}$  for  $j \in \overline{1, l-k+1}$ . If  $l = k-1$ , then (1.1) – (1.3) induce  $A(X) = Y$  for state  $X = (0^{n-1}, p-1)$ . If  $l \geq k$ , we form the state  $X = (y_1 + 1, \dots, y_{l-k+1} + 1, 0^{n+k-l-2}, p-1)$  and according to (1.2) – (1.3) obtain  $A(X) = Y$ .

3.  $2 \leq m \leq \lfloor \frac{n}{k} \rfloor$ . As in the item 2 the state  $Y$  contains coordinates equal to  $(p - 1)$  if and only if the subvector  $(0^{k-1}, 1^s)$ ,  $s \in \overline{0, n-k}$ , precedes them. Form  $Y$  by follows

$$Y = (\underbrace{*, \dots, *}_{i_1}, Y_1, \underbrace{*, \dots, *}_{i_2}, Y_2, \dots, \underbrace{*, \dots, *}_{i_m}, Y_m),$$

where  $* \in \overline{0, p-2}$  and  $Y_j$  is one of the subvectors  $(0^{k-1}, 1^s, p-1)$  such that  $\sum_{j=1}^m (i_j + |Y_j|) = n$  for all  $j \in \overline{1, m}$ . Now form the state

$$X = (\underbrace{\bullet, \dots, \bullet}_{i_1}, 0^{|Y_1|-1}, p-1, \underbrace{\bullet, \dots, \bullet}_{i_2}, 0^{|Y_2|-1}, p-1, \dots, \underbrace{\bullet, \dots, \bullet}_{i_m}, 0^{|Y_m|-1}, p-1),$$

with the symbol  $\{\bullet\}$  denoting coordinates of the state  $Y$  increased by one. From (1.1) – (1.3) we obtain  $A(X) = Y$ . Sufficiency is proved.

**Corollary 2.2.** The state  $Y \in B_p^n$  is reversible for the mapping  $A: B_p^n \rightarrow B_p^n$  if and only if the subvector  $(0^{k-1}, 1^s)$ ,  $s \in \overline{1, n-k}$ , precedes all  $Y$  coordinates equal to  $(p - 1)$ .

**Theorem 2.3.** All connected components of the functional graph of the mapping  $A: B_p^n \rightarrow B_p^n$  are cycles if and only if  $p = k = 2$ .

**Proof.** Necessity follows from theorems 2.1 and 2.2, and sufficiency follows from statement 2.1.

### 3. The number of reversible states for $p = 2$

In the case  $p = 2$  the mapping  $A: B_2^n \rightarrow B_2^n$  is defined on the set  $B_2^n$  of all binary states. According to formulas (1.1) – (1.3) the mapping  $A$  applied to any state  $X \in B_2^n$  gives the state  $X' \in B_2^n$  whose coordinates are calculated by formulas

$$x'_i = \begin{cases} 1, & \text{if } \sum_{j \in D_i} x_j = 0, \\ 0, & \text{if } \sum_{j \in D_i} x_j > 0, \end{cases} \tag{3.1}$$

As before  $D_i$  is the numbers of  $(k - 1)$  vertices which have the output edges leading to the vertex with the number  $i \in \overline{1, n}$  in the graph  $G_{n,k}$ ,  $k \leq n$ .

If  $k = 2$  then by theorem 2.3 the set of reversible states coincides with the set  $B_2^n$ . Therefore, their number in this case is equal to  $2^n$ .

#### 3.1. The recurrent formula for the reversible states number in the case $k \geq 3$

Assume further  $k \geq 3$ . The state  $X = (x_1, \dots, x_n)$  is called a  $(k, n)$ -state if it does not contain the linear occurrences of subvectors  $(1, 0^r, 1)$  for all  $r \in \overline{1, k-2}$ . Denote the subset of such states in  $B_2^n$  by  $\Lambda_{k,n}$  and note that  $\Lambda_{k+1,n} \subset \Lambda_{k,n}$  for all values of  $n$  and  $k$ .

Define the function  $Q: \mathbb{N} \rightarrow \mathbb{N}$  calculating the  $(k, n)$ -states as follows. For any fixed value  $k \in \overline{3, n}$

$$Q(0) = 1, Q(1) = 2, Q(2) = 4 \text{ and } Q(n) = |\Lambda_{k,n}|.$$

**Lemma 3.1.** For all  $n \geq 3$  the function  $Q(n)$  satisfies the recurrent relation

$$Q(n) = 2Q(n-1) - Q(n-2) + Q(n-k). \quad (3.3)$$

**Proof.** The proof is by the induction on  $n$ .

*The induction base.*  $n = k = 3$ . In this case the value  $Q(3)$  is equal to the number of states of the length 3 that do not contain the linear occurrences of the subvector  $(1, 0, 1)$ . There are exactly  $2^3 - 1 = 7$  of such states. Whereas relation (3.3) gives  $Q(3) = 2Q(2) - Q(1) + Q(0) = 7$ .

*The induction step.* Suppose that  $Q(n) = 2Q(n-1) - Q(n-2) + Q(n-k)$  for any fixed value  $k \in \overline{3, n}$ . Fix  $k \in \overline{3, n+1}$  and find the value  $Q(n+1)$ . In the case  $k \in \overline{3, n}$  we have

$$\Lambda_{k,n+1} \subset \{X = (x_1, \dots, x_n, *) \mid * \in \{0, 1\}, (x_1, \dots, x_n) \in \Lambda_{k,n}\}.$$

Denote by  $Q_i(s)$ ,  $i \in \{0, 1\}$ ,  $s \in \overline{3, n+1}$ , the number of states in  $\Lambda_{k,s}$  with the last coordinate equal to  $i$ . Then

$$Q_0(s) = |\Lambda_{k,s-1}| = Q(s-1) \text{ and } Q_1(s) = Q(s) - Q(s-1). \quad (3.4)$$

Because only when  $x_{n-r} = 1$ ,  $x_{n-r+1} = \dots = x_n = 0$  and  $x_{n+1} = 1$  for any  $r \in \overline{1, k-2}$ , then  $X = (x_1, \dots, x_n, x_{n+1}) \notin \Lambda_{k,n+1}$  for the subvector  $(x_1, \dots, x_n) \in \Lambda_{k,n}$ , therefore,

$$Q(n+1) = |\Lambda_{k,n+1}| = 2|\Lambda_{k,n}| - Q_1(n-1) - \dots - Q_1(n-k+2). \quad (3.5)$$

From (3.4) and (3.5) we obtain

$$Q(n+1) = 2Q(n) - Q(n-1) + Q(n+1-k). \quad (3.6)$$

Now let  $k = n+1$ . So far as  $\Lambda_{n+1,n+1} \subset \Lambda_{n,n+1}$ , then deleting the state  $(1, 0^{n-1}, 1)$  from the set  $\Lambda_{n,n+1}$  and taking into account (3.6) we conclude

$$|\Lambda_{n+1,n+1}| = |\Lambda_{n,n+1}| - 1 = 2Q(n) - Q(n-1) + Q(1) - Q(0) = 2Q(n) - Q(n-1) + Q(0).$$

**Lemma 3.2.** The number of  $(k, n)$ -states with the first and last coordinates equal to 1 is given by the value  $F(n) = Q(n-k)$ .

**Proof.** The number of  $(k, n)$ -states of the type  $(0, *, \dots, *, 0)$ , where  $* \in \{0, 1\}$ , is equal to  $Q(n-2)$ . The number of  $(k, n)$ -states of the type  $(0, *, \dots, *, 1)$  is equal to the number of  $(k, n)$ -states of the type  $(1, *, \dots, *, 0)$  and is given by the expression  $Q(n-1) - Q(n-2)$ . Therefore, the number of  $(k, n)$ -states of the type  $(1, *, \dots, *, 1)$  is equal to

$$F(n) = Q(n) - Q(n-2) - 2(Q(n-1) - Q(n-2)) = Q(n) - 2Q(n-1) + Q(n-2). \quad (3.7)$$

According to lemma 3.1  $Q(n) = 2Q(n-1) - Q(n-2) + Q(n-k)$ . Thus, from (3.7) we obtain  $F(n) = Q(n-k)$ .

Lemmas 3.1 and 3.2 provide the number  $F(n)$  to satisfy the recurrent relation

$$F(n) = 2F(n-1) - F(n-2) + F(n-k). \quad (3.8)$$

Denote the number of reversible states of the mapping  $A: B_p^n \rightarrow B_p^n$  by  $H(n, k, p)$ .

**Lemma 3.3.** The number  $H(n, k, 2)$  of reversible states of the mapping  $A: B_2^n \rightarrow B_2^n$  is equal to  $H(n, k, 2) = k \cdot F(n+1) - (k-2) \cdot F(n)$ , where  $F(n)$  satisfies the recurrent relation (3.8).

**Proof.** By theorem 2.1 the value  $H(n, k, 2)$  is equal to the number of  $n$ -states which do not contain subvectors  $(1, 0^r, 1)$  for all  $r \in \overline{1, k-2}$ . Meanwhile lemma 3.1 gives the recurrent relation for the number  $Q(n)$  of  $(k, n)$ -vectors which do not contain the linear occurrences of the subvectors  $(1, 0^r, 1)$  for any  $r \in \overline{1, k-2}$ . Therefore, in order to find  $H(n, k, 2)$ , all states of the type  $(0^s, 1, *, \dots, *, 1, 0^{r-s})$ , where  $* \in \{0, 1\}$ ,  $s \in \overline{0, r}$ ,  $r \in \overline{1, k-2}$ , should be deleted from the set  $\Lambda_{k,n}$ . By lemma 3.2 the number of such states for any  $r \in \overline{1, k-2}$  is equal to  $(r+1) \cdot F(n-r)$ , where the coefficient  $(r+1)$  appears due to the parameter  $s \in \overline{0, r}$ . Hence, we obtain the following sequence of equalities

$$\begin{aligned}
 H(n, k, 2) &= Q(n) - \sum_{r=1}^{k-2} (r+1) \cdot F(n-r) = \\
 &= Q(n) - \sum_{r=1}^{k-2} (r+1) \cdot (Q(n-r) - 2Q(n-r-1) + Q(n-r+2)) = \\
 &= Q(n) - \sum_{r=1}^{k-2} (r+1) \cdot Q(n-r) + \sum_{r=1}^{k-2} 2 \cdot (r+1) \cdot Q(n-r-1) - \sum_{r=1}^{k-2} (r+1) \cdot Q(n-r-2) = \\
 &= Q(n) - \sum_{r=1}^{k-2} (r+1) \cdot Q(n-r) + \sum_{r=2}^{k-1} 2r \cdot Q(n-r) - \sum_{r=3}^k (r-1) \cdot Q(n-r) = \\
 &= Q(n) - 2Q(n-1) - 3Q(n-2) - \sum_{r=3}^{k-2} (r+1) \cdot Q(n-r) + 4Q(n-2) + 2 \cdot (k-1) \cdot Q(n-k+1) + \\
 &\quad + \sum_{r=3}^{k-2} 2r \cdot Q(n-r) - (k-2) \cdot Q(n-k+1) - (k-1) \cdot Q(n-k) - \sum_{r=3}^{k-2} (r-1) \cdot Q(n-r) = \\
 &= Q(n) - 2Q(n-1) + Q(n-2) + k \cdot Q(n-k+1) - (k-1) \cdot Q(n-k).
 \end{aligned}$$

Since by lemma 3.1  $Q(n) = 2Q(n-1) - Q(n-2) + Q(n-k)$ , we conclude  $H(n, k, 2) = k \cdot F(n+1) - (k-2) \cdot F(n)$ .

### 3.2. The reversible states number asymptotic for $k \geq 3$

**Theorem 3.1** The asymptotic behavior of the function  $H(n, k, 2)$  for the fixed parameter  $k \geq 3$  is given by the relation  $H(n, k, 2) \sim c_k R^n$ , where  $c_k$  are the constants depending only on  $k$  and  $1 < R < 2$  is the largest by module real root of the characteristic equation

$$\lambda^k - 2\lambda^{k-1} + \lambda^{k-2} - 1 = 0 \quad (3.9)$$

of recurrent relation (3.8).

**Proof.** Since (3.8) is the linear recurrent relation of  $k$  order with constant coefficients, its solution is sought in the form  $f_n = c\lambda^n$  with constants  $c$  and  $\lambda$ . This leads to the characteristic equation  $\lambda^k - 2\lambda^{k-1} + \lambda^{k-2} - 1 = 0$ ,  $k$  roots of which give solutions of the form  $\lambda_i^n$  for  $i \in \overline{1, k}$ . Show that these roots are different. Denote  $g(\lambda) = \lambda^k - 2\lambda^{k-1} + \lambda^{k-2} - 1$ . Then

$$g'(\lambda) = k\lambda^{k-1} - 2(k-1)\lambda^{k-2} + (k-2)\lambda^{k-3}.$$

So far as  $g'(\lambda) = 0$  if and only if  $\lambda = 0$ ,  $\lambda = 1$  or  $\lambda = \frac{k-2}{k}$  and these values are not the roots of  $g(\lambda)$ , therefore, all roots of equation (3.9) are different. Thus,  $k$  roots of equation (3.9) form the basis of the solution space of recurrent relation (3.8) whose general solution can be written as  $F(n) = \sum_{i=1}^k c_i \lambda_i^n$ . Analyze the asymptotic behavior of the sequence  $F(1), F(2), \dots$ . It is sufficient to consider the term  $c_i \lambda_i^n$  with the largest absolute value of the root and the coefficient  $c_i \neq 0$ . Denote this root by  $R$ . Then the asymptotic behavior of the function  $F(n)$  is given by the relation  $F(n) \sim cR^n$ , where  $c$  is constant. In view of lemma 3.3 this implies  $H(n, k, 2) \sim c_k R^n$ , where  $c_k$  is a constant depending only on  $k$ .

It is remain to show that  $1 < R < 2$  is the real root of (3.9). Let  $\lambda = R_\lambda (\cos \phi + i \sin \phi)$  is an arbitrary root of equation (3.9). Then  $\lambda^{k-2}(\lambda - 1)^2 = 1$  and  $|\lambda - 1|^2 = \frac{1}{|\lambda^{k-2}|} = \frac{1}{R_\lambda^{k-2}}$ . On the other hand

$$|\lambda - 1|^2 = R_\lambda^2 - 2R_\lambda \cos \phi + 1 \text{ and } (R_\lambda - 1)^2 \leq |\lambda - 1|^2 \leq (R_\lambda + 1)^2.$$

So, we obtain

$$(R_\lambda - 1)^2 \leq \frac{1}{R_\lambda^{k-2}} \leq (R_\lambda + 1)^2. \tag{3.10}$$

Since  $g(1) < 0$  and  $g(2) > 0$  for  $k \geq 3$ , there exist the real root of equation (3.9) which is greater than 1 by the function  $g(\lambda)$  continuity on the real axis. Meanwhile (3.10) implies that there are not roots less than  $-1$ . Thus,  $R > 1$ . Then  $\lambda$  reaches the maximum absolute value  $R = R_\lambda$  at the minimum value of  $\frac{1}{R_\lambda^{k-2}}$  which is equal to  $(R_\lambda - 1)^2$ , i.e. when  $\cos \phi = 1$  and  $\sin \phi = 0$ . Hence,  $R$  is the real root of equation (3.9). The estimation  $R < 2$  is obvious because the total number of  $n$ -states for  $p = 2$  is  $2^n$ .

### Conclusion

Investigation of the regulatory circuits functioning represented in this paper provides an opportunity to understand the regulatory mechanisms of the processes under the control of gene networks and possibility for a directional impact on them.

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