

# Equivalent Model of p53 pathway using Boolean Network

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**Abstract**— A Boolean network model is designed to represent the p53 gene regulation and simulate the model response. Digital logic gates are used to realized the model of p53 pathway in CIRCUIT LOGIX environment. The model responses truly reflect the core regulation of p53 gene.

**Index Terms**— Boolean Network, Gene Regulation, Gene Expression, Logic Expression, Logic Diagram, p53 pathway.

## 1 INTRODUCTION

This paper gives us a general framework of Boolean network of Gene Expression.[3]. Gene is a region of DNA which is made up of nucleotides and is the physical and functional unit of heredity. Each gene has a particular set of instructions, usually coding for a particular protein or function. Gene Expression is the process by which a gene's DNA sequence is converted into functional Gene product. To control Gene Expression Level genetic regulation is required which is the process of interaction between DNA-protein and Protein-Protein in an organism [4]. The modeling of different process of gene expression and genetic regulatory system are investigated to differentiate between normal and abnormal (diseased) gene and invention of proper medicine to cure the disease [3].

Genes can be viewed as the nodes in the gene regulatory network, proteins as input and gene expression is as output. For any particular job when the gene is expressed, the gene expression is in 'ON' state and when it is not expressed, it is in 'OFF' state. So, it has two states similar to the Boolean Network which has also two states.

In this paper we proposed an equivalent Boolean model for a particular pathway of oncogene p53. It has significant role used to suppress tumor (cancer) cell and known as "guardian of the genome".

This paper is divided into different sections. A brief description of the biological process is illustrated in the Introduction. Section 2 describes Boolean representation of P53 pathway, a brief description of p53 and the realization of the Boolean network Model. Section 3 describes derivation of logic expression and its implementation.

In Section IV a conclusion is drawn based on the result of the simulation.

## 2 BOOLEAN REPRESENTATION OF P53 PATHWAY

### 2.1 Description of p53

p53 is a tumor protein that suppress the tumor cell of human body and it is located in the seventeenth chromosome. The p53 protein is a phosphoprotein made of by 393 amino acids and plays an important role in the cell cycle control. Defective p53 could allow abnormal cells to proliferate, resulting in cancer. Among the stress signals Gamma or UV irradiation, alkylation of bases, depurination of DNA or reaction with oxidative free radicals all alter the DNA in different ways and for each damaging agent a different detection and repair mechanism is employed by the cell [2].

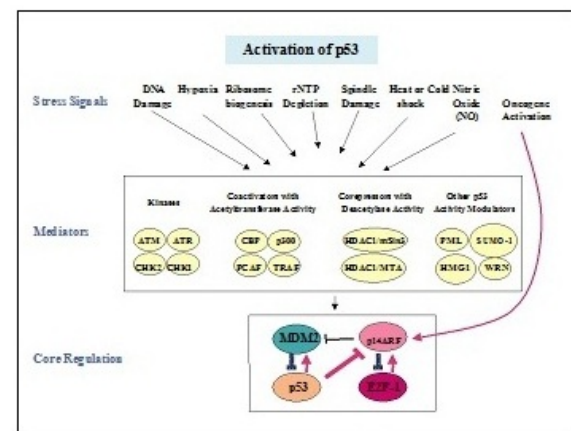


Fig.1: Activation of p53

In each case, the enzyme informs the p53 protein that the DNA is damaged. So modification of p53 protein depends on different enzymes being activated by different type of damaged DNA.

In normal cells, the p53 protein level is low. DNA damage and other stress signals may trigger the increase of p53 protein, which

have three major functions-Growth arrest, DNA repair and apoptosis (cell death)[2].

The growth arrest stop the profession of cell cycle, preventing replication of damaged DNA. During the growth arrest , p53 may activate the transcription of proteins involved in DNA repair. Apoptosis is the “last resort” to avoid proliferation of cells containing abnormal DNA.The cellular concentration of p53 must be tightly regulated because high level of p53 may accerelate the ag-ing processs of apoptosis.

So, regulation of p53 is very important which is done by Mdm2, an oncoprotein plays a central role in this regulatory process. The transcription of the Mdm2 oncogene is induced by the p53 protein after DNA damage, and the Mdm2 protein then binds to p53 and blocks its activities as a tumour suppressor and promotes its degradation.

Here, we can see that p53 activates Mdm2, but Mdm2 inhibits p53 but again p53 inhibits p14ARF which also inhibits Mdm2. p14ARF inhibits E3F which in turn activate p14ARF

## 2.2 BOOLEAN NETWORK

One of the main objectives of Boolean network modeling is to study genetic properties of large genetic networks and the logical interactions of genes without knowing specific details[1].

Genetic Regulatory network lies in the fact that , the cell exhibits a switch like behavior.,which is important for cells to move from one state to another state in a normal cell growth process or in situation when cells need to respond to external signals.

Boolean network is logic based. It consists of a set  $V=\{v_1,v_2,...v_n\}$ of nodes representing genes and a list  $F=\{f_1,f_2,...f_n\}$  of Boolean function  $f_i$  with inputs from specified nodes[5]. A gene can be described as expressed, i.e. ‘ON’ state (1) or not expressed, i.e. ‘OFF’ state (0) at any point of time.Let  $x$  be an n-dimensional binary vector representing the state of a system of n genes, thus the state space of the system consists of  $2^n$  possible states.

## 3 MODELING OF p53 PATHWAY USING BOOLEAN NETWORK

### 3.1 DERIVATION OF LOGIC EXPRESSION FROM P53 PATHWAY

The core regulation of the p53 pathway can be realized using Boolean network

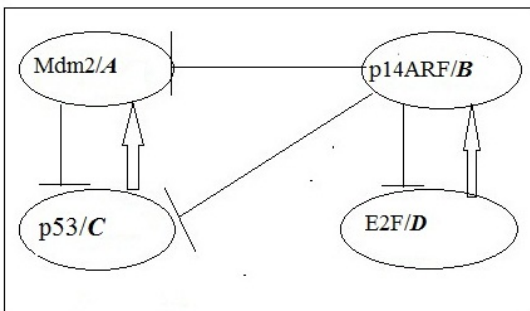


Fig-2: Core Regulation of p53

Here, p53 is regulated by MDM2, p14ARF and E2F.

These four can be represented by four variables as A (MDM2), B(p14ARF), C(p53) and D(E2F). A,B,C & D are interdependent with each other and their interrelation can be expressed as follows: The logic expression for the above diagram is

$$A_{next} = \text{NOT } B \text{ AND } C$$

$$B_{next} = D \text{ AND NOT } C$$

$$C_{next} = \text{NOT } A$$

$$D_{next} = \text{NOT } B.$$

The following is the truth table

A	B	C	D	A <sub>next</sub>	B <sub>next</sub>	C <sub>next</sub>	D <sub>next</sub>
0	0	0	0	0	0	1	1
0	0	0	1	0	1	1	1
0	0	1	0	1	0	1	1
0	0	1	1	1	1	1	1
0	1	0	0	0	0	0	0
0	1	0	1	0	1	0	0
0	1	1	0	1	0	0	0
0	1	1	1	1	1	0	0
1	0	0	0	0	0	1	0
1	0	0	1	0	1	1	0
1	0	1	0	1	0	1	0
1	0	1	1	1	1	1	0
1	1	0	0	0	0	0	0
1	1	0	1	0	1	0	0
1	1	1	0	1	0	0	0
1	1	1	1	1	1	0	0

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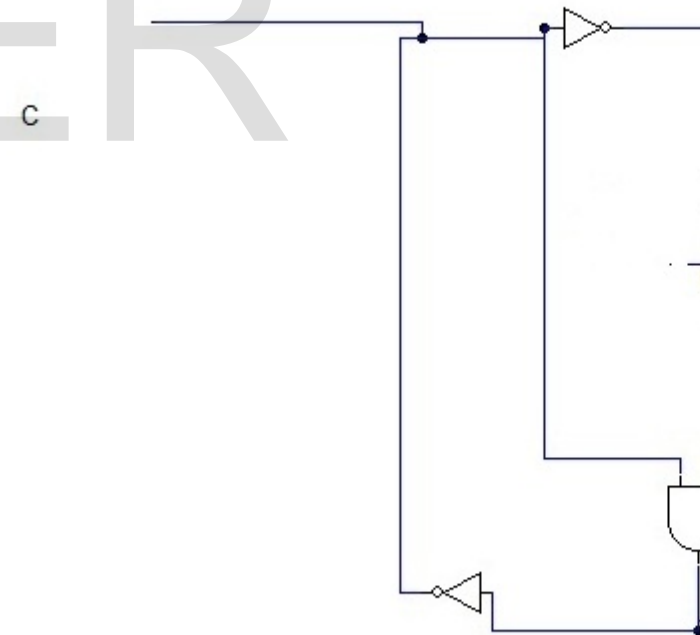


Fig.-3: Logic Diagram

### 3.2 Result & Discussion

From the expression, the logic diagram is drawn and simulated using the software CIRCUIT LOGIX. The simulated outputs are as follows:

Figure -4 gives the output of A.  
 As  $A = \text{NOT } B \text{ AND } C$ , so when B is 0 and C is 1,  $A=1$   
 So, LED connected to A is glowing.

Figure-5 gives the output of B.  
 As  $B = D \text{ AND NOT } C$ , So, When C is 0 and D is 1,  $B=1$   
 So, LED connected to B is glowing.

Figure-6 gives the output of C.  
 As  $C = \text{NOT } A$ , So, When  $A=0, C=1$   
 So, LED connected to C is glowing.

Figure-7 gives the output of D.  
 As  $D = \text{NOT } B$ , So when  $B=1, D=0$ .  
 So, LED connected to D is off.

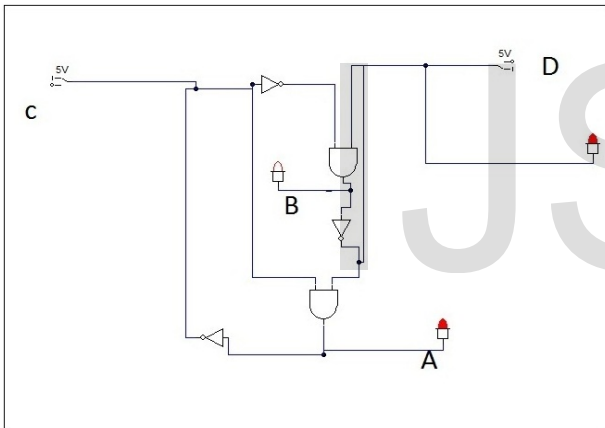


Figure 4: For the output  $A = \text{NOT } B \text{ AND } C$

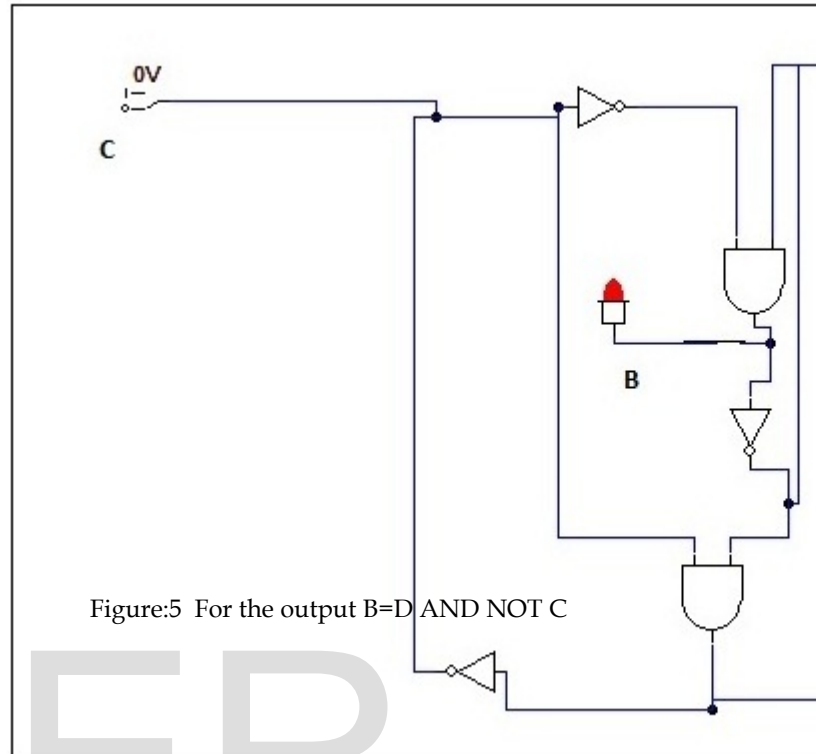


Figure:5 For the output  $B = D \text{ AND NOT } C$

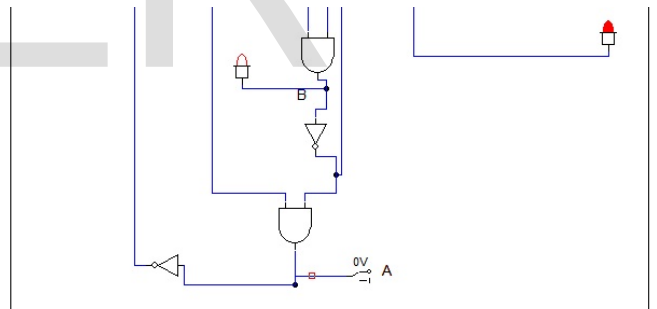


Figure 6: For the output  $C = \text{NOT } A$

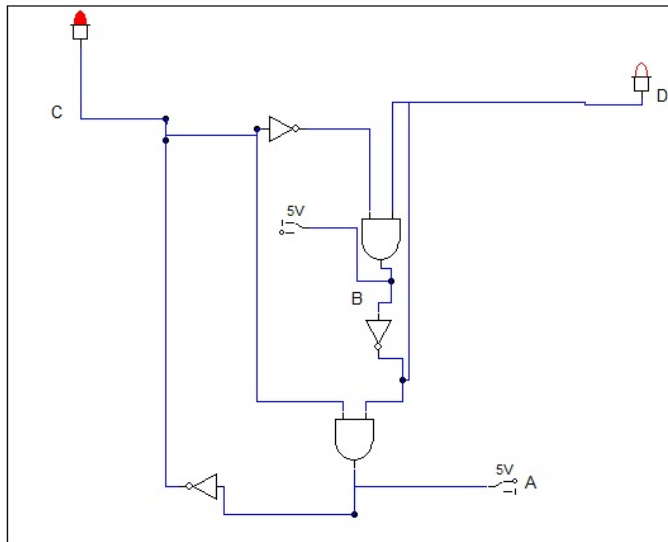


Figure 7: For the output  $D = \text{NOT } B$

## CONCLUSION

Equivalent Boolean network model is realized to represent the p53 gene regulation. The model is designed by digital logic gates in CIRCUIT LOGIX platform and simulates the response. The responses of the digital circuits reflect the behavior of p53 gene. Here the behavior of p53 gene is studied without wet smelly laboratory. This work may further be extended for other genes.

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