Study of Gene Regulatory Network Using Polynomial, Rational Polynomial and Circular function

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Abstract

Genome contains vital genetic information. It becomes necessary to uncover vast genetic information that is hidden in genetic code. Different types of mathematical models have been evolved over the years but still a lot needs to be done. The regulatory function of genes can be modeled mathematically by using various types of polynomials and also by changing its degree, one can conclude whether increase of the degree of polynomial has any impact on predicate value. In this paper, solution of differential equation for analysis of regulatory gene network using different functions has been studied. In section 2 and 3 related research work and mathematical formulation are discussed. In section 4and 5, model is solved using polynomial, circular function and rational polynomial. The degree of the polynomial also changes the influence of one gene on another gene in gene regulatory network which is non-linear in nature the present study. The study shows that gene regulatory network can be expressed as polynomial and rational polynomials of degree two, three and four. The mathematical models are tested on four different organism i.e Yest, E.coli, drosophila and mycobacterium. The results shows that further increasing the degree does not improve the accuracy of prediction but by enlarge remains same in most of the cases. In case of rational polynomial when degree is changed from 2 to 3 accuracy deteriorates.

Keywords: *regulatory function, gene network, gene expression*

1. Introduction

Genome contains vital genetic information. It becomes necessary to uncover vast genetic information that is hidden in genetic code. Different types of mathematical models have been evolved over the years but still lot needs to be done. The regulatory function of genes can be modeled mathematically by using various types of polynomials and also by changing the degree one can conclude whether increase of the degree of polynomial has any impact on predicate value.

Gene Expression refers to the processes involved in converting genetic information from a DNA sequence into an amino acid sequence, or protein. Each gene encodes a protein and proteins are the functional units of life. Genes are present in every cell, but only a fraction of the genes are expressed at any time. Many diseases result from the interaction between genes.

Researchers are trying to analyze gene expression data for finding relationship that exists between the genes using computational algorithms and which may be further corroborated with biological evidences [19]. In this paper we have tried to find out the regulatory effect of one gene on another. Gene regulatory networks help in understanding the interaction between the genes and their functions. The cell function and development are regulated by complex networks of genes, proteins and other components by means of their mutual interactions. These networks are called gene regulatory networks [20].

2. Related Work

Gene regulatory network is intrinsically dynamic in nature and can be modeled by Boolean Network or differential equations. Stuart Kauffman et. al., [1] was amongst the first biologists to use Boolean networks to model genetic regulatory networks. Akutsu et. al., [2] gave an algorithmic analysis of the problem of identifying Boolean networks from data obtained by multiple gene disruption and gene over-expressions in regard to the number of experiments and the complexity of experiments. Ting Chen et. al., [3] has developed a linear transcription model for the gene expression and can be represented as a non-linear dynamic system. J. Geber et. al., [5] has given a piece wise linear differential equation model to describe the regulation process within the cell. The m-RNA concentration model has been considered for modeling. F.B. Vilmaz et. al., [4] has given a differential equation model to represent the behavior of gene expression pattern and solved it by discrete approximation. Gene regulatory network from gene expression data with a state space description of the gene expression model was given by F.X. Wu et. al., [6]. He considered that in a cell genes can be treated as variables and its expression values depends upon internal state variables and external inputs. De Hoon et. al., [9] presented a differential equation model which is continuous in nature and solved the differential equation by using difference equation. Sakamoto and Iba [11] solved the differential equation as a sum of functions of genes and evaluated this function using genetic programming and estimated the parameter by least square method. Jing LIU et. al., [12] has given a model based on differential equation, to study gene regulatory network using Genetic Programming. This method is able to adjust to continuously external changes Fang-Xiang Wu et. al., [13] has given a method for inferring sparse and stable gene regulatory networks from time course gene expression data. The results from computational experiments have shown that the proposed method can correctly find majority of connections in both small-size and large-size networks by using noise and short gene expression profiles. A. Darvish et. al., [14] has proposed a hierarchical model utilizing nonlinear factor analysis methods to analyze time-series DNA microarray data and identify the dynamic regulatory pathways, Yoshihiro Mori et. al., [15] has proposed a synthesis method of gene regulatory networks based on gene expression by network learning. Fang-Xiang Wu [16] et. al., has propose a method to estimate the parameters in the rational models of molecular biological systems they have shown that the proposed method performs better than the general nonlinear optimization methods in terms of the running time, robustness. Haixin Wang et. al., [17] has studied the steady-state behaviors of the nonlinear GRN models. The authors have studied Solution of Differential Equation for Testing the Periodicity of Regulatory Gene Network using Transcendental Function [18].

3. Mathematical Formulation

Many researchers have developed gene expression model using differential equation. Ting Chen et. al. [3] has given a linear transcription model for the gene expression in which transcription and translation processes were modeled. The gene expression has been represented as a non-linear dynamic system and is expressed in matrix form as

$$\frac{dE}{dt} = ME \quad \text{.....(i)}$$

where E is the matrix of m-RNA and protein concentrations

and M is the transition matrix representing regulatory interactions for both protein and genes.

Sakamoto and Iba [13] further modified it as

$$\left(\frac{dE}{dt}\right)_j = f_j\left(E_0, E_1, E_2, ...E_j\right) \text{ (j = 1, 2, ..., n)}.....\text{(ii)}$$

where n being the number of genes and fj being a function of $E_0, E_1, E_2, ...E_n$

F.B.Vilmaz [4] et. al. represented the behavior of the gene expression patterns by a system of ordinary differential equation

$$\frac{dE}{dt} = M(E)E \text{ .....(iii)}$$

They considered

$$\frac{dE}{dt} = \text{F (E)}.....\text{(iv)}$$

where $F = (F_1, F_2, F_3....F_n)^T$ consists of the sum of the quadratic (constant, linear) functions

$$F_j(E) = f_{j,i}(E_1) + f_{j,i}(E_2) + f_{j,i}(E_3)..... + f_{j,i}(E_n) \text{ .....(v)}$$

In this paper model of F. B. Vilmaz [4] is assumed to be the base model and the regulatory pattern is modeled using polynomial, rational polynomial and circular function.

4. Regulatory Function Approach

The model of differential equation can be solved as a initial value problem [4].If the initial states $E(t_0)$ then prediction is done for next state and so on , i.e. iterative state E(t_k) ; k =1,2,3 …….. can be obtained and compare $E_0, E_1, E_2, ...E_{l-1}$ with approximated data

$$\frac{dE}{dt} = M(E)E$$

$$\left(\frac{d\bar{E}_k}{dt}\right)_j = \left(f_{j,1}(\bar{E}_k)_1\right) + \left(f_{j,2}(\bar{E}_k)_2\right) + \left(f_{j,3}(\bar{E}_k)_3\right) + ... + \left(f_{j,n}(\bar{E}_k)_n\right) + (AM_k)_j \text{ .....(vi)}$$

$(\bar{E}_k)_j$ denotes the concentration of gene j at the current state, functions $f_{j,i}(x)$ are the influence functions defined as a polynomial, rational polynomial and circular function. Some approximations have been inferred for the underlying regulatory network for representing the interactions between genes by polynomial, rational polynomial and circular function for genes $j \in \{1,2,3,.....n\}$ and samples $k \in \{0,1,2,3,.....l-1\}$, and $(AM_k)_j$ is used for the approximation error, $f_{j,i} : R \to R$ denotes the influence of gene i to the transcription rate of gene j.

The minimization problem can be separated into n sub problems. Each sub problem including l approximated.

For all j, the minimization of these approximation errors is worked out using least squares method.

$$\min_{(\hat{A}_j)_j} \quad \sum_{k=0}^{l-1}\left(\left(\hat{E}_k\right)\left(\hat{A}\right)_j - \left(\frac{d\overline{E}_k}{dt}\right)_j\right)^2 \quad \text{.....(vii)}$$

where $\hat{A}_j$ is a collection of Vandermonde matrices for polynomials, rational polynomial, circular function.

Case-I: If Regulatory function is defined as a polynomial

$$f_{j,i}(x) = \sum_{n=0}^{p} a_{i,j}\ x^n \qquad :1 \le p \le 4 \quad \text{.....(viii)}$$

where $x = E_i$ denotes the concentration of gene i and $\forall a_{i,j} \in R$ .then

$$\hat{E}_k = \left[1 \quad (\overline{E}_k)_1^1 \ \ldots\ (\overline{E}_k)_1^p, \ \ldots\ldots\ldots, 1 \quad (\overline{E}_k)_n^1 \ \ldots\ (\overline{E}_k)_n^p\right] \qquad 1 \le p \le 4$$

represents the k[th] row vector of the matrix $\hat{E}_k$ and $\hat{A}_j = [(\hat{A}_j)_1\ (\hat{A}_j)_2\ \ldots..(\hat{A}_j)_{3n}]^T$ is a column vector consisting of the coefficients of the polynomials for the regulating functions.

Case-II: If Regulatory function is defined as a

$$f_{j,i}(x) = a_{i,j} + b_{i,j}\sin x + c_{i,j}\cos x \quad \text{.....(ix)}$$

where $x = E_i$ denotes the concentration of gene i and $a_{i,j}, b_{i,j}, c_{i,j} \in R$ .Then

$$\hat{E}_k = \left[1 \quad \sin(\overline{E}_k)_1 \cos(\overline{E}_k)_1 \ \ldots\ldots\ldots 1 \quad \sin(\overline{E}_k)_n \ \cos(\overline{E}_k)_n\right]$$

represents the k[th] row vector of the matrix $\hat{E}_k$ and $\hat{A}_j = [(\hat{A}_j)_1\ (\hat{A}_j)_2\ \ldots..(\hat{A}_j)_{3n}]^T$ is a column vector consisting of the coefficients of the polynomials for the regulating functions.

Case-III: If Regulatory function is defined as a rational polynomial

$$f_{j,i}(x) = \sum_{n=0}^{p} \frac{a_{i,j}}{x^n} \qquad :1 \le p \le 4 \quad \text{.....(x)}$$

where $x = E_i$ denotes the concentration of gene i and $a_{i,j}, b_{i,j} \in R$ .Then

$$\hat{E}_k = \left[1 \quad \frac{1}{(\overline{E}_k)_1^1} \ \ldots\ \frac{1}{(\overline{E}_k)_1^p} \ \ldots\ldots\ldots 1 \quad \frac{1}{(\overline{E}_k)_n^1} \ \ldots\ \frac{1}{(\overline{E}_k)_n^p}\right]; 1 \le p \le 4$$

represents the k[th] row vector of the matrix $\hat{E}_k$ and $\hat{A}_j = [(\hat{A}_j)_1\ (\hat{A}_j)_2\ \ldots..(\hat{A}_j)_{3n}]^T$ is a column vector consisting of the coefficients of the polynomials for the regulating functions.

And error will we calculate by residual

$$R_j = \left[\left(\hat{E}_k\right)\left(\hat{A}\right)_j - \left(\frac{d\overline{E}_k}{dt}\right)_j\right] \quad k = 0,1,2....l-1 \quad \text{.....(xi)}$$

$$Total\ Error = \sum_{j=1}^{m-1} (R_j)^2 \quad \text{.....(xii)}$$

5. Illustration using Yeast, E.coli Data, Drosophila, and Mycobacterium Data Set

GENOWIZ software has been used for comparison. We study the E.coli data of 4224 on 22 sample time point and Yeast data of 1056 on 16 time point , Drosophila data of 18208 on 16 sample time point and mycobacterium data of 22283 on 50 sample time point . The data is first normalized by using min-max method, and then it is filtered for 10 most fluctuated genes.

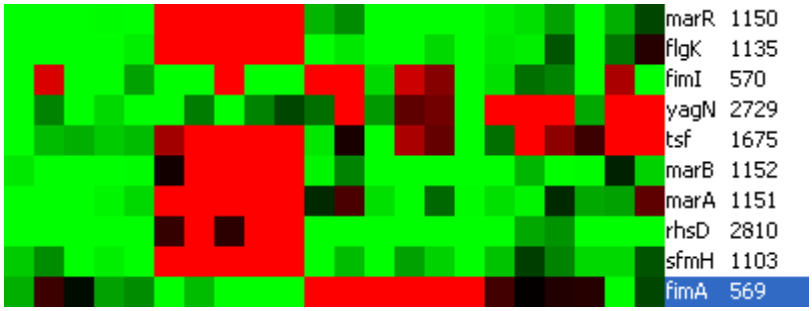


Figure 1. Image Data of 10 Fluctuating Genes of E.coli Dataset

The image contains 10 most fluctuated genes on 22 samples from which a 5×3 matrix is extract which contain 3 genes on 5 sample point.

Table 1. E.coli Data

	Gene1	Gene2	Gene3
$sample(t_0)$	.0860	.1200	. 0220
$sample(t_1)$	.1190	.1230	.8060
$sample(t_0)$	.1440	.0460	.1070
$sample(t_0)$	.1520	.0650	.0100
$sample(t_0)$	.1160	.1720	.2800

Where Gene1, Gene2 and Gene3 are Mar1150, flgk1135 and fimI570 respectively and is represented by column vector.

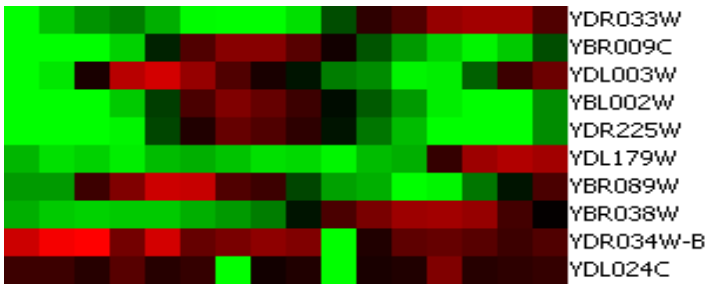


Figure 2. Image Data of 10 Fluctuating Genes of Yeast Dataset

The image contains 10 most fluctuated genes on 16 samples from which a 5×3 matrix is extract which contain 3 genes on 5 sample point.

Table 2. Yeast Data Set

	Gene1	Gene2	Gene3
$sample\ (t_0)$	-0.8321	-0.9799	-0.7174
$sample\ (t_1)$	-0.5364	-0.8275	-0.6394
$sample\ (t_0)$	-0.4150	-0.8973	0.0606
$sample(t_0)$	-0.3380	-0.5761	0.5198
$sample(t_0)$	-0.4921	-0.0925	0.5985

Where Gene1, Gene2 and Gene3 are YDR033W, YBR009C and YDL003W respectively and is represented by column vector.

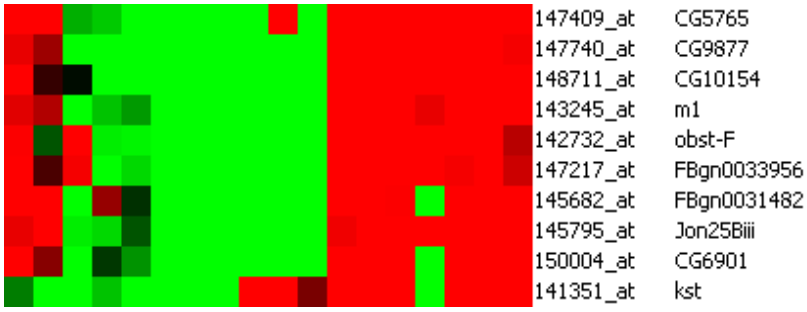


Figure 3. Image of 10 Fluctuating Genes of Drosophila

The image contains 10 most fluctuated genes on 16 samples from which a 5×3 matrix is extract which contain 3 genes on 5 sample point.

Table 3. Drosophila Data Set

	Gene1	**Gene2**	**Gene3**
$sample\ (t_0)$	0.9610	0.6562	0.7395
$sample\ (t_1)$	0.8177	0.4270	0.1446
$sample\ (t_0)$	-0.4680	-0.9132	-0.0255
$sample(t_0)$	-0.5628	-0.9115	-0.9113
$sample(t_0)$	-0.9068	-0.8913	-0.9017

Where Gene1, Gene2 and Gene3 are 147409, 147740 and 148711 respectively and is represented by column vector.

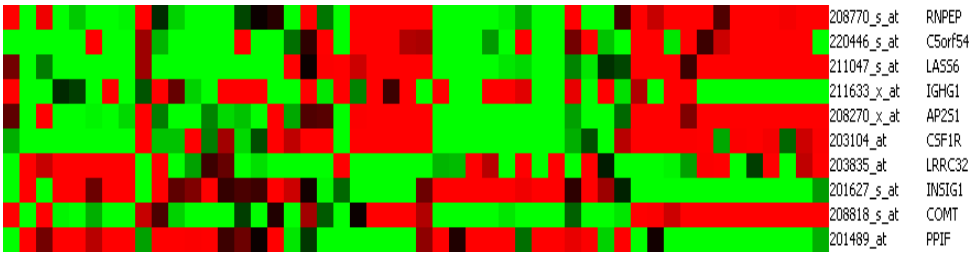


Figure 4. Image of 10 Fluctuating Genes of Mycobacterium

The image contains 10 most fluctuated genes on 50 samples from which a 5×3 matrix is extract which contain 3 genes on 5 sample point.

Table 4. Mycobacterium Data Set

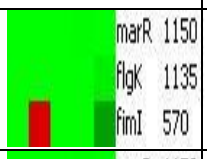
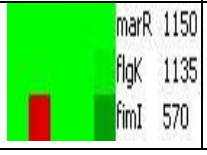
	Gene1	Gene2	Gene3
$sample\ (t_0)$	1.0000	-0.9609	0.3170
$sample\ (t_1)$	-1.0000	-1.0000	-1.0000
$sample\ (t_0)$	0.6751	-0.9669	-0.3295
$sample(t_0)$	-1.0000	-0.8278	-1.0000
$sample(t_0)$	-0.5551	-0.8340	-1.0000

Where Gene1, Gene2 and Gene3 are 208770, 220446 and 211047 respectively and is represented by column vector

5.1. Discussion

Residual norm is used to compare the predicted value with actual one further the comparison of numerical data and image is shown in Table 5, 6, 7, 8.

Table 5. E.coli Data Set

Regulatory function ⇓	Gene 1 Mar 1150 (Error)	Gene2 Fgk1135 (Error)	Gene3 fimI 570	Image of Sample Data set	Images through GENOWIZ for said approximation
Linear: $a+bx$ $\left(\sum_{n=0}^{p} a_{i,j}\, x^n\ ;p=1\right)$	0.0001	0.0001	0.0228		
Quadratic : $a+bx+cx^2$ $\left(\sum_{n=0}^{p} a_{i,j}\, x^n\ ;p=2\right)$	0.3888 * 1.0e-30	0.8454 * 1.0e-29	0.34902 * 1.0e-30		

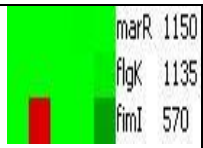
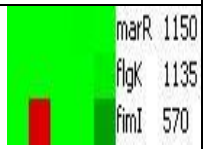
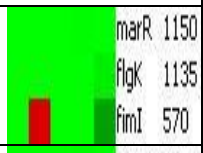
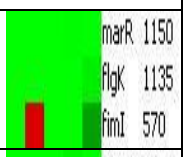
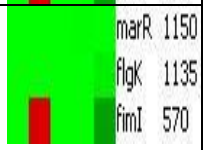
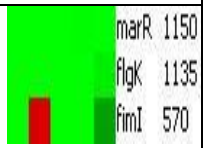
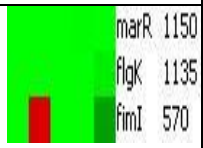
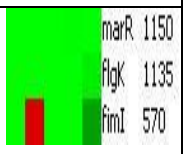
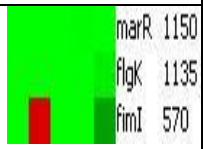
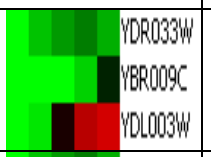
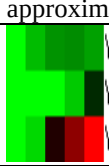
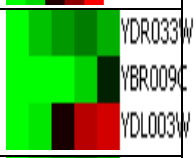
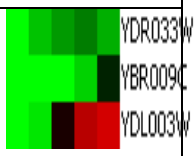
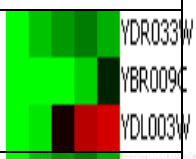
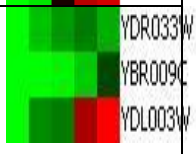
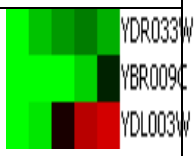
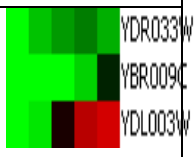
Cubic: $a+bx+cx^2+dx^3$ $\left(\sum_{n=0}^{p} a_{i,j}\, x^n \;;\; p=3\right)$	0.5030 * 1.0e-31	0.1403 * 1.0e-29	0.6500 * 1.0e-31		
Biquadratic $a+bx+cx^2+dx^3+ex^4$ $\left(\sum_{n=0}^{p} a_{i,j}\, x^n \;;\; p=4\right)$	0.5030 * 1.0e-31	0.1403 * 1.0e-29	0.6500 * 1.0e-31		
Circular: $a+b\sin x+c\cos x$	0.3000 * 1.0e-28	0.1137 *10-25	0.1200 * 1.0e-27		
Rational form: $a+\frac{b}{x}$ $\left(\sum_{n=0}^{p} \frac{a_{i,j}}{x^n} \;;\; p=1\right)$	0.0016	0.0161	0.4608		
Rational form $a+\frac{b}{x}+\frac{c}{x^2}$ $\left(\sum_{n=0}^{p} \frac{a_{i,j}}{x^n} \;;\; p=2\right)$	0.1400 *1.0e-29	0.4230 1.0e-29	0.4296 1.0e-28		
Rational form $a+\frac{b}{x}+\frac{c}{x^2}+\frac{d}{x^3}$ $\left(\sum_{n=0}^{p} \frac{a_{i,j}}{x^n} \;;\; p=3\right)$	0.3000 *1.0e-30	0.3210 *1.0e-29	0.8060 *1.0e-28		
Rational form $a+\frac{b}{x}+\frac{c}{x^2}+\frac{d}{x^3}+\frac{e}{x^4}$ $\left(\sum_{n=0}^{p} \frac{a_{i,j}}{x^n} \;;\; p=4\right)$	0.1280 *1.0e-28	0.8670 *1.0e-28	0.2776 *1.0e-27		

Table 6. Yeast Data Set

Regulatory function ⇓	Gene 1 YDL033W (Error)	Gene2 YDL009C (Error)	Gene3 YDL003W (Error)	Image of Sample Data set	Images through GENOWIZ for said approximation
Linear: $a+bx$ $\left(\sum_{n=0}^{p} a_{i,j}\, x^n \;;\; p=1\right)$	0.0037	0.0002	0.0404		
Quadratic : $a+bx+cx^2$ $\left(\sum_{n=0}^{p} a_{i,j}\, x^n \;;\; p=2\right)$	0.7700 *1.0e-33	0.4333 *1.0e-31	0.1849 *1.0e-31		
Cubic: $a+bx+cx^2+dx^3$ $\left(\sum_{n=0}^{p} a_{i,j}\, x^n \;;\; p=3\right)$	0.3640 *1.0e-31	0.8940 *1.0e-31	0.2743 *1.0e-30		
Biquadatric $a+bx+cx^2+dx^3+ex^4$ $\left(\sum_{n=0}^{p} a_{i,j}\, x^n \;;\; p=4\right)$	0.1560 *1.0e-31	0.8936 *1.0e-31	0.6779 *1.0e-31		
Circular: $a+b\sin x+c\cos x$	0.7610 * 1.0e-30	0.4200 * 1.0e-31	0.1359 * 1.0e-29		
Rational form: $a+\frac{b}{x}$ $\left(\sum_{n=0}^{p} \frac{a_{i,j}}{x^n} \;;\; p=1\right)$	0.0000014	0.0748	0.2626		
Rational form $a+\frac{b}{x}+\frac{c}{x^2}$ $\left(\sum_{n=0}^{p} \frac{a_{i,j}}{x^n} \;;\; p=2\right)$	0.2130 * 1.0e-30	0.1830 * 1.0e-30	0.4880 * 1.0e-29		
Rational form $a+\frac{b}{x}+\frac{c}{x^2}+\frac{d}{x^3}$ $\left(\sum_{n=0}^{p} \frac{a_{i,j}}{x^n} \;;\; p=3\right)$	0.8260 *1.0e-27	0.6979 *1.0e-26	0.4337 1.0e-26		

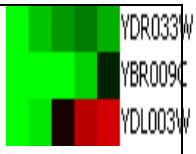
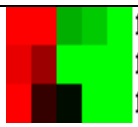
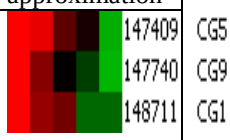
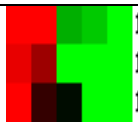
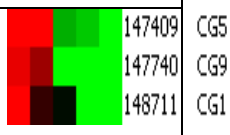
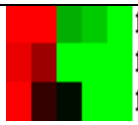
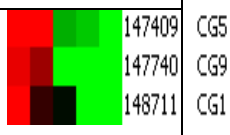
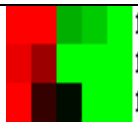
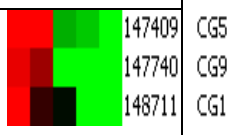
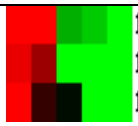
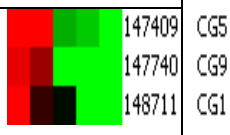
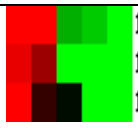
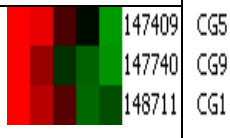
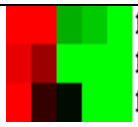
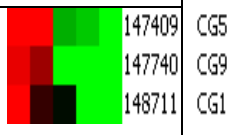
Rational form $a+\frac{b}{x}+\frac{c}{x^2}+\frac{d}{x^3}+\frac{e}{x^4}$ $\left(\sum_{n=0}^{p}\frac{a_{i,j}}{x^n};\ p=4\right)$	0.5300 *1.0e-25	0.2250 *1.0e-24	0.1201 *1.0e-23		

Table 7. Drosophila Data Set

Regulatory function ⇓	Gene 1 147409 (Error)	Gene2 147740 (Error)	Gene3 148711 (Error)	Image of Sample Data set	Images through GENOWIZ for said approximation
Linear: $a+bx$ $\left(\sum_{n=0}^{p}a_{i,j}\,x^n\ ;p=1\right)$	0.3720	0.4824	0.0002		
Quadratic : $a+bx+cx^2$ $\left(\sum_{n=0}^{p}a_{i,j}\,x^n\ ;p=2\right)$	0.1638 * 1.0e-29	0.8660 * 1.0e-30	0.252 * 1.0e-30		
Cubic: $a+bx+cx^2+dx^3$ $\left(\sum_{n=0}^{p}a_{i,j}\,x^n\ ;p=3\right)$	0.1638 * 1.0e-29	0.8660 * 1.0e-30	0.2520 * 1.0e-30		
Biquadratic $a+bx+cx^2+dx^3+ex^4$ $\left(\sum_{n=0}^{p}a_{i,j}\,x^n\ ;p=4\right)$	0.1898 * 1.0e-29	0.1409 * 1.0e-29	0.5170 * 1.0e-30		
Circular $a+b\sin x+c\cos x$	0.1146 * 1.0e-29	0.5080 * 1.0e-30	0.2910 * 1.0e-30		
Rational form: $a+\frac{b}{x}$ $\left(\sum_{n=0}^{p}\frac{a_{i,j}}{x^n};\ p=1\right)$	0.2974	0.2334	0.0530		
Rational form $a+\frac{b}{x}+\frac{c}{x^2}$ $\left(\sum_{n=0}^{p}\frac{a_{i,j}}{x^n};\ p=2\right)$	0.3300 * 1.0e-30	0.1049 * 1.0e-29	0.1002 * 1.0e-29		

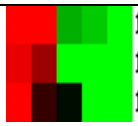
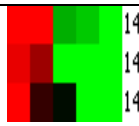
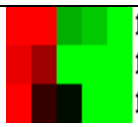
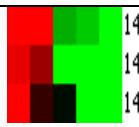
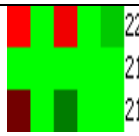
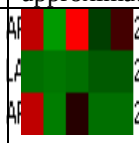
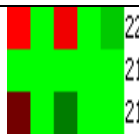
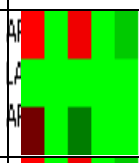
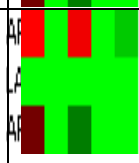
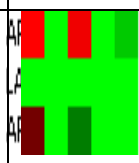
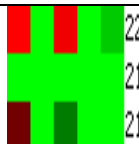
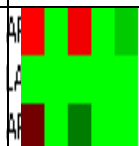
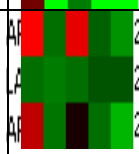
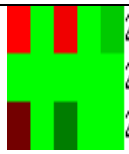
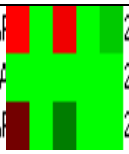
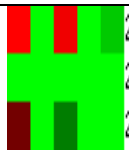
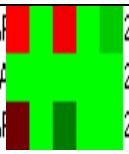
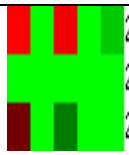
Rational form $a+\frac{b}{x}+\frac{c}{x^2}+\frac{d}{x^3}$ $\left(\sum_{n=0}^{p}\frac{a_{i,j}}{x^n}\ ;\ p=3\right)$	0.2680 *1.0e-28	0.2380 *1.0e-28	0.1128 *1.0e-27		
Rational form $a+\frac{b}{x}+\frac{c}{x^2}+\frac{d}{x^3}+\frac{e}{x^4}$ $\left(\sum_{n=0}^{p}\frac{a_{i,j}}{x^n}\ ;\ p=4\right)$	0.1030 *1.0e-26	0.9300 *1.0e-27	0.8621 *1.0e-25		

Table 8. Mycobacterium Data Set

Regulatory function ⇓	Gene 1 220770 (Error)	Gene2 212446 (Error)	Gene3 211047 (Error)	Image of Sample Data set	Images through GENOWIZ for said approximation
Linear: $a+bx$ $\left(\sum_{n=0}^{p}a_{i,j}\,x^n\ ;p=1\right)$	0.3234	0.0041	0.0109		
Quadratic : $a+bx+cx^2$ $\left(\sum_{n=0}^{p}a_{i,j}\,x^n\ ;p=2\right)$	0.2564 * 1.0e-028	0.8000 * 1.0e-31	0.3900 * 1.0e-29		
Cubic: $a+bx+cx^2+dx^3$ $\left(\sum_{n=0}^{p}a_{i,j}\,x^n\ ;p=3\right)$	0.8875 *1.0e-30	0.6200 *1.0e-32	0.9368 *1.0e-30		
Biquadratic $a+bx+cx^2+dx^3+ex^4$ $\left(\sum_{n=0}^{p}a_{i,j}\,x^n\ ;p=4\right)$	0.1639 *1.0e-29	0.7000 *1.0e-32	0.4326 *1.0e-29		
Circular: $a+b\sin x+c\cos x$	0.1139 *1.0e-28	0.4000 *1.0e-31	0.253 *1.0e-29		
Rational form: $a+\frac{b}{x}$ $\left(\sum_{n=0}^{p}\frac{a_{i,j}}{x^n}\ ;\ p=1\right)$	0.6217	0.0001	0.1246		

Rational form $a+\frac{b}{x}+\frac{c}{x^2}$ $\left(\sum_{n=0}^{p}\frac{a_{i,j}}{x^n}\ ;\ p=2\right)$	0.1787 *1.0e-28	0.1000 *1.0e-31	0.1630 *1.0e-29		
Rational form $a+\frac{b}{x}+\frac{c}{x^2}+\frac{d}{x^3}$ $\left(\sum_{n=0}^{p}\frac{a_{i,j}}{x^n}\ ;\ p=3\right)$	0.1584 *1.0e-029	0.8000 *1.0e-32	0.1141 *1.0e-29		
Rational form $a+\frac{b}{x}+\frac{c}{x^2}+\frac{d}{x^3}+\frac{e}{x^4}$ $\left(\sum_{n=0}^{p}\frac{a_{i,j}}{x^n}\ ;\ p=4\right)$	0.2638 *1.0e-29	0.4000 *1.0e-32	0.1630 *1.0e-30		

In this research we have tried to establish and demonstrate patterns of gene regulatory expression which can be modelled using polynomial, rational and circular functions. This phenomenon has been studied by different researchers to one extent or the other therefore in this paper a detailed comparison of these three approaches has been shown. The parameter of well established model [4] is optimized using least square method and then error is calculated by residual norm. The numerical value where calculated using MATLAB.

6. Conclusion

The degree of polynomial and rational polynomial is changed for performing different experiments. The comparative result indicates that when degree of polynomial is 1, prediction error is large but in case of degree 2, 3 and 4 prediction error is less for polynomial and rational polynomial. In case of E.coli , Yeast and Drosophila data sets, if degree of polynomial increased from 2 to more, then efficacy remains same, but in case of rational form it is just opposite. In case of mycobacterium results are bit off the trend, that is when rational form is applied and degree of polynomial is increased, the error reduces. Initial increase in degree gives significant improvement in most of the cases i.e from degree one to two or more, but this nature varies from one organism to another.

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