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Research Article

Modeling and Simulation of Lac Operon Regulation of E. coli bacterium Using Intelligent Fuzzy System

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Abstract: Current methodologies in displaying dynamic organic frameworks regularly need fathomability, particularly for users without scientific foundation. In this paper propose another way to deal with defeat such confinements by joining the graphical representation gave by the utilization of Petri nets with the demonstrating of flow by effective yet natural fuzzy logic based frameworks. We build a fuzzy reasoning Petri net (FRPN) model for the genetic regulatory network of the lac operon of E. coli bacterium. Depending on the FPN formalism is a decent other option to mathematical equations that require dynamic parameter qualities and better than Boolean Formalism which naturally sets control as "on" or "off" guidelines. The lac operon has been considered as a model framework for comprehension the molecular biology of gene expression with considered to its regulation. We approve our formal model via programmed checking a progression of characteristics that are known for the control of the lactose. In this way, we demonstrate the feasibility of utilizing FRPN to design and reason about biochemical systems.
Keywords: Fuzzy reasoning Petri net; Lac operon of E. coli bacterium; Modeling and simulation; LacY, LacZ, LacA.

INTRODUCTION

PN has capacity to take and investigate in simple way simultaneousness and synchronization wonders, as simultaneous advancements, where different procedures that develop all the while are incompletely autonomous. Moreover, PN approach can be effortlessly consolidated with different methods and hypotheses, for example, question situated programming, fuzzy hypothesis, neural systems, and so forth. These altered PNs are generally utilized as a part of PC, assembling, mechanical, and information based frameworks; prepare control, and in addition different sorts of building applications [1, 2].

Demonstrating and reenactment strategies gave by frameworks hypothesis can help enhancing the level of comprehension of natural marvels, [3]. Specifically, PN are turning into the reference demonstrating formalism for GRNs (see, e.g., [4-7]): actuation and hindrance of quality movement is naturally an on/off system, and the progression administering proteins fixation are portrayed by half and half Petri nets (HPNs), while the initiation and the deactivation of these elements are activated by discrete switches encoding protein focus achieving some edge.

FPN which consolidates fuzzy rationale with PN is helpful device in managing unverifiable and fragmented data. FPN has reliable relationship delineate fuzzy generation manage [8-10]. FPN has intense capacity when utilized for handling parallel data and has the attributes of simultaneous working capacity. FP organize model is anything but difficult to make and its chart expression is likewise straightforward, the graphical perspective makes it less demanding to speak to the diverse associations between discrete occasions, the scientific viewpoint takes into consideration the formal demonstrating of these collaborations and examination of the properties of the displayed framework. It is in this manner a reasonable and helpful displaying instrument.

FPN offers an engaging technique for portraying marvels by an arrangement of tenets and informational collections. These informational indexes relate specifically to ideas utilized regularly, for example, "fast", "strong" or "high", while the standards express learning around a similar way a human master would. A case of a fuzzy govern

would be "if the auto is quick, then the compel connected to the brakes is solid". In this work, we concentrate a FPN model for the lac operon administrative system in the E. coli bacterium. Natural structures for control are generally exhibited as subjective semantic graphical data.

Late work by Aris and Amable proposes that fuzzy rationale formalism is joined with element flux adjust examination (dFBA), may get to be distinctly profitable instrument in demonstrating and recreation of natural frameworks where the association and versatility are essential elements [11]. The field may have a critical effect in seeing how organic frameworks function, giving in the meantime an approach to portray, control, and examine them. Sokhansanj and Fitch built up a URC fuzzy displaying and recreation of quality direction, they exhibited the technique on the lac operon of E. coli [12], and Yildirim and Mackey proposed nonlinear differential postpone conditions to model control in the lactose operon and made correlations with exploratory information [13].

Our commitment in this paper is the utilization of a FPN model to displaying and reenactment the normal conduct of an organic framework. To the best of our insight it is the first occasion when that a FPN is utilized to make subjective derivations of a natural framework. Given the multifaceted nature of frameworks start considered, scientists require a displaying and reproduction structure to comprehend substantial scale information and insightfully plan customary seat beat tests that give the most organic understanding.

Whatever is left of the paper is sorted out as takes after. In area II, major of lac operon is presented, in segment III, a few standards of fuzzy surmising frameworks is given, in segment IV, formal thinking model and fuzzy thinking Petri net in view of network calculation is exhibited, before thinking procedure is started, structure of learning base is speak to, in segment V, building the model of the lac operon in E. coli in light of fuzzy thinking Petri net model and grid calculation plan is depicted, in area VI, the recreation aftereffects of glucose, EIIA-P, and lactose are appeared lastly in segment VII, a few rundowns and conclusions are given.

Regulation Mechanism of Lactose Operon Operation

The lac operon [14] depicts the control of lactose take-up in microbes. The schematic outline of the operon is appeared in Fig. 1. Upon take-up, lactose is separated into glucose and galactose. The lactose operon contains three qualities identified with lactose digestion system. The lac Z, Y and A qualities encode β-galactosidase, galactoside permease and thiogalactoside transacetylase, separately. β-galactosidase changes over lactose to galactose and glucose or, by transglycosylation, to allolactose. Galactoside permease transports lactose into the cell and thiogalactoside transacetylase seems to alter poisonous galactosides to encourage their expulsion from the cell.

Without lactose, the lac operon qualities are subdued — actually, they are deciphered at a basal level. This negative control is finished by a particle called Lac repressor, which ties to a few locales close to the begin of the operon, obstructing the action of RNA polymerase. These locales are called administrators. The administrator to which the repressor ties most firmly is named O1. The lac operon has two optional restricting destinations for the Lac repressor: O2 and O3. To subdue the operon, the Lac repressor ties to both the fundamental administrator and one of the two auxiliary destinations.

At the point when cells are furnished with lactose, the lac operon is initiated. An inducer (flag) particle ties to a particular site on the Lac repressor, bringing on a conformational change those outcomes in separation of the repressor from the administrators. The inducer in the lac operon framework is allolactose, an isomer of lactose. Whenever unrepressed, interpretation of lac qualities is expanded, however not at its more elevated amount. Different variables other than lactose influence the outflow of the lac qualities, for example, the accessibility of glucose — the favored vitality wellspring of microscopic organisms. Different sugars can fill in as the principle or sole supplement, yet additional means are required to set them up for section into glycolysis, requiring the amalgamation of extra chemicals. Plainly, communicating the qualities for proteins that metabolize sugars, for example, lactose is inefficient when glucose is plenteous.

The lac operon manages it through a positive direction. A direction system known as catabolite restraint limits articulation of the qualities required for catabolism of lactose within the sight of glucose, notwithstanding when this optional sugar are additionally present. The impact of glucose is intervened by cAMP, as a coactivator, and an activator protein known as cAMP receptor protein, or CRP (some of the time it is called CAP, for catabolite quality activator protein). CRP has restricting destinations for DNA and cAMP. At the point when glucose is truant, CRP-cAMP ties to a site close to the lac promoter and fortifies RNA translation. CRP-cAMP is along these lines a positive administrative component receptive to glucose levels, while the Lac repressor is a negative administrative component receptive to

lactose. The two demonstrations in show, CRP-cAMP has little impact on the lac operon when the Lac repressor is blocking interpretation, and separation of the repressor from the lac administrator has little impact on translation of the lac operon unless CRP-cAMP is available to encourage translation; when CRP is not bound, the wild-sort lac promoter is a moderately frail promoter.

The impact of glucose on CRP is interceded by the cAMP cooperation. CRP ties to DNA most energetically when cAMP fixations are high. Within the sight of glucose, the union of cAMP is hindered and efflux of cAMP from the cell is fortified. As cAMP decays, CRP official to DNA decreases, consequently diminishing the declaration of the lac operon. Solid acceptance of the lac operon in this manner requires both lactose (to inactivate the Lac repressor) and a brought down convergence of glucose (to trigger an expansion in cAMP and increment official of cAMP to CRP) [15].

Carbon catabolite restraint in E. coli is predominantly intervened by the glucose-particular EIIA of the glucose phosphotransferase framework (PTS). Within the sight of glucose, EIIA ties and inactivates the lactose permease (LacY) and glycerol kinase (GlpK). Without sugars, phosphorylated EIIA (EIIA~P) actuates adenylate cyclase (AC) which creates cAMP from ATP. cAMP ties to catabolite activator protein (CAP) neighboring the lac promoter area. The mind boggling CAP-cAMP expands lac mRNA translation by its connection with the RNA polymerase at the promoter site. An abnormal state of articulation of the lac qualities requires the simultaneous nearness of cAMP and the inducer allolactose [16].

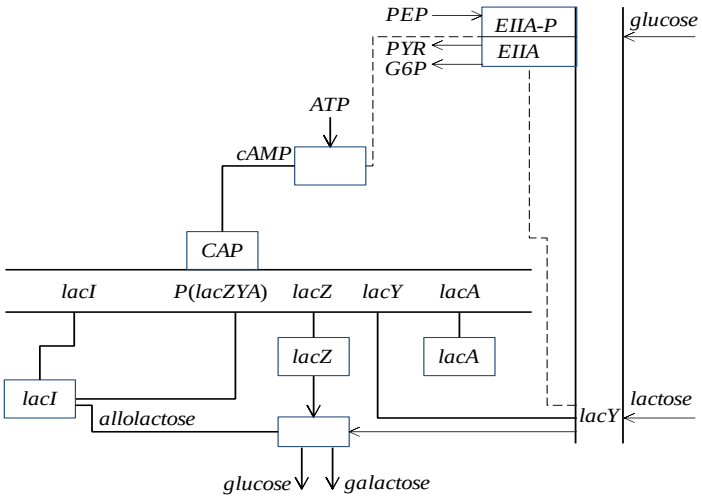


Fig-1: Schematic model of lac operon operation

Description of Knowledge Base of Fuzzy Mechanism in Our System

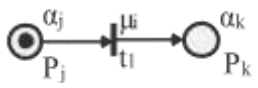
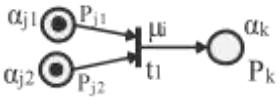
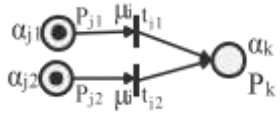
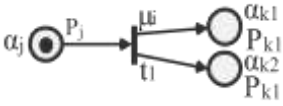
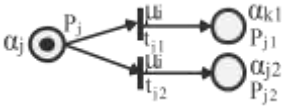
Structure of Knowledge Base

In this paper, the formal description of knowledge based is given as follows and shown in Table 1. The doublet KB = (D, R) is call a knowledge base iff

1) $D = \{d_1, d_2,\ldots, d_n\}$ is just a group of propositions;
2) $R = \{r_1, r_2,\ldots,r_n\}$ is a set of rules, where r_i, i = 1,2,…,n is one of the following forms:
   2.1) If d_{i1} and d_{i2} … and d_{ik} then d_{ik+1};
   2.2) If d_{i1} or d_{i2} … or d_{ik} then d_{ik+1};
   2.3) If d_{i1} then d_{i2} and d_{i3} … and d_{ik+1};
   2.4) If d_{i1} then d_{i2} or d_{i3} … or d_{ik+1}.

Where $d_{i1}, d_{i2}, \ldots, d_{ik+1} \in D$.

Table-1: The Fuzzy Petri Nets Description of Logical Rules

No.	Rules	Fuzzy Reasoning Petri Nets	Truth Degrees α_k
1.	IF d_1 THEN d_2		$\alpha_k = \alpha_j \times \mu_i$
2.	IF d_1 AND d_2 THEN d_3		$\alpha_k = \text{Min}(\alpha_{j1}, \alpha_{j2}) \times \mu_i$
3.	IF d_1 OR d_2 THEN d_3		$\alpha_k = \text{Max}(\alpha_{j1} \times \mu_i, \alpha_{j2} \times \mu_i)$
4.	IF d_1 THEN d_2 AND d_3		$\alpha_{k1} = \alpha_j \times \mu_{i1}$ $\alpha_{k2} = \alpha_j \times \mu_{i2}$
5.	IF d_1 THEN d_2 OR d_3		$\alpha_{k1} = \alpha_j \times \mu_i$ $\alpha_{k2} = \alpha_j \times \mu_i$

Fuzzy Reasoning Petri net

Definition of FRPN

Established PN [1, 2] don't have adequate ability to demonstrate the vulnerability in frameworks [24]. This impediment of Petri nets has urged specialists to augment the leaving models by utilizing the fuzzy thinking hypothesis [25-29].

In what tails, we give a concise depiction about the FRPN demonstrating apparatus. Let consider FRPN = (P, T, D, I, O, F, α, β). A token incentive set up pi P is signified by α (pi) [0, 1], α (pi) = yi, yi [0, 1] and β (pi) = di. This expresses the level of reality of recommendation di is yi. A move ti is empowered if pi I (ti), yi > 0. In the event that this move ti is terminated, tokens are expelled from info places I (ti) and a token is saved onto each of the yield places O (ti). This current token's enrollment incentive to the place pk, (i.e. yk = α(pk)), is a piece of the token and gets ascertained inside the move work. It is anything but difficult to see that CF [0, 1]. On the off chance that CF = 1 then we will state that a given manage is deterministic. Something else (i.e., if CF < 1), we will state that the given govern is non-deterministic.

Case

The formalism of the fuzzy guidelines (IF di1 and di2 ... furthermore, diminish THEN dk) and (IF di1 or di2 ... alternately diminish THEN dk) can be demonstrated as appeared in Fig. 2. In this illustration, β (pi) = di, β(pj) = dj, β(pm) = dm, β(pk) = dk, α(pi) = yi = 0.88, α(pj) = yj = 0.44 and α(pm) = ym = 0.73. Since yi > 0, yj > 0 and ym > 0, move tn is empowered and let go. Tokens are expelled from I(tn), which are pi, pj, pm and stored onto O(tn), which is pk. At that point reality estimation of the yield token (enrollment degree) of the first is ascertained as α(pk) = min(yi, yj, ym) × μi = yk = 0.44 .

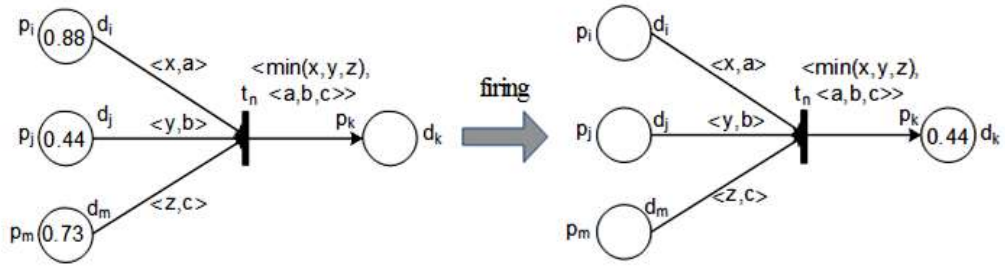


Fig.2. Firing principle of transition PNs

A Mechanism of Solving the Problem Using the Concept of FRPN

As indicated by the components of FRPN, we can depict the thinking procedure of FRPN in the information representation precisely and formally. Give k a chance to indicate the kth thinking step, and then the fuzzy thinking calculation of the FRPN is as per the following:

Step 1: Start with the FRPN: I_i, O_j, F, α^0 and M^0.

Step 2: Let k =0.

Step 3: ([=

(1) Calculate ρ_F^k = neg V_k = $\overline{(Ii)^T \otimes \overline{\alpha^K}}$

$V_k = Ii^T \otimes (neg\alpha^k) = Ii^T \otimes \overline{\alpha^K}$

$neg\alpha^k = 1_m - \alpha^k = \overline{\alpha^k}$

(2) Calculate the value of α^{k+1} from α^k based on

$\alpha^{k+1} = \alpha^k \oplus [(Oj \,.\, f) \otimes \overline{(Ii^T \otimes \overline{\alpha^K})}]$

Step 4: If $\alpha^{k+1} \neq \alpha^k$ then let $k = k+1$, and return to Step 3; otherwise, go to step 5.

Step 5: For every output $\alpha(p_s)$, determine

$$P = \frac{\sum_{i=1}^{n} \mu[i] \times y_i}{\sum_{i=1}^{n} \mu[i]}$$

Step 6: According to step 5, the P_s value becomes an actual output, so the reasoning is over.

The calculate of FRPN will compute the value of (i.e. $\alpha(p_i) = y_i$) and change the vector M^0. According to the definition of FRPN, I, O, and μ.

The test of fuzzy rules of our algorithm include firing rules [25].

1) Any transition of FPN $t_j \in T$ is enabled with respect to p_i is marked, or $M_i = 1$, $\forall p_i \in$ {input values of t_j}.
2) Change the value of M, t_j fires resulting in a new one M′

$$M'(p) = M(p) \oplus O(p_i, t_j), \quad \forall p_i \in P.$$

The degree of FPN places changes from α to α′

$$\alpha'(p) = \alpha(p) \oplus \mu_j \,.\, \rho_j \,.\, O(p, t_j), \quad \forall p_i \in P.$$

where

$$\rho_j = \min_{p_i \in t_j} \{x_i \mid x_i = \alpha_i \text{ if } I(p, t_j) = 1, \; x_i = 1 - \alpha_i\}$$

and

$$\cdot t_j = \{ p_i \mid I(p, t_j) = 1, p_i \in P.$$

3) In FRPNs, transition rules can process in same time. We introduce a firing vector V such that $V_j = 1$ if t_j fires. After firing a set of fuzzy transitions, the values of FPN of the FRPNs become with new values as following here :-

$$M' = M \oplus [O \otimes V]$$
$$\alpha' = \alpha \oplus [(O \,.\, \mu) \otimes \rho]$$

where $\rho = [\rho_1, \rho_2, \ldots, \rho_m]^T$, that refer to the values of FP. $V : T \rightarrow \{0\text{-}1\}$ is a proceeding vector. $V = (V_1, V_2, \ldots, V_m)^T$.

Consider the example shown in Fig. 3,

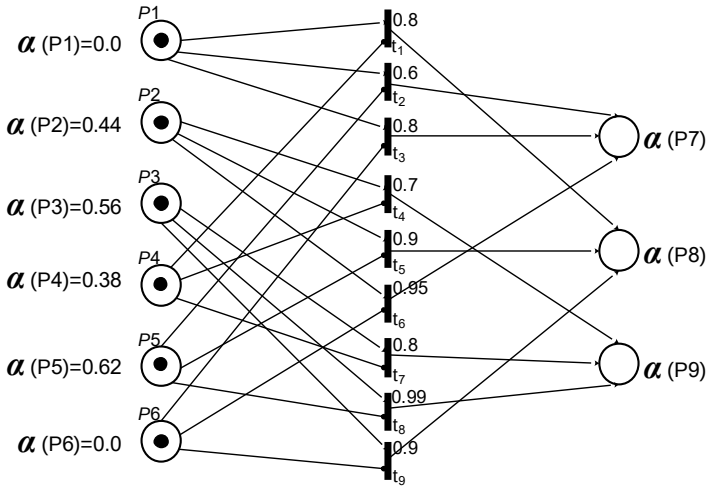


Fig-3: A FRPN model representation of predicting shift values of the target gene in our model.

Where
P = {P_1 (activator _low), P_2 (activator _medium), P_3 (activator _high), P_4 (repressor_low), P_5 (repressor_medium), P_6 (repressor_high), P_7 (target_low), P_8 (target_medium), P_9 (target_high)}, and T = {T_1, T_2… T_8, T_9}.

According to the definition of FRPN, I, O, μ are

$$I=\begin{Bmatrix} 1&1&1&0&0&0&0&0&0\\ 0&0&0&1&1&1&0&0&0\\ 0&0&0&0&0&0&1&1&1\\ 1&0&0&1&0&0&1&0&0\\ 0&1&0&0&1&0&0&1&0\\ 0&0&1&0&0&1&0&0&1\\ 0&0&0&0&0&0&0&0&0\\ 0&0&0&0&0&0&0&0&0\\ 0&0&0&0&0&0&0&0&0 \end{Bmatrix} \quad O=\begin{Bmatrix} 0&0&0&0&0&0&0&0&0\\ 0&0&0&0&0&0&0&0&0\\ 0&0&0&0&0&0&0&0&0\\ 0&0&0&0&0&0&0&0&0\\ 0&0&0&0&0&0&0&0&0\\ 0&0&0&0&0&0&0&0&0\\ 0&1&1&0&0&1&0&0&0\\ 1&0&0&0&1&0&0&0&1\\ 0&0&0&1&0&0&1&1&0 \end{Bmatrix} \quad \mu=\begin{Bmatrix} 0.8&0&0&0&0&0&0&0&0\\ 0&0.6&0&0&0&0&0&0&0\\ 0&0&0.8&0&0&0&0&0&0\\ 0&0&0&0.7&0&0&0&0&0\\ 0&0&0&0&0.9&0&0&0&0\\ 0&0&0&0&0&0.95&0&0&0\\ 0&0&0&0&0&0&0.8&0&0\\ 0&0&0&0&0&0&0&0.99&0\\ 0&0&0&0&0&0&0&0&0.9 \end{Bmatrix}$$

Its start value of tokes as a vector of M,

$$M^0 = (1,1,1,1,1,1)^T .$$

and start value degree vector

$$\alpha^0 = (0, 0.44, 0.56, 0.38, 0.62)^T.$$

Using the algorithm we obtain

$$neg(\alpha^0) = (1.0, 0.56, 0.44, 0.62, 0.38, 1.0, 1.0, 1.0, 1.0)^T,$$

$$V_0 = (1.0, 1.0, 1.0, 0.62, 0.56, 1.0, 0.44, 0.44, 1.0)^T,$$

$$\rho_F^0 = (0.0, 0.0, 0.0, 0.38, 0.44, 0.0, 0.56, 0.56, 0.0)^T,$$

$$\alpha^1 = \alpha^0 \oplus [(O \,.\, \mu) \otimes \rho_F^0]$$

$$\alpha^1 = (0.0, 0.44, 0.56, 0.38, 0.62, 0.0, 0.0, 0.39, 0.55)^T,$$

In the same way we can have,

$$\alpha^2 = (0.0, 0.44, 0.56, 0.38, 0.62, 0.0, 0.0, 0.39, 0.55)^T,$$

As $\alpha^2 = \alpha^1$ the final state of places P is $(0.0, 0.44, 0.56, 0.38, 0.62, 0.0, 0.0, 0.39, 0.55)^T$ and the marking vector is $M^1 = (1,1,1,1,1,1)^T$. Next, no transition (rule) can be enable and the net is in a stable stat. After the execution mentioned

above, the truth degrees of "α (p_7)= Low ", "α (p_8)= Medium ", and "α (p_9)= High ", are 0.0, 0.39 and 0.55 respectively.
Therefore, we can obtain the target gene. Convert the values into a crisp according to "gravity".

$$\text{Target\_Level}= \frac{0\times 0.25+0.39\times 0.5+0.55\times 0.75}{0+0.39+0.55}\approx 0.64$$

The finally, we can say the final value depending on our model in target level is 0.64 or 64%.

An Example of E. coli lac operon network Model of LacY, LacZ, LacA

We take after an approach in which FRPN is built specifically from given lead definitions. Development calculation takes the principles determined in a predefined language structure as info. At that point it produces the comparing FRPN structure consequently. All the more particularly, first the administer definitions are acquired from the client. For every run, a run question is made, and the occasion, condition and activity parts of the control are analyzed. In that, related FRPN places, for example, glucose take-up, Normalized EIIA-P, LacY, LacZ, LacA generation and so on, are made. At that point, the fuzzy induction bunches, which are the simultaneous run sets are resolved finally, moves are developed over these FRPN places. The pseudo-code of the calculation is given in Algorithm 1.

Algorithm 1. Construct_FRPN algorithm

```
Begin
  While there are still some rules do
    Create a rule object
    Examine Event, Condition, Action parts
    For each one of them do
      Create related FRPN places
    end for
  end while
Construct fuzzy inference groups
Construct transitions
End
```

Amid the moves development, some particular reason capacities are doled out to moves for esteem goes between the spots. For instance, we allocate an AND administrator to a few moves where required for the conjunctions of unmistakable occasions. The moves give the surmising ventures to be acknowledged with the assistance of these capacities.

Displaying the lac operon is conceptualized in two sections, catabolite constraint and acceptance. Hence, simulink fuzzy control arrangement of the lac operon in Escherichia coli is partitioned into two sections; one will actualize the catabolite constraint because of glucose and the other will execute enlistment. Catabolite restraint brought on by the nearness of glucose is the aftereffect of the aggregation of the non-phosphorylated type of EIIA which represses lactose permease. Current trial ponders have demonstrated that the intracellular cAMP increments fleetingly when glucose is drained [11, 16]. The CAP-cAMP complex applies a beneficial outcome on the outflow of the lac operon.

Since we utilize fluffiness, every token has an enrollment incentive to the place it is allocated. This is a piece of the token and gets figured inside the move work. Fig. 4 indicates how we understand the means of Fuzzy Inference utilizing the FRPN structure that we show above of lac operon catabolite restraint. Amid the FRPN development, first the administer definitions are acquired from [11]. The thinking motor performs basic leadership in view of the fuzzy rationale thinking rules with first request predicate rationale. Every govern can be characterized as an If-Then proviso, which decides the etymological estimation of yield as indicated by the phonetic estimations of info.

The glucose take-up rate is measured inside five unique conditions of Very High (VH), High (H), Medium (ME), Low (L), and Very Low (VL).

In the catabolite constraint part, the relationship between glucose take-up rate and the standardized EIIA~P rates are acquired from the fuzzy IF–THEN controls as takes after:

R1: IF Glucose uptake is VL THEN Normalized EIIA-P is VH;
R2: IF Glucose uptake is L THEN Normalized EIIA-P is H;
R3: IF Glucose uptake is M THEN Normalized EIIA-P is M;
R4: IF Glucose uptake is H THEN Normalized EIIA-P is L;
R5: IF Glucose uptake is VH THEN Normalized EIIA-P is VL;

At that point, the aftereffects of the IF–THEN standards are joined in the progression called induction, and the numerical estimations of EIIA-P rates are acquired from the defuzzification step. In unequaled strides, EIIA-P focus is recorded to portray EIIA-P time profile which gives a sign of the move from glucose use to lactose use. The principles got for the connection between the standardized EIIA-P and LacY generation rates are the accompanying:

R1: IF Normalized EIIA-P is VL THEN Normalized LacY, LacZ, LacA production is VL;
R2: IF Normalized EIIA-P is L THEN Normalized LacY, LacZ, LacA production is L;
R3: IF Normalized EIIA-P is M or H THEN Normalized LacY, LacZ, LacA production is H;
R4: IF Normalized EIIA-P is VH THEN Normalized LacY, LacZ, LacA production is VH;

The fuzzified LacY creation rates are utilized to decide lactose take-up rates and the defuzzified qualities are recorded in the Lactose take-up result workspace. The principles acquired were the accompanying:

R1: IF LacY production is VL THEN Lactose uptake is VL;
R2: IF LacY production is L THEN Lactose uptake is L;
R3: IF LacY production is M or H THEN Lactose uptake is M;
R4: IF LacY production is VH THEN Lactose uptake is H;

In the enlistment part, the declaration of the qualities will be actuated by allolactose. Allolactose ties to the repressor particle which permits the interpretation of the lacY, lacZ, and lacA qualities. Therefore lactose can be made up by the move of the LacY permease. Fig. 5 demonstrates how we understand the means of Fuzzy Inference utilizing the FRPN structure for lactose take-up enlistment. The guidelines acquired for the relationship between the rates estimation of lactose take-up and standardized estimation of Allolactose, were the accompanying:

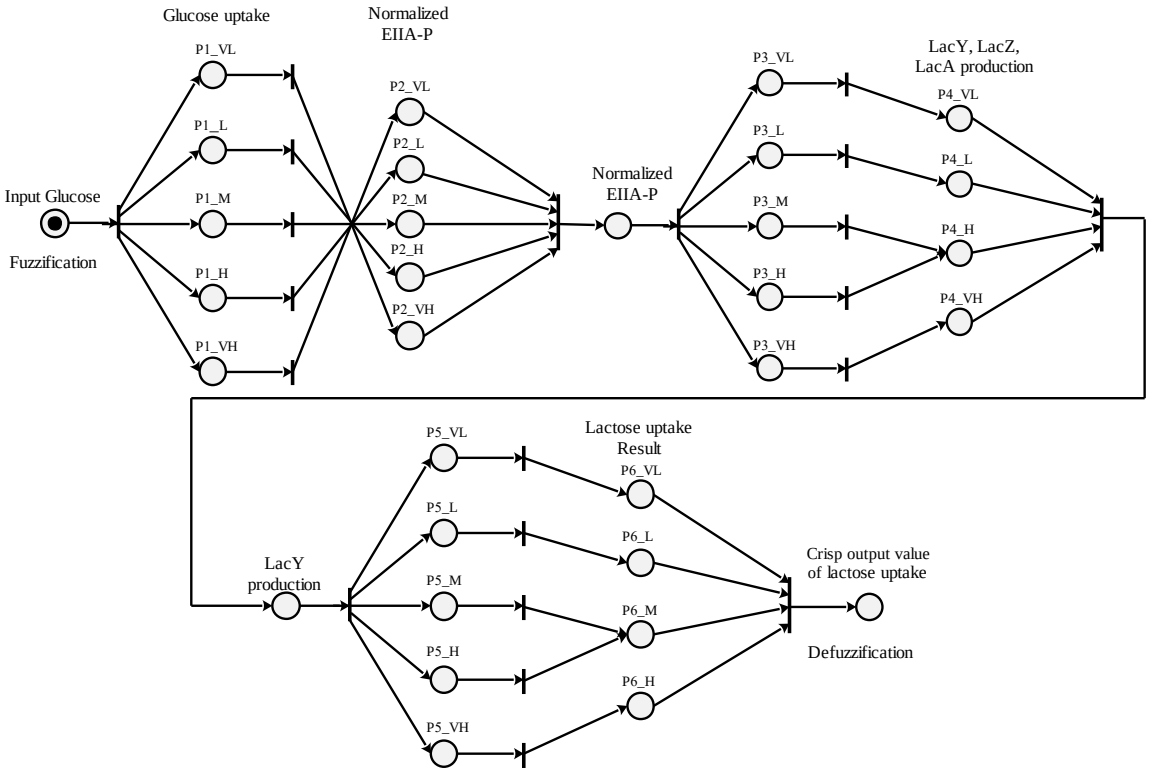


Fig-4: The FRPN Model of lactose operon in Escherichia coli catabolite repression.

R14: IF Lactose uptake is VL or L or M THEN Allolactose (normalized) is L;
R15: IF Lactose uptake is H or VH THEN Allolactose (normalized) is H;

A numerical outcome is taken from the controller after the deduction and defuzzification of a fuzzy outcome has been finished. The relationship between the rates of creation of allolactose and the LacZYA proteins were the accompanying:

R16: IF Allolactose is VL or L or M THEN Normalized LacY, LacZ, LacA production is M;
R17: IF Allolactose is H or VH THEN Normalized LacY, LacZ, LacA production is H;

According to the following two rules, the relationship between LacY and lactose uptake are:

R18: IF LacY production is VL or L or M THEN Lactose uptake is L;
R19: IF LacY production is H or VH THEN Lactose uptake is M;

At long last, the lactose take-up rates originating from both the enlistment and the catabolite suppression consequences for lac operon are included request to decide the subsequent lactose take-up rate.

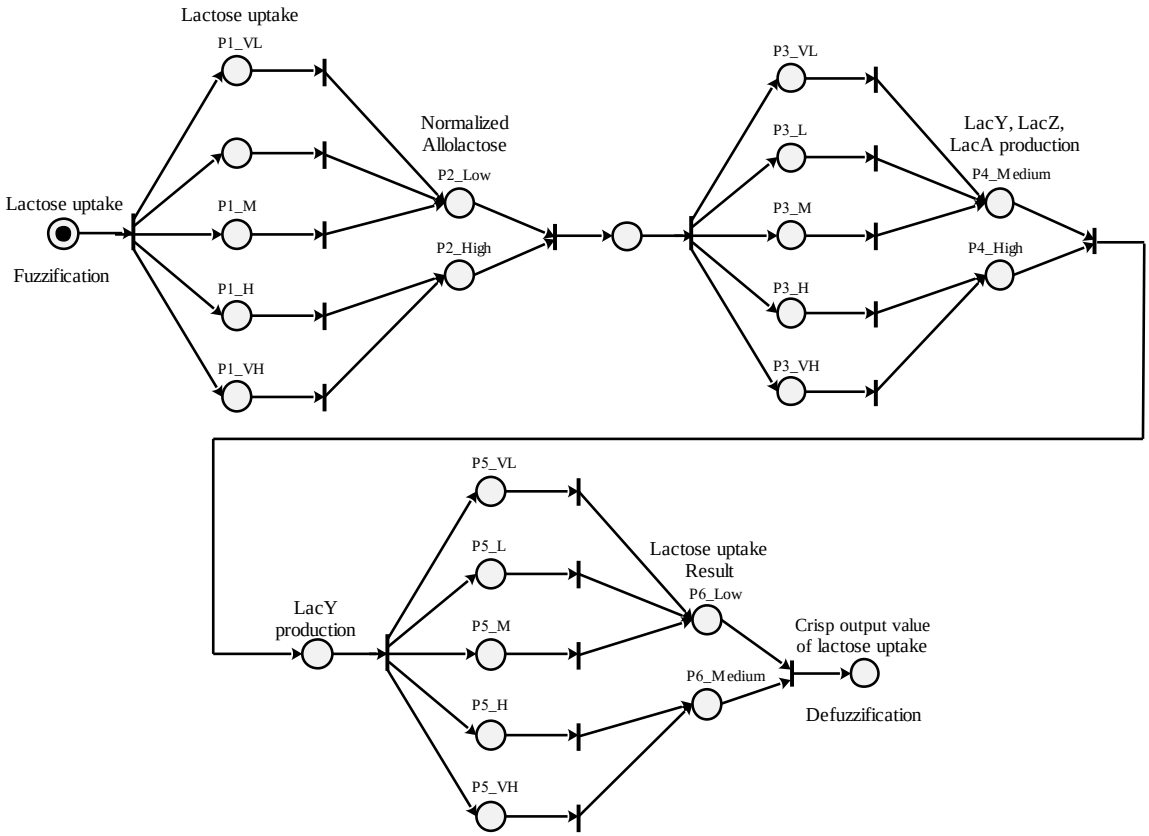


Fig.5. the FRPN Model of lactose operon in Escherichia coli induction.

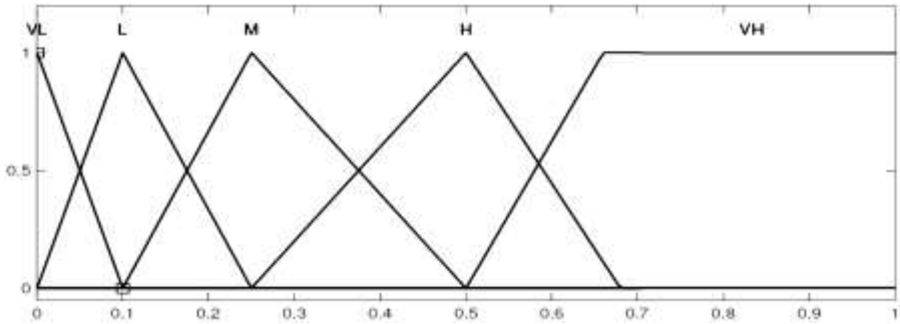


Fig-6: The fuzzy input MFs lac operon (Catabolite repression and induction) level

Glucose take-up rates are fuzzified with a specific end goal to figure EIIA-P values as in Fig 6. The numerical estimation of 0.34 could be doled out a semantic estimation of 0.63 medium and 0.37 high as appeared in Table 2. The aggregate of the weights of the semantic qualities ought to be 1.00. These enrollment work esteem can be utilized as reality level of every suggestion.

Table-2: input data for the model of MFs

Input Data	Crisp Value	Membership Function Value				
		Vlow	low	medium	high	Vhigh
Glucose Uptake	0.34	0.0	0.0	0.63	0.37	0.0

Given α^0 and M^0, the proposed model of FRPN used to obtain the outputs. According to the definition of FRPN algorithm is

$$I=\left\{\begin{matrix}
10000000000000000000\\
01000000000000000000\\
00100000000000000000\\
00010000000000000000\\
00001000000000000000\\
00000100000000000000\\
00000100000000000000\\
00000100000000000000\\
00000100000000000000\\
00000100000000000000\\
00000010000000000000\\
00000001000000000000\\
00000000100000000000\\
00000000010000000000\\
00000000001000000000\\
00000000000100000000\\
00000000000010000000\\
00000000000010000000\\
00000000000010000000\\
00000000000010000000\\
00000000000001000000\\
00000000000000100000\\
00000000000000010000\\
00000000000000001000\\
00000000000000000100\\
00000000000000000010\\
00000000000000000001\\
00000000000000000001\\
00000000000000000001\\
00000000000000000001
\end{matrix}\right\}
\qquad
O=\left\{\begin{matrix}
00000000000000000000\\
00000000000000000000\\
00000000000000000000\\
00000000000000000000\\
00000000000000000000\\
00001000000000000000\\
00010000000000000000\\
00100000000000000000\\
01000000000000000000\\
10000000000000000000\\
00000100000000000000\\
00000010000000000000\\
00000010000000000000\\
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00000001000000000000\\
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00000000011000000000\\
00000000000100000000\\
00000000000010000000\\
00000000000001000000\\
00000000000001000000\\
00000000000001000000\\
00000000000001000000\\
00000000000001000000\\
00000000000000100000\\
00000000000000010000\\
00000000000000001100\\
00000000000000000010
\end{matrix}\right\}$$

From the rule base, confidence matrix μ = diag(0.95, 0.9, 0.8, 0.9, 0.95, 1.0, 1.0, 0.95, 0.8, 0.8, 0.8, 0.95, 1.0, 1.0, 0.95, 1.0, 1.0, 0.95, 0.8, 0.8, 0.8, 0.95, 1.0).

Its start point as a vector

$$M^0 = (1,1,1, 0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0)^T .$$

and start values of our models as a vector

α^0= (0.0,0.0,0.63,0.37,0.0,0.0,0.0,0.0,0.0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0)^T.

Using the algorithm we obtain

neg(α^0) = (1,1,0.37,0.63,1,1,1,1,1,1,1,1,1,1,1,1,1,1,1,1,1,1,1,1,1,1,1,1,1,1,1,1)^T,

$V_k = I^T \otimes (neg\alpha^k)$ V_0 = (1,1,0.37,0.63,1,1,1,1,1,1,1,1,1,1,1,1,1,1,1,1)^T,

ρ_F^k = neg V_k ρ_F^0 = (0,0,0.63,0.37,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0)^T,

$\alpha^1 = \alpha^0 \oplus [(O \,.\, \mu) \otimes \rho_F^0]$

α^1 = (0,0,0.63,0.37,0,0,0.33,0.50,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0)^T,

$M^1 = M^0 \oplus [O \otimes V^0]$

M^1 =(1,1,1,1,1,1,1,1,1,1,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0)^T .

For the FRPN Model of lac operon (catabolite restraint), the execution result is appeared in Fig. 4. Take note of that the calculation still proceeds at the second step, in spite of the fact that M7 = 1n. The checking and truth degree in the fourth thinking venture is the same as those in the eighth step. In this way, the thinking ends after ninth thinking steps. The last truth degree is α7 = (0,0,0.63,0.37,0,0,0.33,0.50,0,0,0.54,0,0,0,0.66,0.34,0,0, 0.524,0.323,0.595,0,0,0,0.5,0.5,0,0,0.4,0.475)T. Reality degrees of the concerned lac operon in Escherichia coli catabolite restraint can be grabbed by defuzzification, as appeared in Fig. 4. In this manner, the framework in all probability has the estimation of "The catabolite restraint" with a certainty of 0.635.

Thus, the FRPN Model of lac operon in Escherichia coli enlistment the execution result is appeared in Fig. 5. From the lead base, certainty network μ = diag(0.8, 0.8, 0.8, 0.9, 0.9, 1.0, 1.0, 0.8, 0.8, 0.8, 0.9, 0.9, 1.0, 1.0, 0.8, 0.8, 0.8, 0.9, 0.9, 1.0). Its underlying stamping vector

M^0 =(1.0,1.0,1.0,1,1,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0)^T .

and underlying degrees as a vector

α^0= (0.0,0.0,0.623,0.367,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0)^T.

The reasoning steps:

The truth degree and marking vectors at the 1st step:

0,0,0.63,0.37,0.504,0.333,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0

1,1,1,1,1,1,1,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0

The truth degree and marking vectors at the 2st step:

0,0,0.63,0.37,0,0.504,0.333,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0

1,1,1,1,1,1,1,0,0,0,0,0,0,0,0,0,0,0,0,0,0,0,

The truth degree and marking vectors at the 3st step:

0,0,0.63,0.37,0,0.504,0.333,0.33,0,0,0,0,0,0,0,0,0,0,0,0,0,0

1,1,1,1,1,1,1,1,0,0,0,0,0,0,0,0,0,0,0,0,0,0

The truth degree and marking vectors at the 4st step:

0,0,0.63,0.37,0,0.504,0.333,0.33,0,0,0.635,0.365,0,0,0,0,0,0,0,0,0,0

1,1,1,1,1,1,1,1,1,1,1,1,0,0,0,0,0,0,0,0,0,0

The truth degree and marking vectors at the 5st step:

0,0,0.63,0.37,0,0.504,0.333,0.33,0,0,0.635,0.365,0, 0.508,0.3285,0,0,0,0,0,0,0

1,1,1,1,1,1,1,1,1,1,1,1,1,1,0,0,0,0,0,0,0,0

The truth degree and marking vectors at the 6st step:

0,0,0.63,0.37,0,0.504,0.333,0.33,0,0,0.635,0.365,0, 0.508,0.3285, 0,0,0,0.65,0.35,0,0,0

1,1,1,1,1,1,1,1,1,1,1,1,1,1,1,1,1,1,1,1,0,0,0

The final truth degree is α^7 = (0,0,0.63,0.37,0,0.504,0.333,0.33,0,0,0.635,0.365,0,0.508,0.3285,0.32,0,0, 0.65,0.35,0,0.52,0.315)^T,

As shown in Fig. 6, after the defuzzification, the system most likely has the value of “induction” with a confidence of 0.717.

The Final Outputs Simulation

The adaption of fuzzy sets for speaking to states and properties and fuzzy rationale based thinking for portraying procedures can be utilized to show organic frameworks [30]. Fuzzy sets catch the commonly indeterminate and fragmented, subjective learning about natural substances and are appropriate to speak to restricted information, estimated estimations and also mistake inclined information. Because of the way that they can remain for self-assertive properties,

it is conceivable to consistently speak to a wide range of outside and inward components affecting a framework. Fuzzy sets can be composed unreservedly by a client as indicated by his needs. Fuzzy thinking Petri net frameworks permit the definition of organic procedures utilizing straightforward yet capable govern frameworks, which can be planned utilizing characteristic dialect. In this way, theories concerning the conduct of elements or impacts between substances can be made an interpretation of specifically into executable frameworks.

For instance, in Fig. 7, the focus practices of glucose, EIIA-P, and lactose are appeared. In this figure the model subjectively mirrors the swaying conduct of glucose, EIIA-P, and lactose. The expressed five tenets suffice to make a wavering conduct subjectively as takes after:

R1: IF Glucose uptake is VL THEN Normalized EIIA-P is VH;
R2: IF Glucose uptake is L THEN Normalized EIIA-P is H;
R3: IF Glucose uptake is M THEN Normalized EIIA-P is M;
R4: IF Glucose uptake is H THEN Normalized EIIA-P is L;
R5: IF Glucose uptake is VH THEN Normalized EIIA-P is VL;

We first test the concentration of glucose and EIIA-P. For doing this we simulated the system in the time interval [0, 14] with different initial total concentration ranging from 1 to 5. The right figure in Fig. 7 gives the concentration levels of lactose at and different glucose concentrations.

The dynamics of system (Fig. 5) is reported. Here we only give the concentrations of EIIA-P and lactose with different total glucose concentrations.

When simulating system (Fig. 5), we found that the ratios of the concentration levels glucose, EIIA-P, and lactose are nearly the same with regard to different total glucose concentrations.

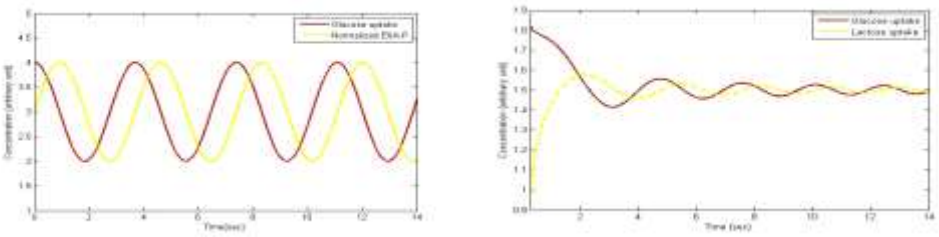

Fig-7: The dynamical mechanism of the system of figure 5. The FRPN model qualitatively reflects the oscillating behavior

CONCLUSIONS

In the paper, we have built up a fluffy thinking Petri net (FRPN) show for the hereditary direction of the lac operon in E. coli. Transcriptional direction by the operon was demonstrated by FRPN formalism. A FRPN model is proposed to execute lac operon direction parallels, which joins the benefits of both of fluffy rationale and Petri net hypothesis. The proposed calculation receives a lattice condition design that is like that in the standard PNs. Utilizing this calculation; we can rapidly get reality degrees of the considerable number of suggestions from the underlying ones.

This work surprisingly proposes to utilize FRPNs for lac operon control. The significant elements of our approach are: (1) Since the FRPN is a graphical instrument, we can give a depiction of the commonplace strategy of fluffy thinking; (2) imagine the structure of a manage based fluffy thinking framework; (3) with the scientific establishment of FRPN, we develop the thinking ventures for FRPN thinking; and (4) Finally, we portray the FRPN based demonstrating for hereditary direction of the lac operon in E. coli (catabolite suppression and acceptance) to approves the achievability of FRPN model. The outcomes found in this review demonstrate that FRPN can be superior to Boolean rationale. FRPN controlling activity due to the quality translation display inside its surmising can start and screen constant quality articulation of fitting chemicals because of modifications in fixation levels of activators and repressors. The administrative qualities are considered either "on" or "off" in Boolean rationale, along these lines, the adjustment of administrative structure to changes in substrate fixation in the medium can't be reflected as it really happens.

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