



## Methodology Article

# The Exchangeable Markov Multi-states Growth Process Incorporate with an Artificial Neural Network of Preterm Infants in an Incubator

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**Abstract:** The standard incubator used to monitor the development of preterm infants, with much attention for random optimization can interrupt the three main parameters (oxygen, environmental temperature, and humidity) responsible for preterm growth. The artificial neural network (ANN) has been recently proposed as a novel technique to control those parameters to provide a better and stabilized environment in an incubator. Unfortunately, this novel technique cannot continuously provide and indicate the update challenge of preterm growth. The objective of this paper is to apply a Markov multi-state growth process incorporates with multilayer feed-forward artificial neural network as an improved methodology to continuously control and provide an update of preterm growth in an incubator. The exchangeable Markov growth process, transition graph, and artificial neural network discussed on and applied in the designed incubator as methodology in paper and then make a joint density function of Markov multi-states growth process through multi-steps designed Algorithm to get the theoretical results. The updated measurements (weight, height, and head-perimeter) associated with controlled parameters used as input to the threshold logic unit (TLU) of ANN and then distinguish whether the growth process is abnormal or normal at each state. The summarized algorithm and multilayer feed-forward ANN utilized the panel data collected at Murunda hospital in Rwanda as input to show the application of improved methodology proposed in this paper, specifically, multi-state growth process of preterm infants across gender. As results, the continuous exchangeability of the growth process at each state has updated and may show abnormal or normal of growth process, and then sensors may notify these change through the joint density function of Markov multi-states growth process. Thus, improved methodology can increase the security and minimize time consumption in continuous monitoring growth process in an advanced way in time this idea has been implemented.

**Keywords:** Preterm Growth, Artificial Neural Network, Markov Multi-state Process, Incubator

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## 1. Introduction

Preterm birth is any birth before 37 completed weeks or fewer than 259 days of gestation. With those of less than 1000 grams need to be transferred into the incubator to optimize oxygen and energy consumption, and provide a well environmental condition regulated between 22 to 26°C without hostile effects to ensure their growth as a normal live condition [1-3].

The functionalities of an incubator have been improved to facilitate the rapid and safety preterm growth, and for minimizing the challenge of exchangeability of environmental temperature, which was suggested to be an issue to concern for its sensitivity with preterm infants [4]. Unfortunately, preterm infants faced several challenges as skin-to-skin contact (SSC) [5]. Several studies conducted to demonstrate the growth of preterm infants by using fat mass (FM), lean mass (LM), and body mass index (BMI) [6, 7], dual-energy X-ray absorptiometry (DXA), bioelectrical

impedance analysis (BIA), isotope dilution, magnetic resonance imaging (MRI), and air displacement plethysmography (ADP) [8].

Recently, the artificial neural network (ANN) implemented as back-propagation method was used to control the internal environment of the premature infant incubator, where Sensors were used to indicate temperature, humidity, and oxygen concentration of the incubator internal environment, and their output was entered to the ANN to identify the corresponding case and decide the proper reaction upon previous training [9].

In this current study without loss of generality of the ANN application in an incubator, ANN used to detect and control the continuous growth of preterm. The time-varying and environmental temperature, humidity, and oxygen concentration adjustment in an incubator lead to the concept of exchangeable Markov multi-states growth process, and incorporation with artificial neural network can be monitored.

The initial theory of Markov multi-states identified the role of integrating the "Survival and theory of stochastic processes" into the framework application of event history analysis [10]. These stochastic processes applied when there is observed and unobserved information about data as has been introduced first by Markov, and explained by the study [11]. When the concerned observations were related to the health aspect, especially for the patient covariates, the Markov multi-state approach intervenes for further analysis. For example, parametric models such as continuous-time Markov process has been considered for under alternating observations [12-14], while the non-parametric models are not suitable for the highly variable health process [15]. Joseph, et al., discussed the importance of multi-states process and completing of risk models for complex models but this concept has been applied in another field [16]. This Markov multi-states extended in health, where Walter Dempsey established the exchangeable Markov multi-state survival process that can be applied in several health studies. This approach was concentrated on the balancing between parametric and non-parametric approaches [17]. These models take care of the assumption about the underlying states space process and focused on the recruitment process of the patients.

Therefore, from this, Walter's approach cannot work on the panel data whose multiple explanatory variables. The proposed approach here is a particularity of Walter's approach and accurately analyze the growth process of preterm infants with little care on the participant's independence or dependence. However, mainly this paper develops the new insight to monitor multi-states growth process of preterm in an incubator. Of special interest, this approach may show the exchangeable effect among the preterm infant's sex. Both continuous and discrete-time for nutrition and treating preterm in the multi-states process were assumed to be the same for all preterm.

## 2. Methods

The physical growth index (PGI) of preterm infants is defined as the variables (weight, height, and head perimeter)

that indicate the physical growth of preterm infants. The multilayer feed-forward NN was applied to determine the exchangeability of growth process in multi-states of preterm infants. The successive time-varying correspond with the recorded data, multi-states and node-points in artificial neural network (ANN) used to show how improved incubator may produce updated information on continuous growth of the infant. To get the application of this methodology, the proposed design of improved incubator and recorded data from current incubators provided by Murunda district hospital have been applied in this study.

### 2.1. Improved Incubator

The incubator normally serves as the microenvironment, controlling light, sound, smell and protecting from infection can disturb the development of preterm infant inside the incubator. The current infant incubator provides stable levels of environmental temperature, relative humidity, light condition, and oxygen level up to an extent so that the preterm maintain the same condition as in the womb. The artificial neural network (ANN) used to control the internal environment and closed-loop system to regulate temperature, humidity and light intensity of an incubator [9]. This application of ANN illustrated below on (A) can be improved and used to indicate and update the continuous preterm growth. The improved design illustrated on (B) contains may contains automatic system to display the update measurements of preterm (weights, height, and head perimeter), environment temperature, humidity and oxygen controlled by ANN and threshold logic unit (TLU) for not only used to control but also to indicate continuous growth process of preterm in an incubator. The detail of the internal circuit of the novel techniques (ANN) applied in an incubator illustrated in this reference [9].

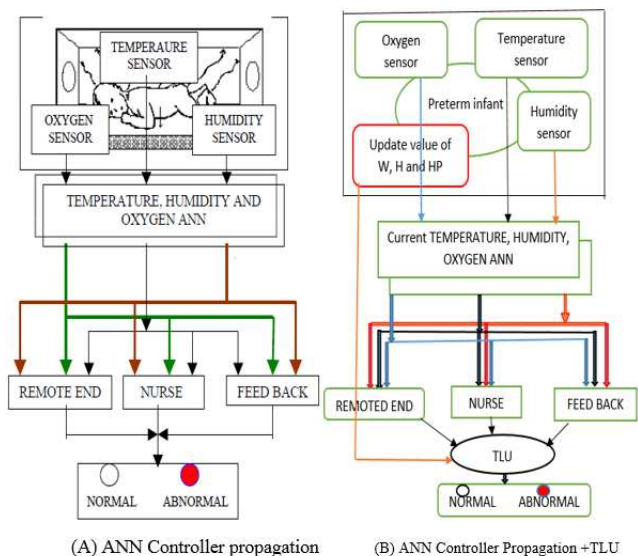


Figure 1. Improved incubator.

### 2.2. Markov Multi-State Growth Process

The Markov multi-states growth process is defined as the

function  $Y$  from the set  $\mathbb{N} \times \tau$  in the state space  $S$ . We assume now that the state space is finite, i.e.  $|S| < \infty$ . We do this, since the growth process of preterm infants is in continuous time, despite the collected panels usually are in discrete time, and external and internal temperature in an incubator also measured continuously but are recorded in discrete time. On the hand of this, the growth process can be considered in both discrete and continuous time. If  $\mathbb{N} = \tau$ , the response variable is in discrete time, and if  $\tau = \mathbb{R}^+$ , the response variable is in continuous time. Each  $Y$  is a pair of  $(U_{u(t,T)}, t)$ , and the value of  $Y(U_{u(t,T)}, t)$  where  $U_{u(t)}$  is an element of  $S$  corresponding to the state of the preterm infant  $U_{u(t,T)}$  at time  $t$  with specific temperature ( $T$ ). The script  $u(t, T)$  of  $U$ , is the function determined by Neural Network that combines weight, height and head perimeter. Since at any state sequence, there can enter or remove the preterm infants, we have to define the absorbing state. This state is taken in the survival process, particularly, in the recruitment process of the new preterm, it can be defined as  $\delta \in S$  so  $Y(U_{u(t,T)}, t) = \delta$  implies  $Y(U_{u(t,T)}, t)$  for all  $t > t$  [17]. Therefore, the survival time which is the same as the growth length of time of the preterm infant  $T_U$  is a deterministic function of the multi-state growth process  $Y$ :

$T_U = \inf\{t \geq 0: Y(U_{u(t,T)}, t) = \delta, \text{ for } U_{u(t)} \in \mathbb{N}, Y(U_{u(0,0)}, 0) \neq \delta, T_U > 0, \text{ at this stage of the recruitment, preterm infants do not yet enter into an incubator.}$

### 2.3. The Transition Graph of the Multi-states Growth Process

The transition graph of preterm infant's growth states represents the set of underlying transitions between growth processes out of the set of  $|S|^2$  possible transitions, for  $|S|$  is finite states number. The transition graph is the directed graph of vertex  $V$  and edge  $E$  denoted  $G = (V, E)$ . This theory of graph representation was explained by Walter and applied in the multi-states survival process [17]. We define vertex  $V$  as the set of all states and directed edge  $E$  contains the set of all edges that represent all transitions  $(i, j)$  so preterm infants' growth at time  $t$  can shift from  $i$  to  $j$  where  $j$  be the next states, and the exchangeabilities phenomena can exist from initial to next state. The clear assumption of this directed graph is that,  $(i, i)$  or  $(j, j)$  is not an edge. In this study, we assume that the preterm infants' growth process is straight forward but not backward, i.e we consider an edge  $(i, j)$  but not  $(j, i)$  although there can be the trends of the growth process, if  $V \in |S|$ ,  $j = i \notin S$ . We can write  $P_G$  to represents the set of  $|S|$  by  $|S|$  transitions matrix  $P$  satisfy  $\sum_{j \in V} P_{i,j} = 1, P_{i,j} \geq 0$ , for all  $i, j \in V$  and  $P_{i,j} = 0$  for all  $(i, j) \in E$ . The interested part here is that on the trend-states, the transition probabilities can be reduced or increased but not equal to zero.

### 2.4. The Exchangeable Markov Process

Walter defined exchangeability as  $Y_{[n]}$  to be partially exchangeability if for the permutation  $\sigma: [n] \rightarrow [n]$ , the patient rebelled process  $Y_{[n]}^\sigma = \{Y(\sigma(1), t), \dots, Y(\sigma(n), t) | t \in \tau\}$  is a version of  $Y_{[n]}$ . This definition leads to define again  $Y_{[n]}$  like

the time-homogenous Markov process for every  $t, t \geq 0$ , with condition distribution of  $Y_{[n]}(t + t)$  given the multi-state survival process from history up to time  $t$ , and  $H_{[n]}(t)$  only depends on  $Y_{[n]}(t + t)$  [17]. This time-homogeneous Markov process characterized by continuous-time and discrete-time process. This factor leads to two approaches for estimating the growth process probabilities. A discrete-time,  $U_{u(t,T)} \in \mathbb{N}$ , the transition probability distribution are given by

$$P[Y(U_{u(t,T)}, t) = j | Y(U_{u(t,T)}, t) = i] \sim [P_t]_{i,j} \quad (1)$$

Where  $(i, j) \in E$  of  $P_t$ . The discrete-time process obtained by this procedure with probability measure is called an exchangeable Markov multi-state growth process in discrete-time. In the fact that  $U_{u(t,T)} \in \mathbb{R}^+$ , the process called continuous-time exchangeable Markov multi-state growth process and the associated transition probability distribution estimated as follow:

$$[P_t]_{i,j} = \int (1 - P_{min}) \sum (dp) < \infty, P_{min} P_{i,i} \text{ for } i \in |S| \quad (2)$$

And  $c = c_{i,j} \geq 0 | (i, j) \in E$  so the continuous-time process obtained by this procedure with probability measure which is a version of  $Y_{[n]}$  [17]. The estimated of these probabilities follow the core assumption of hidden Markov models, where the current state depends only on the previous state, not on the whole history of the states. The hidden Markov models associated with the Markov multi-state growth process either in discrete-time or continuous-time estimated with using the detailed and proved theorems illustrated in this book [11] and the EM Algorithm [18].

### 2.5. Artificial Neural Network (ANN)

The growth process of preterm infants in an incubator can be understood in a continuous neural functional system. The physical outlook of this growth process can take much more time, for example, we cannot wake up in the morning, and know how much weight increases to a child of one month of birth, and also the current incubator cannot indicate continuously information about the growth of infants.

Recently, the artificial neural network (ANN) used as novel techniques in an incubator to control environmental temperature through three parameters (temperature, humidity, and oxygen) [9]. The current technique is based on using the monitored parameters' values and linked with physical measurements (weights, height, and head-perimeter) of preterm to show continuous growth process of preterm.

An ANN is simulated as the human brain, where the brain can adapt to a new changing of the environment [19], it contains the set of processing elements known as nodes or neurons. These elements connected themselves and produce a directed graph discussed in the previous section and in [20]. Referring to applications of ANN, we pleased to use it in this study for merging its performance to the Markov multi-state to control and show the continuous growth of infants. This approach illustrated at figure 2 works:

- a) The input is the PGI (weight, height, and head-perimeter) and the ANN weights are the

environmental temperature ( $T_i$ ) which are the same at each Input, for  $i = 0, 1, 2, \dots, n$ ,  $n$  is the number of states correspond with the occurred event and at  $j = 1, 2, \dots, m$  number of preterm infants;

- b) The activation key or jumping condition has to be determined by the conventional average of BMI multiplied with updating parameter  $\beta$ . This average has to be estimated on each multi-states growth process. Let  $\mu$  is the average of BMI, then  $\beta\mu = \theta_i$ ,  $\theta_i$  will be the activation key for  $i = 0, 1, 2, \dots, n$  at  $m$  number of

preterm infants;

- c) The logical assumption is that to assess the exchangeability, we have to conduct pre-training the individual Input and then combine all together for confirming the decrease or increase of preterm infant's growth.
- d) The sigmoid function used in threshold unity to indicated the exchangeable multi-state growth process of preterm.

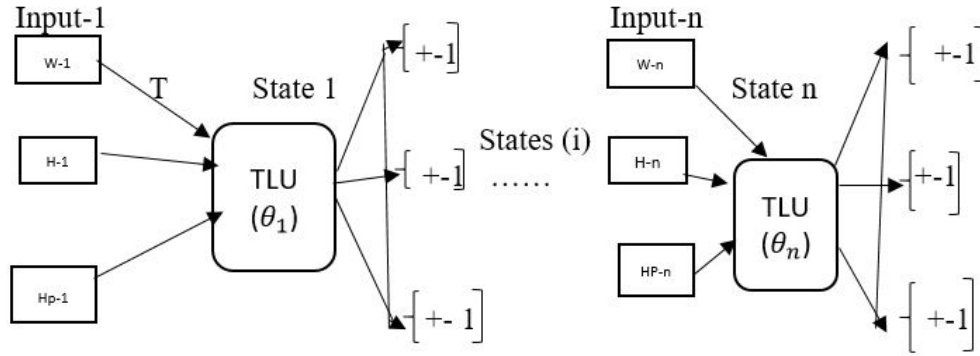


Figure 2. Markov multi-states incorporate with multilayer feed-forward ANN design.

Note: W, H, and HP are the preterm infants' weight, Height, and Head perimeter respectively, T is the environmental temperature, TLU is Threshold Logic Unit associates with each Markov multi-state and  $\theta_i$  is the TLUs parameter on each state.

In pre-training of each Input, we have to estimate the activation key denoted as  $a$  and computed as follow:

$$\begin{cases} a_i = \Delta T_i w_i \text{ for Input weight} \\ \dot{a}_i = \Delta T_i HP_i \text{ for head perimeter} \\ \ddot{a}_i = \Delta T_i H_i \text{ for height Input} \end{cases} \quad (3)$$

After the pre-training step, we then make combined training, where the activation key will be equal to all Input at each node ( $\mu$ ), and then can be written as follow:

$$\mu_i = \sum_{i=0}^n \Delta T_i w_i + \Delta T_i HP_i + \Delta T_i H_i \quad (4)$$

This equation can be written as:

$$\mu_i = \sum_{i=0}^n \Delta T_i (w_i + HP_i + H_i) \quad (5)$$

The training process at each node is then worked as follow:

$$y_i = \begin{cases} +1 \text{ for } a_i \geq \theta_i \\ -1 \text{ for } a_i < \theta_i \end{cases} \quad (6)$$

The actual values of the output can be estimated as:

$$y_i = f_i(\sum_{i=0, j=1}^{n, m} \Delta T_i (w_{ij} + HP_{ij} + H_{ij})) \quad (7)$$

Where  $y_i$  is the final output, and  $f_i$  is the transfer function from one node to the next node, and it called the sigmoid function [20, 21], which can be written as

$$f_i = 1 / (1 + \text{Exp}(-\Delta T_i (w_i + HP_i + H_i))) \quad (8)$$

## 2.6. The Joint Density Function of Markov Multi-state and ANN

We above discussed on the transition probability distribution on both discrete-time and continuous-time exchangeable Markov multi-state for preterm infants 'growth, equations (1) and (2). We then discussed applying ANN in the growth process of preterm infants, where a sigmoid function works as a transfer function from one node to the next, equations (8) and (7). The main idea of this paper is to determine the density function that joins Markov multi-state and ANN. This function will always indicate the update of the growth process of preterm infants in multi-state at any time for every adjustment of environmental temperature. The combination of (1), (2), (7), and (8) give the new equation that can be denoted as  $G(t)$  and defined as the growth process of preterm infants, and it can be written as:

$$G(t) = \beta y_i [P_t]_{i,j} \quad (9)$$

This equation (9) can also be written as

$$G(t) = \beta f_i (\sum_{i=0, j=1}^{n, m} \Delta T_i (w_{ij} + HP_{ij} + H_{ij}) [P_t]_{i,j})$$

Where  $f_i$  is the transfer function from the initial node to the next node or state,  $[P_t]_{i,j}$  is the transition probability distribution from  $i$  state to  $j$  state, and  $\beta$  is the updating parameter ranged  $0 \leq \beta \leq 1$ . This update needed also on the environmental temperature since at every node or state, there is an update recorded values [21].

*Multilayer feed-forward Algorithm*

Initial step: Pre-training the Inputs

For  $i = 0$ , compute  $\begin{cases} a_i = \Delta T_i w_i \text{ for weight} \\ \dot{a}_i = \Delta T_i HP_i \text{ for headperimeter} \\ \ddot{a}_i = \Delta T_i H_i \text{ for height} \end{cases}$

Search the optimum at each node or state;

Compute  $y_i = \begin{cases} +1 \text{ for } a_i \geq \theta_i \\ -1 \text{ for } a_i < \theta_i \end{cases}$

Let  $P_t = \pi(0)$  be the initial transition probability at  $i = 0, j = 0$ ;

Second step: for  $i = 1, 2, \dots, n$

Compute  $f_i = 1 / (1 + \text{Exp}(-\Delta T_i (w_i + HP_i + H_i)))$ ;

Compute  $y_i = f_i (\sum_{j=0}^{n,m} \Delta T_i (w_{ij} + HP_{ij} + H_{ij}))$ ;

Compute  $[P_t]_{i,j} = [P_t]_{i-1,j-1} \text{Exp}(-\Delta T_i (w_i + HP_i + H_i))$ ;

Last step: choose  $\beta$  as constant;

Compute  $G(t) = \beta f_i (\sum_{i=0}^{n,m} \Delta T_i (w_{ij} + HP_{ij} + H_{ij})) [P_t]_{i,j}$

### 3. Analysis and Application

The sheets of data contained weight (kg), height (m), and head perimeter (m) of twelve preterm infants collected with the variation between the external and internal environmental temperature at Murunda hospital has been applied to get an understanding about the theoretical application of improved incubator. The exchangeability Markov multi-state incorporate with multilayer feed-forward artificial neural network (ANN) used as addition novel method to show the growth process of preterm infants.

Table 1. Activation key on each Threshold logic units (TLU) correspond to each state.

TLUs	Activation key for Female (beta = 0.2)		Activation key for Male (beta = 0.2)	
States	BMI (kg/m <sup>2</sup> )	Key-values	BMI BMI (kg/m <sup>2</sup> )	Key-values
S-1	10.36	2.07	10.48	2.09
S-2	11.12	2.22	11.21	2.24
S-3	12.17	2.43	11.95	2.39
S-4	11.36	2.27	11.09	2.21
S-5	sessme3.25	3.25	15.86	3.17

This table represents the multi-state growth process state at s-1, BMI (body mass index) at each state and key-values which update whether the growth of preterm is normal or abnormal across gender.

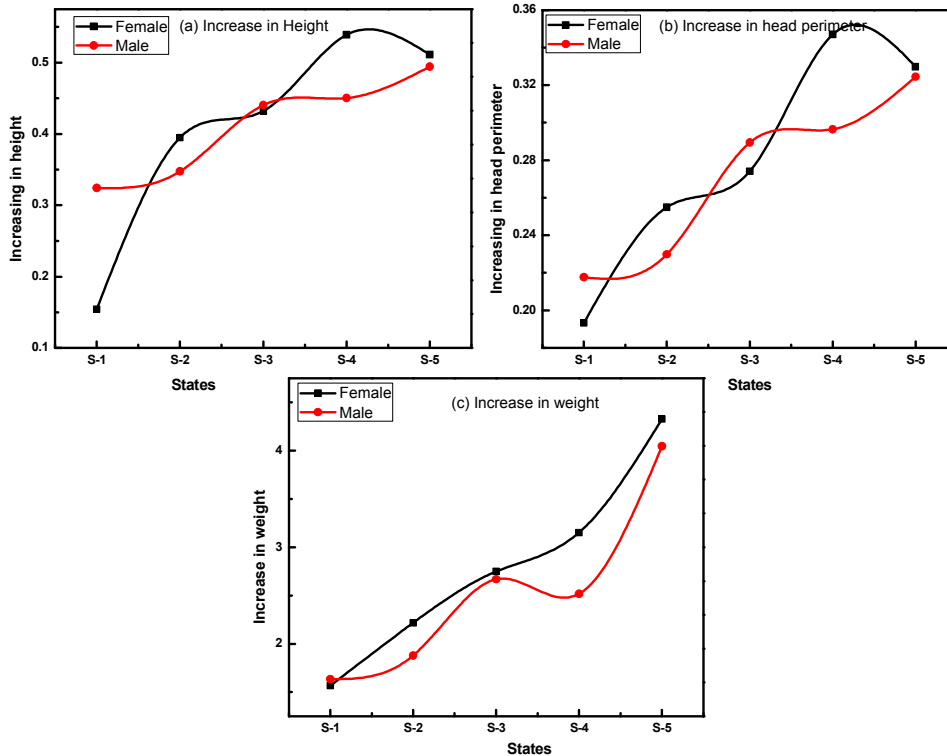


Figure 3. The internal exchangeability of preterm growth in weight, height, and head-perimeter.

This figure represents the individual Input parameter of preterm infant's increases in multi-state growth process across gender. The value of these parameters is to be read after being controlled by ANN which means are updated internal growth exchangeability. This internal multi-state

exchangeability growth (increase or decrease) of an infant at each state can be seen even by traditional computation and plot the recorded sheets of data in different states. The increase or decrease in the three parameters (weight, height, and head perimeter) of preterm infants in an incubator are

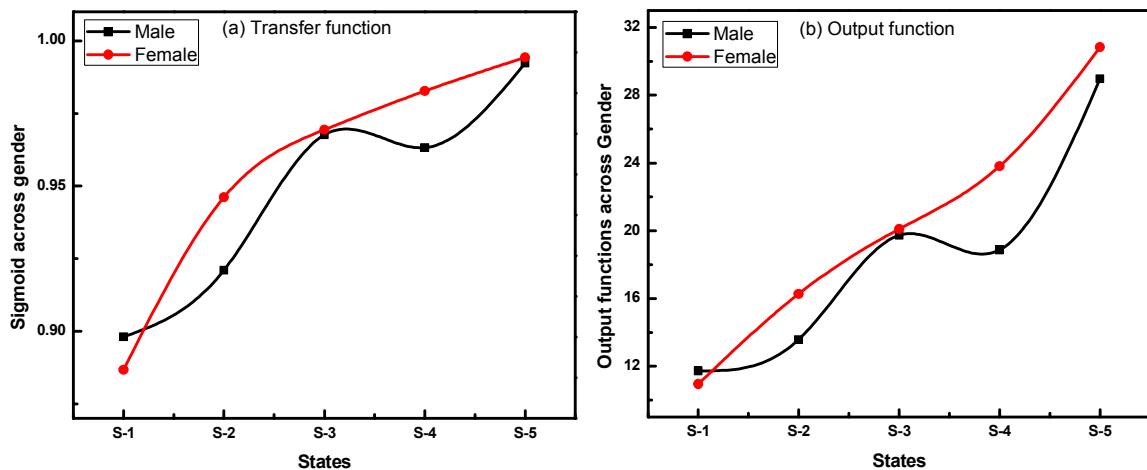
slightly different, where the exchangeable growth in female preterm infants is higher than that of male (Figure 3).

This table shows the results from TLU of each preterm infant in an incubator. The positive one (+1) and a negative one (-1) indicate NORMAL and ABNORMAL of the multi-state growth process of preterm infants respectively. At first, second and third states, the growth of two females were abnormal. The updated output indicate three successive abnormalities of one preterm, and on first and third states, there was an abnormality of another preterm. On the side of the male, the growth of three preterm infants was successively abnormal from first and second states, two successive

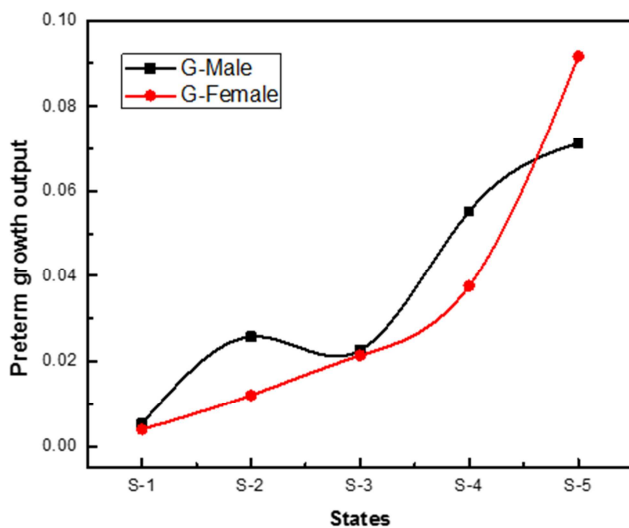
abnormals from state 4 and 5 on one preterm (Table 2).

**Table 2.** The output of ANN on each Input corresponds to each state across gender.

The growth process of Preterm infants									
Female					Male				
S-1	S-2	S-3	S-4	S-5	S-1	S-2	S-3	S-4	S-5
-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	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	1	-1	-1	1



**Figure 4.** The transfer and output functions in exchangeable multi-states growth across Gender.



**Figure 5.** The update joint multi-state growth process with ANN across Gender.

This figure shows the sigmoid transfer and output functions inside of threshold logic unit respectively. The transfer function plays a key role in the multi-state growth process to transfer the preterm infant growth level to the next state level even if it can be abnormal growth process. The output function controls the outlook of the growth process as a result of the threshold logic unit (TLU) before being

updated (Figure 4).

This figure represents the joint density function of the Markov multi-state and multilayer feed-forward ANN that showing the update continuous growth process of preterm infants in an improved incubator. Those outputs occurred by applying the combined designs from Figure 1 and Figure 2. The growth process in male decreases continuously from the second state up to the third state, and then slight decrease from the middle of fourth state up to fifth state. Similar to the growth process of female, it slight decrease from third state up to the middle of third and fourth. The sensors of this improved incubator will continuously notify these abnormalities or exchangeability during growth process of preterm infants (Figure 5).

However, all output of the theoretically improved incubator are subjected to be displayed by automatic system cooperated with controlled parameters in an incubator. Referring to the obtained results, the designed incubator may provide and indicate the multi-state growth process of a preterm infant at each stage of growth.

## 4. Conclusion

Artificial neural network (ANN) used to control environmental temperature, oxygen, and humidity in an incubator to provide a better environment to grow for preterm infants. The exchangeable multi-state Markov



process incorporates with artificial neural network proposed as an improved methodology to continuously control and provide an update growth process of preterm infants in an incubator. The hand-computing and challenges from recorded data may be resolved by using the theoretically designed incubator for saving time and improving the preterm infants' safety. The summarized algorithm of multilayer feed-forward ANN cooperated with sensors may apply to identify abnormal and normal and display the updated growth curve of preterm infants at each state. To show the theoretical application of the current improved methodology, the panel data collected and recorded in five successive stages at Murunda hospital used as input to the threshold logic unit to show the multi-state growth process of preterm infants across gender. The results of the continuous exchangeability of the growth process of preterm infants at each state are the important points to be notified by sensors of improved incubator. However, this methodology may establish the novel technological incubator instead of using the traditional to secure and continuous monitoring growth of preterm infants in an advanced way. This improved methodology can be applied in several technological aspects related to growth process by considering the related effective parameters, as the detection of the continuous growth process of microbes cultivated in laboratory, survival process of patients with a certain disease, resistance of certain virus on the drugs in clinical trials, etc. In this current study, we used the adjusted environmental temperature, therefore, further research will consider all three parameters (temperature, humidity, and oxygen) and design a full internal circuit.

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