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Research Article

A Tumor Growth Model with Unmolded Dynamics Based on an Online Feedback Neural Network Model

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Abstract: In this study, we identify tumor growth system by an online feedback neural network model based on back-propagation method. The modeling and identification of nonlinear dynamic systems is the process of developing and improving a mathematical representation of a system using experimental data. So, it is a problem of considerable importance through the use of measured experimental data in biomedical modeling. As is obvious, in biomedical researches it is really difficult and in some cases impossible to implement research on real patient or such a system which is not possible to empirical tests. To deal with, we need sometime a model close to real system in order to forecast dynamic systems so as to perform researches on models and design controller for control of system.

Keywords: Back-propagation, multi-layer perceptron, online feedback neural network, system identification, tumor growth model

INTRODUCTION

In order to control modern systems one requirement is having structured knowledge about the system which should be pictured in terms of differential or difference equation. The Model of the system has several usages such as simulation, prediction, fault detection and control system design. Models can be obtained by two main methods:

- Using physics laws
- According to a set of data collected during a practical experiment

The first method can be simple, but in many cases is excessively time-consuming; it would be unrealistic or impossible to obtain an accurate model in this way. The second way, which is commonly referred as system identification. A satisfactory model can be often obtained with reasonable efforts. In this study, we focus on the second method (Farrell and Polycarpou, 2006; Norgaard, 2000).

Identification of nonlinear systems can be found in various applications such as neural networks, fuzzy logic and combined neuro-fuzzy systems algorithms (Manel *et al*., 2006; Rouss and Charon, 2008; Johnson *et al*., 2009; Luitel and Venayagamoorthy, 2010; Vieira *et al*., 2005; Fu *et al*., 2009; Lendaris, 2009; Elfelly *et al*., 2010). Recent results show that neural network technique seems to be very effective in identifying a broad category of complex nonlinear systems when complete model information cannot be obtained. Neural networks can be classified as feed Forward Neural Network (FNN) and Recurrent Neural Network (RNN).

The Artificial Neural Network (ANN) is based on information with the ability to imitate and emulate biological neural networks. It is inspired by the capability of the human brain to discover from observation and generalize by abstraction. Also, is a proper method to solve the complex and ill-defined problems. Therefore, it is possible to use them as a powerful data modeling tool which are able to capture and present complex input/output relationships. That is to say, they are specifically applicable in system modeling, like implementing complex mapping and system identification**.**
The main advantages for ANNs are as follows:

- The neural weights are tuned online without any pre-training phase
- The stability and performance of the closed-loop systems can be guaranteed

The main drawback of these neural networks is that the weights' updating do not utilize information on the local data structure and the function approximation is sensitive to the training data (Parlos *et al*., 2001). Since

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recurrent networks incorporate feedback, they have powerful representation capability and can successfully overcome disadvantages of feed forward networks (Kosmatopoulos *et al*., 1995).

There are different kinds of neural networks, such as Multi-Layer Perceptron (MLP), Radical Basis Function neural network (RBF), Self-Organization Mapping net (SOM), Hopfield neural network, Back Propagation neural network (BP), etc. Neural networks are greatly used for approximating functions owing to its simplicity and faster convergence (Eberhard and Dobbins, 1990; David, 1996; Alexander, 2010). Functions approximations by neural networks have done without requiring mathematical description and any relation between inputs and outputs. So, they are often referred to as model-free estimators. The basic modeling philosophy of model-free estimators is that they learn from examples without any knowledge of the model type (Shi and Gao, 2012).

An effective method for learning neural networks is Back-Propagation (BP) (Rumelhart and McClelland, 1986; Yuan and Yu, 2012). A typical BP consists of input layers, hidden layers and output layers. It can perform the mapping between input signals and output signals (Eberhard and Dobbins, 1990; David, 1996). The working principle of the BP learning algorithm is based on a gradient approach in which incremental steps are made in the direction of the steepest descent with respect to the mapping errors. This is achieved by a definition of a least Mean-Square-Error (MSE) function and the use of steepest gradient descent.

In this study, the aim is modeling a virtual patient by online feedback neural network due to void of accessibility to real patient. That is to say, with respect to the assumption, we take the model as a real patient. In order to model, we use a back propagation neural network with three layers as well as some feedbacks from hidden layer and output layer. There are five neurons in the hidden layer and one neuron in the output layer. So, since the number of layer is low the speed of computation is increased. The obtained model can be used in order to do theatrical research such as control of tumor growth.

MATHEMATICAL MODEL

In this study, we use the simple ODE model of Panetta and Kirschner (Kirschner and Panetta, 1998) which represents the interactions between the effect or cells, tumor cells and the cytokine (IL-2) as follows:

$$\dot{E} = cT - \mu_2 E + \frac{p_1 E I_L}{g_1 + I_L} + s_1 \tag{1}$$

$$\dot{T} = r_2 T \, (1 - bT) - \frac{aET}{g_2 + T} \tag{2}$$

$$\dot{I_L} = \frac{p_2 ET}{g_3 + T} - \mu_3 I_L \tag{3}$$

Despite the simplicity of this model the related dynamics are in qualitative agreement with experimental findings, such as tumor recurrence (Blumberg *et al*., 1990; Hirao *et al*., 1992) and short and long term tumor oscillations, (Kennedy, 1970; Gatti *et al*., 1973). The model represents the reciprocal interactions between cells and concentration of Interleukin-2 (IL). In brief, the effectors decay at rate μ_2 and stimulate by the interaction with the tumor and the presence of Interleukin-2; the tumor follows a logistic growth and is reduced by the effectors; Interleukin-2 is produced when the effectors interact with the tumor and decays at rate μ_3. The parameters s_1 appearing in Eq. (1) incorporate the therapeutic factor.

It is assumed that the model is a black box and anyone do not know anything about it and only access to output signals is obtained by implying of input signals to the plant is possible.

DYNAMIC IDENTIFICATION STRATEGY

Black-box models such as neural networks (see e.g., [30, 36 and 25]) are greatly used to build models from measured input/output data. Although ANN method is an approximate solution to problems, but is a really powerful tool for identification of systems and is a popular empirical modeling method. Neural networks can be classified as feed forward and recurrent (or feedback). In the present study, the feedback neural network is adapted for the identification of a structural dynamic model. The multilayer feed forward neural network with sigmoid activation function in the hidden layer and linear activation function in output layer can identify a nonlinear system appropriately if the number of neurons in the hidden layer is sufficiently large. The feedback neural network used in this study is shown in Fig. 1.

A typical three-layer feedback neural network is shown in Fig. 1 and consisted of the input layer, hidden layer and output layer where input vector (I) as network inputs contains system output, the outputs of hidden layer and error. Also, the differentiable activation function $F_H(x)$ is the sigmoidal function as represented as follows:

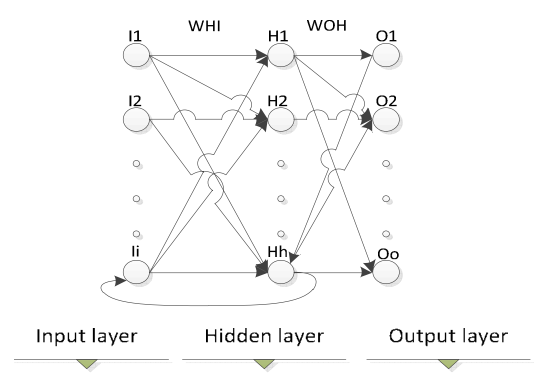

Fig. 1: Three-layer feedback neural network

$$F_H = \frac{e^n - e^{-n}}{e^n + e^{-n}} \tag{4}$$

W_{IH} represents weights associated with input nodes and hidden nodes and WHO presents weights associated with hidden nodes and output nodes in the network. For feed forward, the output vector O (t) is calculated by feeding the input vector I (t) through the hidden layer of the neural network. The output of the node h in the hidden layer $H_h(t)$ is:

$$H_h(t) = F_h(\sum_k W_{hk} I_k(t)) \tag{5}$$

The output of hidden layer of the network is feedback to its input. So, the output of the network is a function not only of the weights and network input, but also of the outputs of hidden layer of the network and error. The output of the node O in the output layer O(t) for the given input layer I(t) is:

$$O(t) = \sum_h W_{Oh} F_H (\sum_k W_{hk} I_k(t)) \tag{6}$$

Therefore, the output layer is the total input to the node O. The error back propagation is presented by the following equation:

$$Error = \frac{1}{2}\sum (O_d(t) - O(t))^2 \tag{7}$$

where, $O_d(t)$ is the desired output (system output) and O(t) is the neural network output. To determine the output adaptive rule for the weight W_{OH} as the link between the input layer and output layer, the following relations exist:

$$W_{OH}(t+\Delta t) = W_{OH}(t) + \Delta W_{OH}, \tag{8}$$

$$\Delta W_{OH} = -\gamma \frac{\partial E}{\partial W_{OH}}, \tag{9}$$

$$\Delta W_{OH} = -\gamma \sum_t \Delta_H(t) H_H(t), \tag{10}$$

$$\Delta_H(t) = \frac{dF_O(Net_O)}{dNet_O}(O_d(t) - O(t)) \tag{11}$$

Also, there are following adaptive rule as a link between input layer and the hidden layer WHI:

$$\Delta W_{HI} = -\gamma \frac{\partial E}{\partial W_{HI}} \tag{12}$$

$$\Delta W_{HI} = -\gamma \sum_t \Delta_H(t) I_I(t), \tag{13}$$

$$\Delta_H = \frac{dF(Net_H)}{dNet_H} \sum_O W_{HO} \Delta_O(t) \tag{14}$$

The coefficient γ is the learnig rate. It can be feasible to expand the error backpropagation rules as shown in equations (8-14) with any number of hidden layers.

SIMULATION AND RESULTS

This section aims to present the result of identification of nonlinear system (1-3) with parameter values (Cappuccio *et al*., 2007): c = 1.009, $\mu_2 = 0.378$, $p_1 = 0.044$, $g_1 = 0.02$, $r_2 = 0.123$, b = 1, a = 0.018, $p_2 = 0.9$, $g_3 = 10^{-5}$, $\mu_3 = 1.8$. Figure 2 Shows the general scheme of system identification process using feed back neural network model. Here y is the output of the plant, uis the plant input and ŷ is the output of model. What is more, $H_1, \ldots, H_5$ are the outputs of the hidden layer of neural network which became feedback to the model and e is the error for updating weights in model. According to Fig. 2, the represented feedback neural

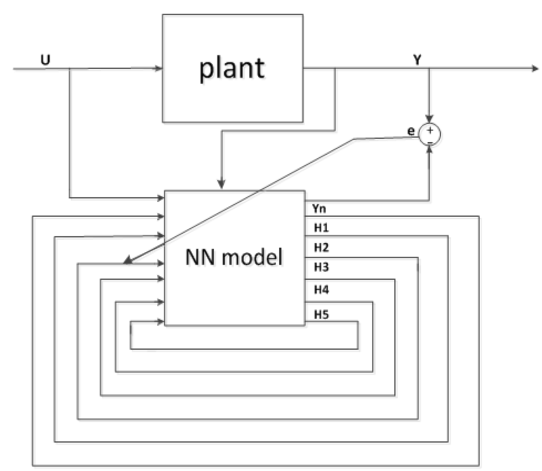

Fig. 2: The general block scheme of the NN model

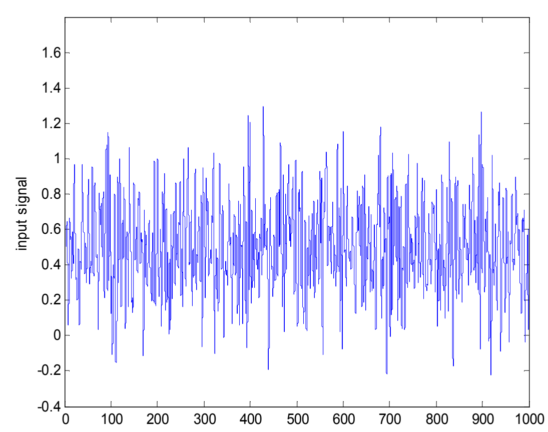

Fig. 3: Input signal

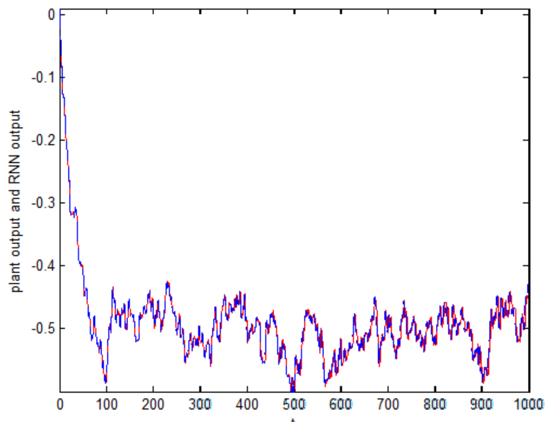

Fig. 4: Output of the identifier model and plant model

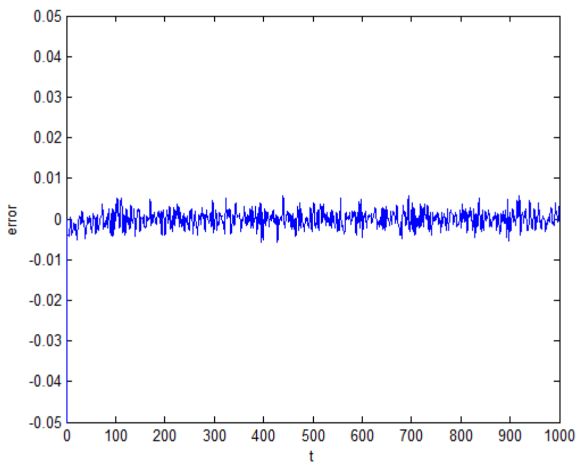

Fig. 5: Identification error

network model for the tumor growth model has eight inputs, six node in hidden layer and one node in output layer.

The output of the feedback neural network model and the plant for a random signal uniformly distributed in the interval [-1 1] (Fig. 3), is shown in Fig. 4. The error of system identification is also shown in Fig. 5 and indicate the efficiency of the presented online feedback neural networks.

CONCLUSION

ANNs have been applied over a wide range of fields for modeling and prediction in complex systems. Based on the knowledge of the system dynamics, the inputs and outputs of the neural network are chosen properly so that the structural model can be identified efficiently. Therefore, in this study, a feedback neural network is used for identification of tumor growth with assumption on lack of knowledge about tumor dynamics. So, we have shown that online feed back neural network with BP can identify a tumor growth model very accurately. What is more, we as a future work will apply different kinds of control methods in order to control tumor growth with respect to neural network model theoretically and make it applicaple after some precaution and consideration in real world.

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