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Journal of Military and Information Science
Institute of Science

Demand Forecasting in Pharmaceutical Industry Using Artificial Intelligence: Neuro-Fuzzy Approach

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Abstract - Because of human healthcare, the pharmaceutical industry is considered as one of the most significant industrial sectors. For that reason, demand forecasting in pharmaceutical industry has more complex structure than other sectors. Human factors, seasonal and epidemic diseases, market shares of the competitive products and marketing conditions are considered as main external factors for forecasting pharmaceutical product. Additionally, active ingredients rate is also important factor for forecasting process. The objective of this study is to predict future demands from previous sales quantity with considering effects of the external factors by employing a neuro-fuzzy approach. Because of the biases of the external effects in Artificial Neural Network (ANN) topology, an ANFIS is applied as a neuro fuzzy approach. Given application illustrates the effectiveness of the approach.

Keywords - Demand forecasting, Neuro-Fuzzy, Fuzzy Logic, Pharmaceutical Industry

1. Introduction

Today, health and treatment services are leading issues in prosperity and democracy concept. Therefore the pharmaceutical industry can be defined as a strategic sector. The pharmaceutical industry develops rapidly and differently from other sectors such as raw material and production process. The characteristics of pharmaceutical industry can be summarized as follows. (Giuffrida, 2001)

- Uncertainty of diseases, their curing and the availability of drugs
- Patients, doctors and health insurance expectations are different
- Patent protection and brand loyalty determine the market power
- Highlighting the market power, industrial policy and politics in health policy which practitioners have to make choices.

Drug companies manufacture pharmaceuticals for gaining profit to the company like other companies. They are different from other companies with respect to risks of drug business. Too much money and effort are spent to approve a given drug. (Ogbru, 2012) .

In this study, the actual sales amounts of a pharmaceutical company for seven years period were considered in order to forecast next period's demands. The company has five production departments; solid, liquid, pomade, penicillin and cephalosporin. A product was chosen from pomade products that have dynamic demand activities because of seasonal effects. It is a dermatologic lotion used to eliminate the pain temporarily against insect bites, simple skin irritation and itching bond cases. In this study, we predict future demands of this product from previous sales quantity data with considering effects of the external factors by employing a neuro-fuzzy approach.

2. Materials and Methods

2.1.Demand Structure of the Pharmaceutical Industry

Demand forecasting is one of the main processes of planning. Its objective is to determine which products are purchased, where, when, and in what quantities. Pharmaceutical manufacturers are affected by the political and economic relations of incomplete forecasting techniques. Balanced market power and valuable information are seen on developed markets. In other sectors, gathering of the forecasting methods' condition, sharing available information systematically and demanding scenarios develop independently from political conditions with greatest accuracy.

Pharmaceutical companies are in a close relationship with doctors, patients pharmacies and lawyers. They should manufacture according to regulations such as Food and Drug Administration (FDA), and GMP (Good Manufacturing Process) (Prest, 2012). Pharmaceutical market's complex structure for demand supply is seen in Figure 1.

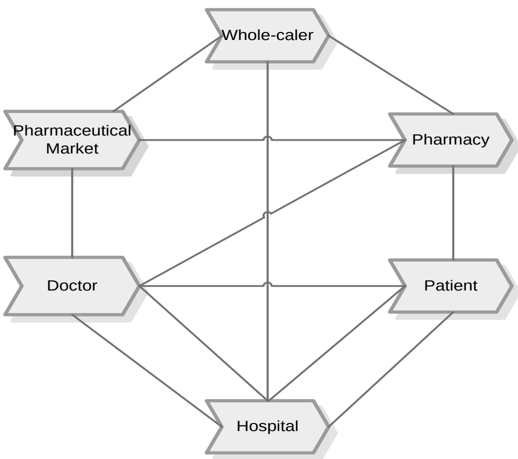

Fig. 1. Complex Structure of Pharmaceutical Market

Pharmaceutical companies make a lot of changes to compete with the new challenges of the modern economy. Manufacturing management and supply chains effect development of new drugs (Papageorgiou et al. 2001). The pharmaceutical industry; contributing to the economy for many countries in the world, offers the world population alleviation and cure from a variety of medical conditions. The importance of these benefits has made the industry an area of discussion, criticism and praise. The demand for pharmaceutical products is a derived one, as desired for the benefits they can provide. They are not demanded for their product value. It is also a directed demand, as the patient has no choice but to take the prescribed drug. The demand for pharmaceuticals is sensitive to quality differences; therefore, a high degree of product differentiation is found. The aim of such differentiation is to cement brand loyalties and establish a secure market share for the product and the company (Craig and Malek, 1995).

Rotstein et al. (1999), described an optimization based approach to select both a product development, an introduction strategy, a capacity planning and investment strategy in a pharmaceutical company. The development and solution of mathematical programming models is to support a holistic approach to product portfolio management in the pharmaceutical industry. Papageorgiou et al (2001), studied an optimization based approach for supply chain optimization problem in the pharmaceutical industry. They tried to decide product development, capacity planning and investment strategy. This problem was formulated with a mixed-integer linear programming (MILP) model. Saritas et al (2009), studied to determine appropriate drug dose for patients by using fuzzy expert system. Pharmaceutical companies produce drugs with high efficiency because of economic reasons. However, producing more than one dose is important for patients. Fisher et al. (2010), provided an overview of the regulation of pharmaceuticals and examined the ways that regulatory agencies accounted for sex and gender in their review of scientific data and marketing materials. Case studies illustrated the importance of considering sex and gender in pharmaceutical development and marketing. Confessore et al. (2011), proposed an approach for solving the dispatching problem in an Automated Guided Vehicles (AGV) system. The problem was modeled through a network by relying on the formulation of a Minimum Cost Flow Problem. The proposed approach has been

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exploited for optimizing the AGVs performance in a pharmaceutical production system. This work was limited to the study of the material handling operations within a pharmaceutical production plant. Thus, it mainly focused on internal logistics factors related to the movements of bins/pallets among the workstations by means of AGVs. Abdollahzade et al. (2012), proposed two models for simulation and prediction of complex dynamic systems. An emotional learning fuzzy inference system (ELFIS) and locally linear neuro-fuzzy (LLNF) methods were modeled to predict stock price of a pharmaceutical company. Considering the obtained results, these two methods exhibited more desirable performances with respect to other models in terms of accuracy and structural transparency for modeling and simulation of the aforementioned dynamic systems. Fruggiero et al. (2012), studied demand forecast management of local pharmacies. Forecast of the requirements obtained through the implementation of a Radial Basis Function (RBF) neural network. This accurate forecast allowed reducing the average level of stock and consequently the costs of warehousing and space needed for storage.

2.2 The proposed methodology

Improved forecasting methodologies exist, but the methods most commonly used in pharmacy are fairly straightforward, relying on direct human judgments with implicit rather than explicit assumptions and limited quantitative data. Two most commonly used methods are “Consumption Method” and “Morbidity Method” (2001). The consumption method was employed in the study. This method uses historical data of past consumption to predict future requirements. When good consumption data are available, this is obviously the most reliable method for existing products and for products where used patterns are well established., In this study, a neuro-fuzzy approach was employed for determining next period’s demands.

2.3 Neuro-fuzzy approach

The available range of forecasting methods is widely used in the management science. The evolution of soft computing techniques has increased the understanding of various aspects of the problem environment and, consequently, the predictability of many events. Methods of neuro computing, neuro-fuzzy computing, evolutionary algorithms and several hybrid techniques which connectionist models make use of some of the popular soft computing techniques. In contrast with the conventional AI techniques, which deal only with precision, certainty and rigor, connectionist models are able to exploit the tolerance for imprecision, uncertainty and, they are often very robust (Abraham and Nath, 2001)

Neuro-fuzzy modeling has been recognized as powerful tool that can facilitate the effective development of models by combining information from various sources, such as empirical models, heuristics and data. Hence, in most cases neuro-fuzzy models can better explain solutions than black box models such as neural networks (Babuška and Verbruggen, 2003).

2.3.1 Artificial neural network (ANN)

Artificial neural network (ANN) is a new technology that has been used for classification, prediction, clustering, and alerting to patterns (Haykin, 1994). The capability of learning examples is probably the most important property of neural networks in applications and can be used to train a neural network with the records of past response of a complex system (Wei, 1997). For creating a functional model of the neuron, there are three basic components. First, the synapses of the neuron are modeled as weights. The value of the weight is noted as strength of the connection between an input and a neuron. Negative weight values reflect inhibitory connections, while positive values designate excitatory connections. The next two components model actual activity within the neuron cell. An adder sums up all the inputs modified by their respective weights. This activity is referred to linear combination. Finally, an activation function controls the amplitude of the output of the neuron. An acceptable range of output is usually between 0 and 1, or -1 and 1 (Jang, 1995).

Once trained properly, ANN is a mostly used technique in modeling the nonlinear relationship between inputs and outputs of a process (Mok and Kwong, 2002; Erkollar et al, 2013). Engineers use Artificial Neural Networks (ANN) as novel signal-processing technologies.

A general and mathematical structure of this process is described in Figure 2 and Figure 3 respectively.

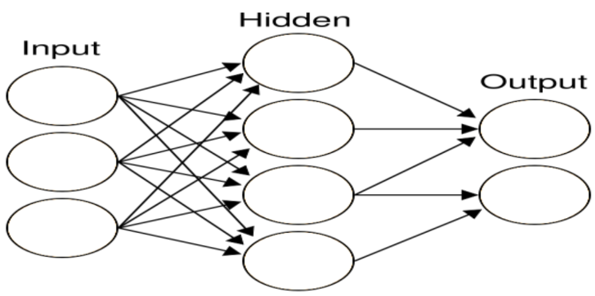

Fig. 2. General structure of ANN (Watson, 2010)

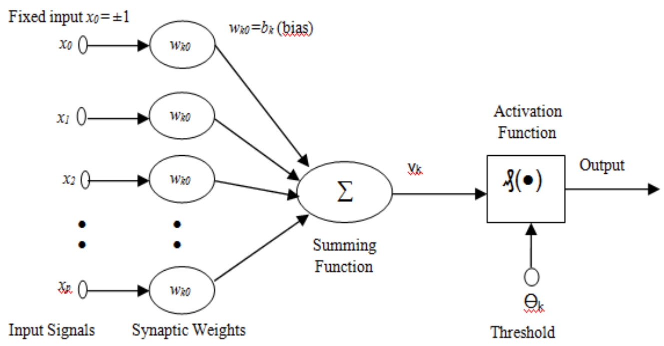

Fig. 3. Mathematical structure of ANN

The interval activity of the neuron can be defined as follows:

$$v_k = \sum_{j=1}^{p} w_{kj} x_j \qquad (1)$$

The output of the neuron, y_k, would therefore be the outcome of some activation function on the value of v_k (Jang, 1995).

2.3.2 Adaptive Network Based Fuzzy Inference System (ANFIS)

ANFIS is the implementation of fuzzy inference system (FIS) for adaptive networks to develop fuzzy rules with suitable membership functions to have required inputs and outputs. In ANFIS (Adaptive Network Based Fuzzy Inference System) structure, both artificial neural networks and fuzzy logic are employed Alizadeh, 2012).

An ANFIS is a fuzzy inference system that can be trained for modeling some collections of input–output data. The training module allows the system to tune its parameters to learn the input–output relationship hidden in the data set (Alizadeh, 2012). In ANFIS, the relationship between variables are represented by means of fuzzy if–then rules with imprecise predicates. In this case, the advantage of using an ANFIS model is the possibility to interpret the obtained result, which is not possible with truly black-box structures like neural networks (Babuška and Verbruggen, 2003).

ANFIS applies several functions to model with obtained data whereas analytical methods provide a single function. For this reason, the representation of the data with fuzzy logic models involves smaller errors than from a single crisp function (Erginel, 2010). A critical issue of using ANN is avoiding over fitting the network. If an ANN is over fitted, noise factors will be modeled in the network, which affects the generalization capability of ANN, and thus affects the prediction accuracy (Tian, 2012). ANFIS has a five-layer feed forward neural network structure. These structures are as follows (Caner and Akarslan, 2009);

- In the first layer; the node number is equal to the number of input variables. Membership functions of these variables are used as node functions. Membership functions of these parameters, are called "the premise parameters"
- In the second layer; the nodes are constant and node number is equal to the number of rules
- Normalizing weights of the rules is completed in the third layer.
- The nodes in the fourth layer are adaptive. The node function comes from the Sugeno method.

- The output of the fifth layer consists of a single node and crisp character as the output of the model.

The layers of the ANFIS are illustrated in Figure 4.

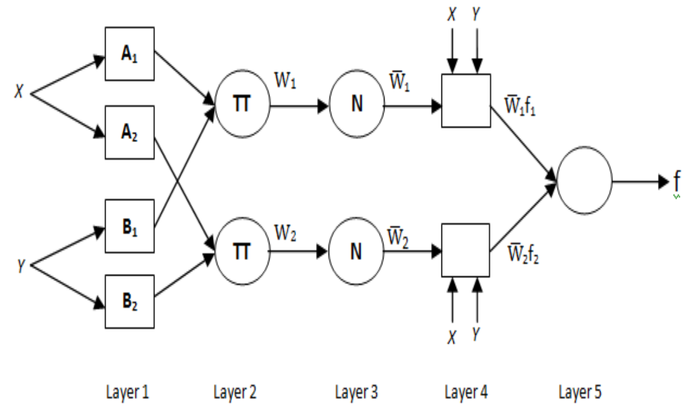

Fig. 4. Layers of ANFIS (Caner and Akarslan, 2009)

Adaptive learning type is chosen generally as hybrid learning. There is a type of a hybrid learning system defined by Jang is shown in Figure 5.

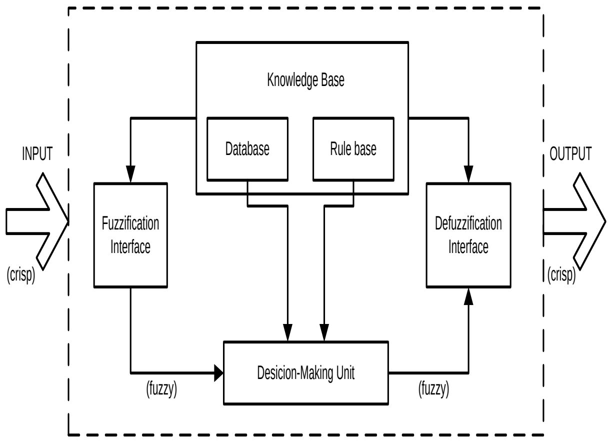

Fig. 5. Learning System of ANFIS (Jang, 1993)

A fuzzy controller was designed to interface with ANFIS edit, with the following steps at Table 1 (Jang, 1993);

Table 1. Fuzzy controller stages

Stages	Activities
1	Collect the system data and ANFIS edit interface for introducing the system data.
2	Build an appropriate "fismat" structure
3	Train the proposed neural network and training error is expected as zero value
4	Determine and control Fismat structure obtained by using performance data and present graphically.

While designing a fuzzy logic controller with ANFIS, the following arrangements should be met

- "Sugeno" type must necessarily to be established for controller.
- There should be input and output data pairs to identify the system better.
- ANFIS is employed as predefined Matlab® membership function
- In the system, each rule must be worked on a single output member

3. Proposed Model

A product which has three active raw materials called zinc oxide, lidocain HCI, diphenhydramine HCI was chosen for prediction. It is a dermatologic lotion and it is used to eliminate the pain temporarily against insect bites, simple skin irritation and itching bond cases. A year was divided to four periods by marketing departments. Because of the selling quantity is affected from seasonal demands, next period demand was predicted with employing previous periods' demands.

According to demand structure, the whole sales in a year were divided in four periods. Each of the period's effect on the output variable with a bias constant. The membership functions were employed in order to describe the sales volumes of the periods. The Membership functions consist of three variables such as low, normal and high. Next period's demand quantity was forecasted with employing defined membership functions.

Matlab® is a well-known program used for modeling purposes. Its neural networks toolbox is user-friendly and the creation of neural networks is performed by using a small amount of commands; the program has data base with functions, algorithms and commands for this purpose (Markopoulos et al. 2008). Our problem was modeled into Matlab® to solve with FIS (fuzzy inference system) editor.

The general "FIS" structure was illustrated in Figure 6a. The model consisted of four periods as four inputs, next period's demand as one output and Sugeno method was chosen. The classification and the description of membership functions in inputs is illustrated as follows in Figure 6b.

According to demand structure of pharmaceutical industry, the rules for evaluation were defined with using the Rule Viewer in Figure 7. The numerical volumes of inputs and next period's amount were calculated by ANFIS model. It was realized that periodical variations of inputs directly affected the output demand amount.

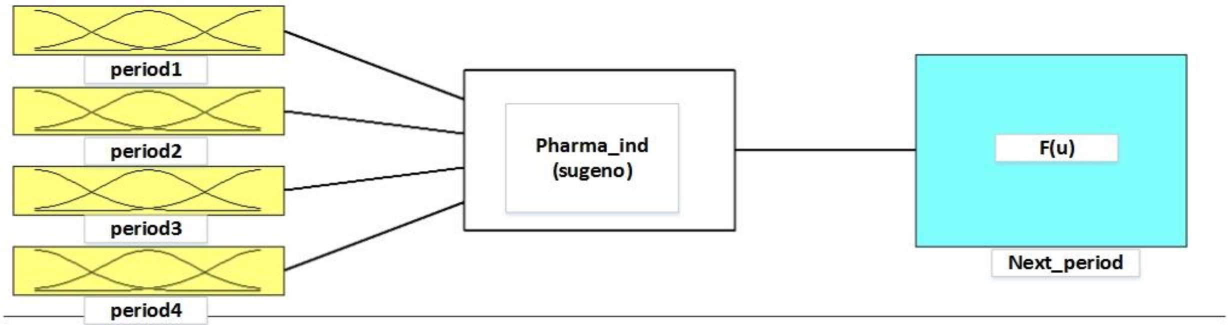

Fig. 6a. General FIS Structure of Model

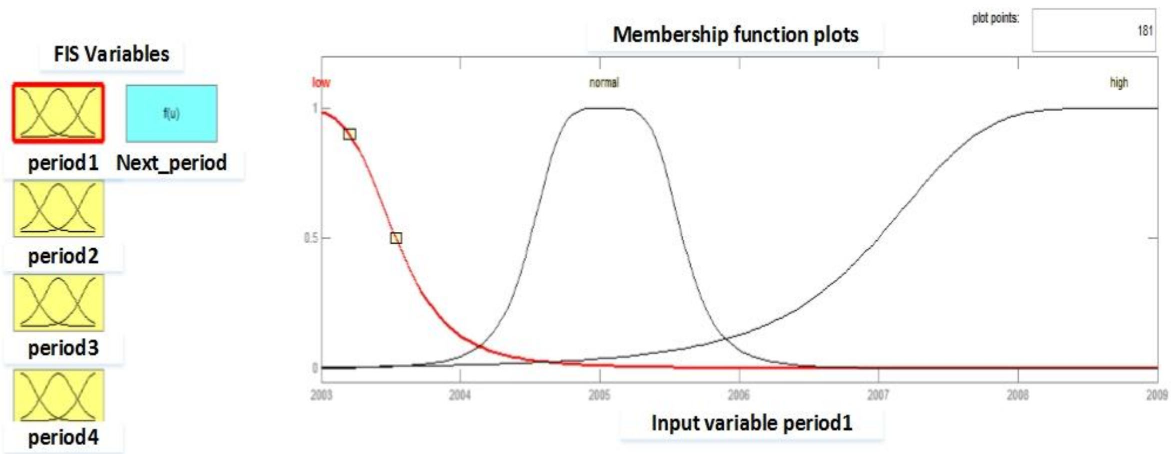

Fig. 6b. Membership Functions of Input2

The inputs, membership functions of inputs and output, rules, etc. in a whole structure were described in the ANFIS. The proposed ANFIS model structure is shown in Figure 8. Actual and predicted data are shown at Table 2.

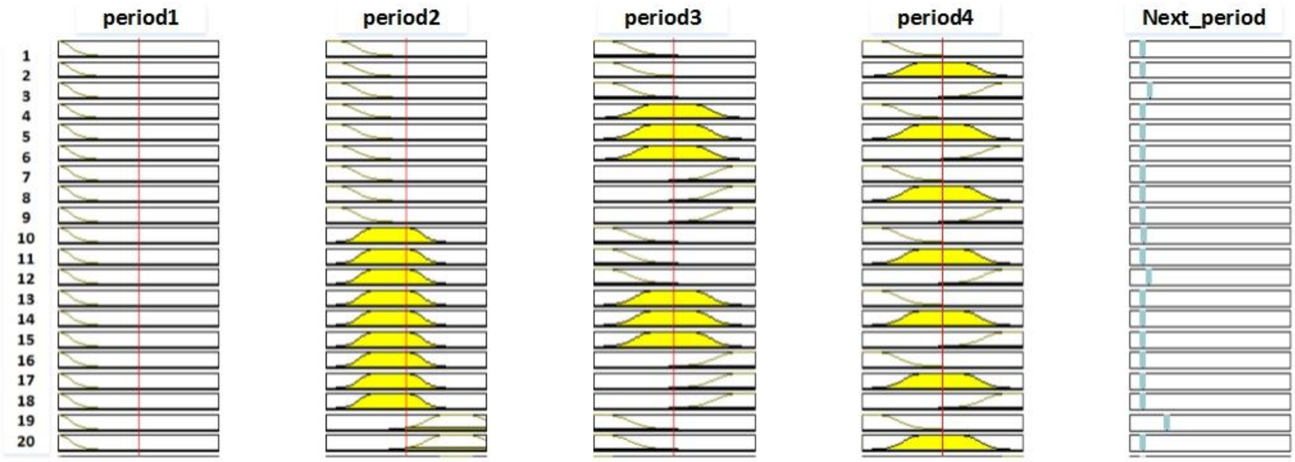

Fig. 7. Rule Viewer

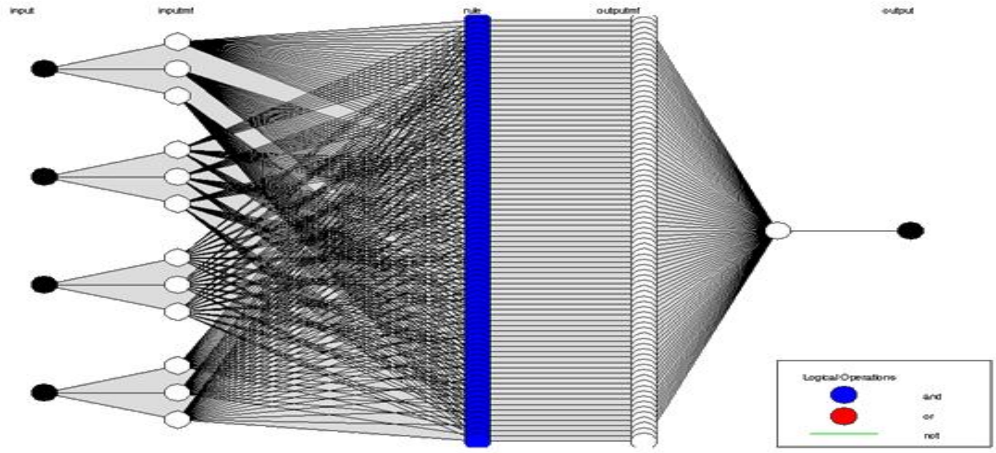

Fig. 8. ANFIS Model Structure

Table 2. Actual and predicted demand value of the product

Periods	1		2		3		4	
Year	**Actual**	**Predicted**	**Actual**	**Predicted**	**Actual**	**Predicted**	**Actual**	**Predicted**
2006	153814	165000	187958	192000	92000	92000	46172	50000
2007	106574	105000	131295	135000	252000	252000	26508	27500
2008	88009	92000	196490	198000	223000	223000	92731	90250
2009	137126	138000	314252	300000	175000	175000	51109	52500
2010	138045	142000	337552	325000	155000	155000	71400	72500
2011	162821	180000	149113	150000	203000	203000	170245	173000
2012	99878	105000	493709	500000	242500	242500	261800	265000

After 200 epochs, average testing error was found as 0,18169. The error between the training data and the output is shown in Figure 9.

Because of the product's dermatological effect, there are large amounts of the product in period 2 and period 3. The same effect results can be seen in Figure 10.

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Fig. 9. Error Graphic of Model

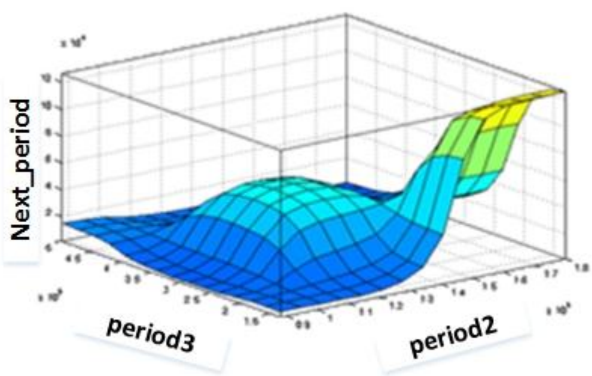

Fig. 10. Surface Analysis between Period2 and Period3

A t test under %95 confidence interval was completed in order to investigate difference between actual and predicted values. The test result showed that there is no significant difference. The t test values and its result were given at Table 3.

Table 3. Paired T for actual and predicted

	N	Mean	StDev	SE Mean
Actual	28	192201	87206	16480
Predicted	28	171437	99023	18714
Difference	28	20764	55058	10405

95% CI for mean difference: (-586; 42113), T-Test of mean difference = 0 (vs not = 0): T-Value = 2,00 P-Value = 0,056

4. Conclusion

Marketing department should predict the amount of product for each period in the company. In the production planning department, the predicted values are considered as production quantity to achieve with taking into consideration of technical production constraints.

Actual demands quantity of the product for six years period, were taken into consideration. It is seen that the proposed approach predicts demands value within reasonable error ranges. As a result of the proposed approach, it can be employed in order to achieve some expectations such as

- Purchasing order can be completed with more realistic data
- Costs of inventory quantity and over production can be reduced dramatically.
- Workforce saving can be achieved
- Idle machine capacity can be reduced
- Considerable important resource saving can be gained.
- Quick reaction to the market can be achieved.

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