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Application of artificial neural networks for Zeta potential of copolymer

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One of the measure of stability of the colloidal system is Zeta potential. In this study, artificial neural networks based prediction of the zeta potential of the copolymer was investigated. Multilayered perceptron and generalized regression neural networks were developed for zeta potential measurements of the copolymer as a function of pHs. Performance indices were demonstrate that structured generalized regression neural networks can predict the zeta potential of the copolymer quite efficiently than multilayer perceptron neural networks. The results showed that generalized regression neural networks could be useful to predict the zeta potential of the copolymer at different pH values.

Keywords: zeta potential, artificial neural networks, multilayer perceptron, generalized regression neural network

1. INTRODUCTION

Artificial neural networks (ANNs) can be summarized as an information processing system consisting of many neurons in the human brain that connected to one another in parallel with different levels of effect. Artificial neural network is an artificial simulation of the biological structure of the human nervous system and the working system of the human brain. Artificial neural networks are algorithmic systems that can grasp nonlinear relationships between different parameters, can order large quantities of input data and transform them into a graphical pattern of the output data. In chemistry, several problems are composed of complex systems and and artificial neural networks (ANNs) are tools that provides accurate results for complex and nonlinear problems requiring high computational costs [1-2].

In addition to fast computation superiority, the basic advantages of ANNs are learning, generalization ability of data, fault tolerance and inherent contextual information processing [3].

Drug carriers that succeed several goals like anhancement of biovailability,satability, preventing the drug interactions are the most important ways among new drug delivery systems. These carrier systems which include, cellular carriers, particulate carriers, lipoidal carriers, etc. were developed for different aims depending on the requirements [4]. The aim of this article is to estimate the zeta potential at different pHs of the copolymer

as an alternative drug carrier system using algorithms and methodologies based on the ways in which the human brain solves the problems. For this purpose, we developed two type of neural network: multilayer perceptron neural network (MLPNN) and generalized regression neural network (GRNN). The neural networks were

compared in order to the prediction capacity of the zeta potential of copolymer at different pH values.

2. ARTIFICIAL NEURAL NETWORKS

Recently there has been a growing interest on the applications of neural networks in biomedical research [5]. Artificial neural networks are designed to simulate some of the functions of the human brain using different learning algorithms. ANNs, have notable information working properties of human brain such as nonlinearity, high parallelism, robustness, fault and failure tolerance, learning, to handle imprecise and fuzzy information and their ability to generalize [6]. Using this feature, ANN can be used to solve complex real-life problems such as classification, clustering, function approximation and optimization[7].

Depending on the nature of the problem, different neural network modeling arrangements are made. These schemes are called artificial neural network architecture and define the number of hidden layers, the number of hidden nodes, the number of nodes in the input and output layers,the nature of activation functions and the learning algorithm [8].

The two main categories can be divided into ANN architectures, feed forward neural networks and feedback neural networks. In the feed forward neural networks, learning is a very important. Supervised and unsupervised are the two type of learning. Supervised learning occurs presenting input and output data to the network [9].

The measurement types used to measure the accuracy of the prediction are based on comparisons between the predicted output and the actual values in

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supervised neural network. Coefficient of determination (R^2) and mean square error (MSE) are the most common network performance measurements [9].

Unsupervised neural network uses only the input data to expose models in the characteristics of the data. Unsupervised learning is to make the computer learn how to do something we do not say how to do it. Classification, data mining, and self-organizing maps are most common unsupervised neural networks. Supervised feed forward neural networks has two different types: feed forward neural networks trained with backpropagation algorithm and statistical neural networks [9]. In this article, we used the multilayer perceptron neural network and generalized regression neural network. MLPNN is the most common and successful supervised learning architecture with multilayer backpropagation algorithm. GRNN is the type of neural networks that mainly depend on statistical methods and probability theory.

2.1. Multilayer perceptron neural network

With multilayer perceptron the data information only flows forward, which means that the output of a layer is used only as the input of the next layer [10]. These algorithms are organized by several neurons of different layers and are thus called multilayered. Each connection between the input and hidden layers (or more hidden layers) is like a synapse, and the input data is replaced with a certain weight.

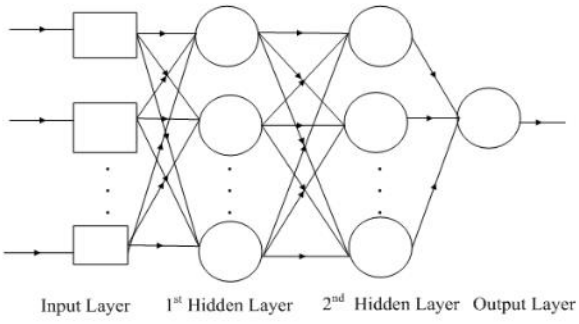

Figure 1. General structure of MLP NN.

A three layer feed-forward network is composed by an input layer, two hidden layers and the output layer as shown in Fig. 1[11].

The value coming out of an input unit is labeled x_j. Each hidden node computes the weighted sum of its inputs and applies a threshold value function to determine the output of the hidden node [12]. The weighted sum of inputs for hidden node z_h is calculated as follows:

$$\sum_{j=0}^{d} w_{hj} x_j \qquad (1)$$

Where w_{hj} a weight going to hidden unit z_h from input unit x_j would be labeled w_{hj} .

Step or sigmoid functions are generally chosen as threshold functions performed in the hidden node. In the hidden node, using the sigmoid function, z_h becomes as follows

$$z_h = sigmoid\left(\sum_{j=0}^{d} w_{hj} x_j\right) = \frac{1}{1+e^{-\sum_{j=0}^{d} w_{hj} x_j}} \qquad (2)$$

for h=1,2,…,H, where H is the number of hidden nodes. Output is computed by the weighted sum of inputs such that

$$o_i = \sum_{h=0}^{H} v_{ih} z_h \qquad (3)$$

to produce the output. We can apply several functions on each of the output nodes, such as Sigmoid [12]. If we apply the "softmax" function to the weighted sum

$$y_i = softmax(o_i) = \frac{e^{o_i}}{\sum_{i=1}^{K} e^{o_i}}$$

$$= \frac{e \sum_{h=0}^{H} v_{ih} z_h}{\sum_{i=1}^{K} e \sum_{h=0}^{H} v_{ih} z_h} \qquad (4)$$

2.2. Generalized regression neural network

The generalized regression neural network proposed by Specht (1991) does not require a recurrent training procedure, such as the back propagation method. GRNN predicts the function between input and output vectors using training data. GRRN has a rapid training capability on sparse data sets such as probabilistic neural networks.As the training set expands, the prediction error is reduced. GRNN use just for the estimation of continuous variables as standard regression techniques. GRNN, which is similar to radial-based functions, is based on standard regression. When a training set is given, GRNN predicts the joint probability density function of x and y [9].

If the joint probability density function f (x, y) is known;

$$E[y/X] = \frac{\int_{-\infty}^{+\infty} y f(X,y) dy}{f(X,y) dy} \qquad (5)$$

If the probability density function is not known

$$\hat{f}(X,Y) = \frac{1}{2\pi^{\frac{(p+1)}{2}} s^{(p+1)}} *$$

$$\frac{1}{n} \sum_{i=1}^{n} exp\left[-\frac{\left(X-X^i\right)^T \left(X-X^i\right)}{2s^2}\right] *$$

$$exp\left[-\frac{(Y-Y^i)^2}{2s^2}\right] \quad (6)$$

In this equation, p is the size of the x vector, n is the number of observations, s is the correction parameter. As D_i^2 is a scalar function,

$$D_i^2 = \left(X - X^i\right)^T (X - X^i) \quad (7)$$

regression of dependent variable y according to independent variable x is

$$\hat{Y}(X) = \frac{\sum_{i=1}^{n} Y^i \exp\left(-\frac{D_i^2}{2s^2}\right)}{\sum_{i=1}^{n} \exp\left(-\frac{D_i^2}{2s^2}\right)} \quad (8)$$

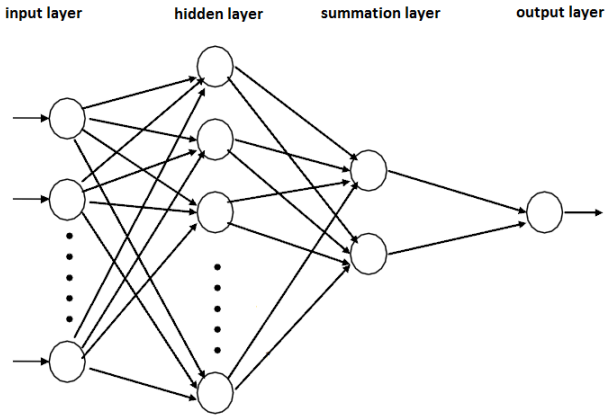

Figure 2. General structure of GRNN

A four layer generalized regression neural network is shown in Fig.2 [9].

3. EXPERIMENTAL STUDY

3.1. Instrument and materials

The particle size of copolymer in water was measured via Brookhaven 90 Plus/BI-MAS (Multi Angle Particle Sizing) and zeta potential measurements of copolymer were also determined by Brookhaven Zeta Potential Analyzer in water as a function of pH at physiological temperature 37ºC. [13].

Zeta potential is the measurement of the push or pull value between the particles. Zeta potential measurement gives detailed information about the distribution mechanisms and is the key to the electrostatic distribution control. A certain overhead grain pulls counter-load ions in the suspension resulting in a strong bond surface on the surface of the loaded grain. And then form an outwardly spread surface from the loaded grain. Within this diffused surface there is a boundary called "sliding surface". Loaded grain and its surrounding the portion of the ions up to the sliding surface boundary acts as a single piece. Potential on this slip surface is called zeta potential and is affected both by the surface texture of the grain and by the content of the liquid it contains. The behavior of granules in polar liquids determines the potential values of zeta, not the electric charge on their surface [14].

The most important reason for determining the zeta potential is to determine the size of the diffuse double layer around the particle. Zeta potential provides an understanding of many important properties of the colloidal systems and allows them to be controlled and to determine the electrical charge or potential on the particles. It is also very important for the understanding of dispersion and aggregate processes. The size of the zeta potential stabilizes the colloidal suspensions by preventing aggregate formation [14].When all the particles have a very large negative or positive zeta potential, the particles push each other and the dispersion becomes stable. When the particles have low zeta potential, there is no force to prevent the particles from accumulating, so dispersion imbalance (aggregation and sedimentation) occurs.

Zeta potential is dependent on surface charge density and double layer thickness. The surface charge density depends on the concentration of the potential determining ions. Since the H^+ ion is the potential determinant ion in many systems, the zeta potential is dependent on pH [14]. In this study, the particle size and zeta potential of the copolymer in the water was measured at different pHs [13].

Nano Particles with a zeta potential value that is more positive than +30 mV and negative than -30 mV are considered stable and particles with a zeta potential value of +30 mV to -30 mV are considered unstable [15].

One of the most important factors that affect the Zeta potential is pH. In this study, the effects of different pHs and particle sizes of copolymer on the zeta potential were investigated by using GRNN and MLPNN. And estimation results are compared by mean squared error and coefficient of determination.

4. RESULTS AND DISCUSSION

Model included two input variables (the particle size (nm), the pH) and one output variable (the zeta potential (mV)). The pH was measured at 17 different values, the lowest being 2.5 and the highest being 11.7. The particle size was measured 5 times

for each pH value and the zeta potential was calculated for each value [13].
Figure 3 shows the relationship between input and output variables.

In the MLPNN and GRNN models, 70% (60 zeta potential measurements) of the data were randomly selected for the training and 30% (25 zeta potential measurements) were used for testing. After preparing the data, code for GRNN was implemented and then the code was processed.

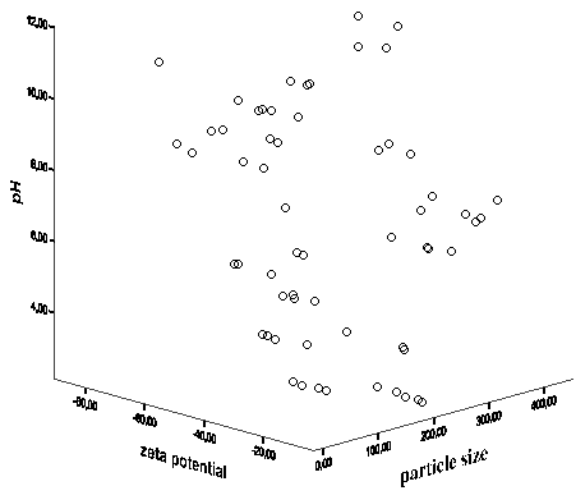

Figure 3. The relationship between input and output data of experimental measurements [13]

Using Weka software 3.8.1, the MLPNN model is developed using ANN fitting tool. In the MLPNN, a hidden layer was used in the network. To find the optimal number of neurons in hidden layers of the model, the size was expanded by adding 1 neuron at each step starting from 1. The maximum number of hidden layer neurons, which l is the number of input variables, should be at most 2l+1 as discussed by Caudill (1988). MPNNs having one to five hidden neurons were trained and one hidden neurons were used for optimal network. Different transfer functions were investigated and sigmoid transfer function was used to achieve the best performance in model. Learning rate and momentum were equal to 0.1 and 0.01, respectively. The initial weight matrices were randomly selected and the learning process continued until a sufficiently low mean square error was obtained. Training started with a small number of epochs (50) and the maximum number of epochs to train was chosen as 500 [16].

Table 1. Result comparison of MLP and GRNN Model

Model	Training set results		Testing set results	
	MSE	R^2	MSE	R^2
*MLP*NN	15.68	0.8692	12.87	0.7437
GRNN	6.23	0.8943	10.65	0.8371

As shown in Table 2, GRNN gives better result than MLPNN both training and testing sets to predict the zeta potential of copolymer solution. The regression plot for training and testing data of GRNN is shown in Fig.4 and Fig.5, respectively.

The GRNN results of training and test data were good fit with the experimental results as shown in Fig. 4 and Fig.5.

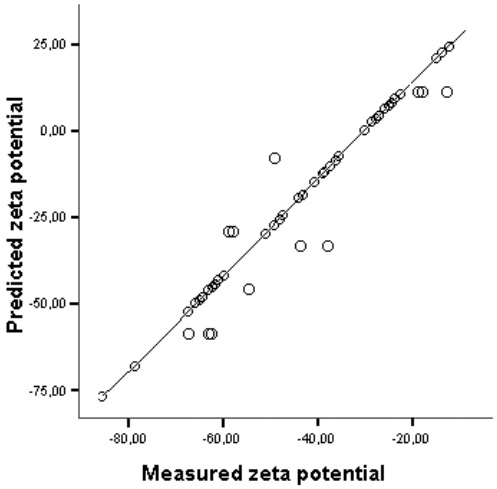

Figure 4. Regression plot of training data of the GRNN model

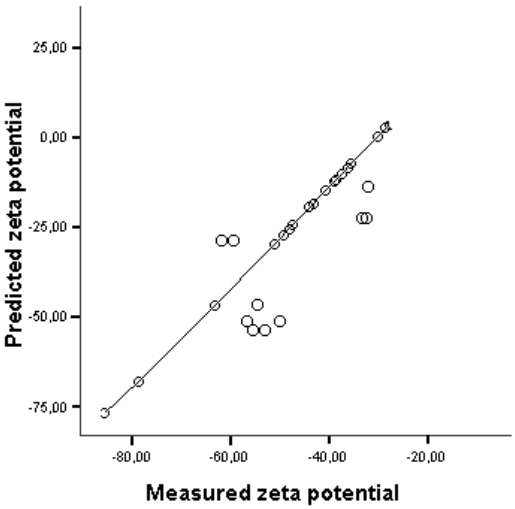

Figure 5. Regression plot of testing data of the GRNN model

5. CONCLUSIONS

In this article, the two artificial neural network algorithms, MLPNN and GRNN, were used to predict the zeta potential of the copolymer and the performance of these were compared. In order to determine the stability of the copolymer, the particle size and zeta potential in water were measured as a function of pHs. The zeta potential behavior of the copolymer solution is complex and important at different pHs. The experimental data [13] were

randomly divided into two groups as sets of training and test. The models of MLPNN and GRNN were built separately for these sets. In this study, coefficient of determination (R^2) and mean square errors (MSE) for both models are considered to compare prediction prerformance of the models. The experimental data were compared to the predicted values of zeta potential of copolymer based on both models for training and test sets. The GRNN model that has higher R^2 values and lower MSE values than MLPNN model showed better performance in terms of prediction accuracy. As a result, GRNN model of pH on the zeta potential of the copolymer can be preferred to MLPNN models in prediction with articifical neural network.

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