

PREDICTION OF THE SIZE OF NANOPARTICLES AND MICROSPORE SURFACE AREA USING ARTIFICIAL NEURAL NETWORK

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Received

January, 2017

Accepted

May, 2017

Published

June, 2017

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Genetics &

Applications, The

Official Publication of

the Institute for

Genetic Engineering

and Biotechnology,

University of Sarajevo

Abstract

This paper presents development of Artificial Neural Network (ANN) for prediction of the size of nanoparticles (NP) and microspore surface area (MSA). Developed neural network architecture has the following three inputs: the concentration of the biodegradable polymer in the organic phase, surfactant concentration in the aqueous phase and the homogenizing pressure. Two-layer feedforward network with a sigmoid transfer function in the hidden layer and a linear transfer function in the output layer is trained, using Levenberg-Marquardt training algorithm. For training of this network, as well as for subsequent validation, 36 samples were used. From 36 samples which were used for subsequent validation in this ANN, 80,5% of them had highest accuracy while 19,5% of output data had insignificant differences comparing to experimental values.

Key words: *artificial neural network, nanoparticles, polymeric nanoparticles, prediction, microspore surface area*

Research article

Introduction

A nanoparticle is the most fundamental component in the fabrication of a nanostructure, and is far smaller than the world of everyday objects that are described by Newton's laws of motion, but bigger than an atom or a simple molecule that are governed by quantum mechanics (Estelrich, 2014). In general, the size of a nanoparticle spans the range between 1 and 100 nm. Metallic nanoparticles have different

physical and chemical properties from bulk metals (e.g., lower melting points, higher specific surface areas, specific optical properties, mechanical strengths, and specific magnetizations), properties that might prove attractive in various industrial applications. However, how a nanoparticle is viewed and is defined depends very much on the specific application (Horikoshi and Serpone, 2013). Polymeric nanoparticles (PNPs) are structures with diameter ranging from 10 to 100 nm. The PNPs are obtained from synthetic polymers,

such as poly-caprolactone, polyacrylamide and polyacrylate or natural polymers, e.g., albumin, DNA, chitosan gelatin (Hosseini et al., 2016). Based on in vivo behavior, PNPs may be classified as biodegradable, i.e., poly (L-lactide) (PLA), polyglycolide (PGA), and non-biodegradable, e.g., polyurethane. PNPs are usually coated with nonionic surfactants in order to reduce immunological interactions (e.g., opsonization or presentation PNPs to CD8 T-lymphocytes) as well as intermolecular interactions between the surface chemical groups of PNPs (e.g., van der Waals forces, hydrophobic interaction or hydrogen bonding). The application of biodegradable nanosystems in the development of nanomedicines is one of the most successful ideas (Wilczewska et al., 2012). Nanocarriers composed of biodegradable polymers undergo hydrolysis in the body, producing biodegradable metabolite monomers, such as lactic acid and glycolic acid (Pavot et al., 2014). Drug-biodegradable polymeric nanocarrier conjugates used for drug delivery are stable in blood, non-toxic, and non-thrombogenic. They are also non-immunogenic as well as non-proinflammatory, and they neither activate neutrophils nor affect reticulo-endothelial system (Babahosseini, 2015). A few strategies can be employed for polymeric nanoparticles preparation: solvent evaporation, salting-out, dialysis, supercritical fluid technology, micro-emulsion, mini-emulsion, surfactant-free emulsion, and interfacial polymerization (Rao and Geckeler, 2011).

According to Rizkalla and Hildgen (2005), prediction of size of nanoparticles can be done using either Artificial Neural Network, Genetic algorithm or Polynomial Regression Analysis. Based on their work, different batches were prepared by varying surfactant and polymer concentration as well as homogenization pressure. Two commercial ANN programs were used: Neuroshell predictor, a black-box

software adopting both neural and genetic strategies and Neurosolutions, allowing a step-by-step building of the network. Results are then compared with those obtained by statistical method. It has been stated that Artificial Neural Networks offer a successful tool for nanoparticle preparation analysis and modeling.

Materials and methods

Obtaining desired nanoparticle's property, determination of their size, affinity and other important features is generally time, money and effort consuming (Giokas et al., 2010). Also, instruments used to carry out experiments are not widely available in any institute or research laboratories, so other more applicable tools are preferred to obtain results of interest. Artificial Neural Network (ANN) is one of those tools that are able to select data, create a network and evaluate its performance using mean square error (MSE) and regression analysis.

The network learns based on adjusting the interconnection weights between layers of input-output relations. Once the training is completed, ANN can predict outputs for new set of data when only input values are introduced. This describes the generalization ability of the network. Based on this, ANN system seems to be ideal for prediction of size and surface area determination (Singaram, 2011).

Feedforward, back-propagation, commonly used network in this type of research (Horikoshi and Serpone, 2013) is used for neural network training. The typical back-propagation network has an input layer- which consists of network inputs only. It is then followed by a hidden layer which consists of number of neurons, or hidden units which are placed in parallel. The network output is also formed by weighted summation that consists of outputs of the neurons in the hidden layer. Formed layer is called output layer. Usually number of output neurons equals

the number of outputs of the approximation problem. In this case, linear activation function for the output layer is used, since it is commonly used in regression problems, where powerful tool for predicting and interpreting information is needed (Wilczewska et al., 2012).

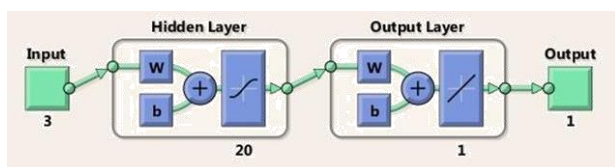


Figure 1. ANN architecture

TRAINLM is a network training function that updates weight and predicts values according to Levenberg-Marquardt optimization. Levenberg-Marquardt Algorithm (LMA) is commonly used training algorithm in data classification, as well algorithm that was used in previous experiment (Rizkalla and Hildgen, 2005). It is often the fastest backpropagation algorithm, although it does require more memory than other algorithms (Fojnica et al., 2016). Network performance function that is used is Mean Squared Error. It measures the network's performance according to the mean of squared errors. Mean Squared Error measures the network's performance according to the mean of squared errors. It is an average of the squares of differences between the actual observations and those predicted. The squaring of errors tends to heavily weight statistical outliers, affecting the accuracy of the results (Fojnica et al., 2016).

Input layer consisted of three network inputs that are followed by a hidden layer containing 20 neurons. Output layer consists of one neuron and output value parameter is the nanoparticle size (Figure 1). The network has been tested with different number of neurons in hidden layer so that best results for nanoparticle size could be observed. Thus, it was tested with 3, 7, 15, 20 and 31 neurons. Figure 1 illustrates ANN architecture and shows that with three parameters and 20 neurons in hidden layer ANN

was trained to give final output-size of nanoparticles.

Input parameters to developed ANN were: concentration of biodegradable polymer in the organic phase, surfactant concentration in the aqueous phase and the homogenizing pressure. Output data was nanoparticle size which we have compared to experimental results in the research we were following (Figure 2). Absolute error was used for comparing the results obtained as outputs and NP size. Small absolute error means higher performance.

$$\text{Absolute Error} = |\text{target}(\text{NP size}) - \text{ANN}|$$

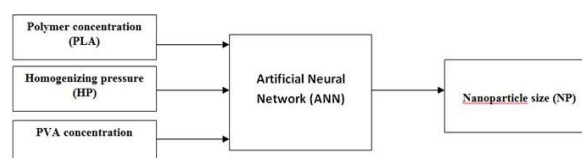


Figure 2. Block diagram of ANN for nanoparticle size

Data used from research paper (Hosseini et al., 2016), consisted of 36 samples implemented for training purposes. Also, they were used for the subsequent validation in order to determine the percentage of overlap with experimental data.

Results and discussion

In this study, impact of number of neurons in hidden layer, training functions as well as dataset distribution during training and transfer function on ANN output accuracy was examined. Based on the ANN performance, the optimal architecture was chosen for solving problem of prediction of the size of nanoparticles (NP) and microspore surface area (MSA). Five different networks were developed with different number of neurons in the hidden layers: 3, 7, 15, 20, and 31. The performance of networks (obtained from performance plot) was compared. As a result, network with 20 neurons achieved the best performance. Figure 3

represents performance plot of the network with 20 neurons in the hidden layer. It is evident that the training line perfectly follow its course however, validation and testing lines do not follow the training line and they almost overlap. Regardless, good results were obtained at the end of the process.

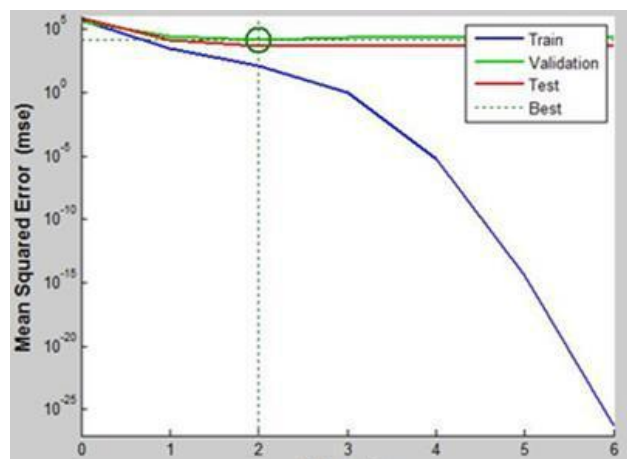


Figure 3. Performance plot of ANN

36 samples were used as a validation data. Absolute errors between outputs and targets were calculated and compared for each network. As a result, network with 20 neurons in the hidden layer has the lowest error rate, which means it has the best performance.

Table 1 (Appendix I) represents the results obtained from the validation process in terms of absolute error. It is clear that 22 out of 36 samples achieved 0% errors which is the best performance to be achieved. Errors appeared in 14 out of 36 samples.

Conclusions

In this study, Artificial Neural Networks (ANNs) were used to predict nanoparticle size and microspore surface area of polylactic acid nanoparticles, prepared by double emulsion method. Different batches were prepared while varying polymer and surfactant concentration, as well as homogenization pressure. In similar studies, researchers used two commercial ANNs

programs: Neuroshell® Predictor, a black-box software adopting both neural and genetic strategies, and Neurosolutions®, allowing a step-by-step building of the network.

Since we did not have an opportunity to work with such commercial ANN programs, an ordinary ANN tool was used to predict nanoparticle size and microspore surface area of polylactic acid nanoparticles. So, in order to develop a system for prediction of nanoparticle size and microspore surface area, three variables were used as inputs: the concentration of the biodegradable polymer in the organic phase (5%, 7.5% and 10% w/v of PLA), surfactant concentration in the aqueous phase (0.1%, 0.5%, and 1% w/v of PVA) and the homogenizing pressure (5000, 10000, 15000 and 20000 psi of HP). NP size experimental data, in this case target data, were already given in the table of default research paper (Hosseini et al., 2016).

Neural network was trained with 36 samples and validated with 36 samples each with three different input variables. Training of Neural Network was performed on few occasions by using Matlab and its nnstart fitting tool. Every time the number of hidden neurons was changed and performances, regressions and Mean Square Errors (MSE) were recorded. So, at first ANN was trained with 3 and then with 7, 15, 20 and 31 neurons, until conclusion that the best results were recorded using 20 neurons. Thus, by selecting 20 neurons, the best possible performance and regression were reached and after inserting all samples in order to do subsequent validation, 22 out of 36 samples were obtained which completely match target data and show 0% relative error.

At the end, a comparison between two commercial ANN programs used in the research was made and we made the following conclusions:

1. Artificial neural networks offered successful tool for nanoparticle preparation analysis and modeling. Genetic algorithm represented fast and reliable method to determine the relative importance of inputs. Predictions from ANNs were closer to experimental values than those obtained using polynomial regression analysis.
2. Results obtained using NeuroSolutions® confirmed that a flexible, rather than a “black-box” program, was more advantageous as it would enable the free selection of different network parameters in manner appropriate for each problem. Also, pre-processing of the training data has proved to play an important role in modeling applications by neural computing.

Considering all things, ANNs represent a promising tool for the analysis of processes involving preparation of polymeric carriers and for prediction of their physical properties.

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Appendix 1

Table 1. Comparison of experimental target data with output data

Batch number	Polymer concentration (%w/v)	Pressure	PVA concentration (%w/v)	NP size (nm)	Outputs	Absolute error
1	5	5000	0.1	295.3	295.3	0%
2	5	5000	0.5	225.5	225.5	0%
3	5	5000	1	141.3	140.7	0.4%
4	5	10000	0.1	214.5	214.5	0%
5	5	10000	0.5	177.0	177.0	0%
6	5	10000	1	137.8	137.8	0%
7	5	15000	0.1	229.0	228.9	0.04%
8	5	15000	0.5	178.1	178.1	0%
9	5	15000	1	128.2	128.2	0%
10	5	20000	0.1	205.4	205.4	0%
11	5	20000	0.5	176.3	249.0	41.24%
12	5	20000	1	152.4	209.1	37.20%
13	7.5	5000	0.1	387.0	316.0	18.35%
14	7.5	5000	0.5	197.1	197.1	0%
15	7.5	5000	1	169.8	169.8	0%
16	7.5	10000	0.1	343.3	311.2	9.35%
17	7.5	10000	0.5	197.0	197.0	0%
18	7.5	10000	1	158.1	131.9	16.57%
19	7.5	15000	0.1	290.6	290.7	0.06%
20	7.5	15000	0.5	196.8	196.8	0%
21	7.5	15000	1	153.2	153.2	0%
22	7.5	20000	0.1	413.6	413.4	0.04%
23	7.5	20000	0.5	188.5	188.3	0.1%
24	7.5	20000	1	173.4	57.2	67.01%
25	10	5000	0.1	545.2	469.6	13.8%
26	10	5000	0.5	211.8	211.8	0%
27	10	5000	1	192.6	192.6	0%
28	10	10000	0.1	502.2	502.2	0%
29	10	10000	0.5	194.4	194.4	0%
30	10	10000	1	183.5	181.7	0.98%
31	10	15000	0.1	437.9	437.9	0%
32	10	15000	0.5	219.4	149.3	31.90%
33	10	15000	1	178.9	178.9	0%
34	10	20000	0.1	500.2	500.2	0%
35	10	20000	0.5	214.9	215.1	0.09%
36	10	20000	1	178.0	178.0	0%