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PREDICTION OF THE ISOTHERMS OF HUMAN IgG ADSORPTION ON Ni(II)-IDA-PEVA MEMBRANE USING ARTIFICIAL NEURAL NETWORKS.

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ABSTRACT: The use of artificial neural networks to predict the adsorption isotherms of human IgG on Ni(II)-IDA-PEVA hollow fiber membranes was studied. Neural networks were trained using the Levenberg-Marquardt algorithm combined with Bayesian regularization technique and experimental data for different temperatures. The resulting neural network demonstrated to be able to interpolate the behavior of the adsorption pair in the temperature range [4ºC,37ºC]. Correlation coefficients achieved for interpolated isotherms were all greater than 0.97. Therefore, similar to that obtained using the Langmuir model.

KEYWORDS: Artificial neural networks; Adsorption isotherms; Immunoglobulin G.

1. INTRODUCTION.

Adsorption processes have a large range of application in different fields (Ruthven, 1984). However, the implementation of rigorous environmental policies and high quality requirements have highlighted the importance of adsorption in several areas, such as the removal of pollutants of effluent streams (Çelekli et al., 2013; Dutta and Basu, 2013; Yetilmezsoy and Demirel, 2008) and in chromatography for downstream processing aiming at protein purification (Labrou and Clonis, 1994). Besides, adsorption can be carried out using environmentally friendly adsorbents like lentil straw (Çelekli et al., 2013), Antep Pistachio shells (Yetilmezsoy and Demirel, 2008), or using shelled Moringa oleifera seed (Raj et al., 2013).

In order to optimize the adsorption process is necessary to know the behavior of the adsorbent-adsorbate pair. This knowledge is commonly represented by means of isotherms models, e.g. Langmuir and Freundlich models. However, in the last years artificial neural networks proved to be a efficient alternative (Çelekli et al., 2013; Dutta and Basu, 2013; Yetilmezsoy and Demirel, 2008; Morse et al., 2011). Morse et al. (2011) indicated the use of neural networks to model adsorption isotherms due to the inherent complexities of adsorption process. Indeed, the adsorbent-adsorbate interaction depends on several conditions like temperature, pH, compositions and/or the nature of adsorbent material. As confirmed, by De Laurentiis and Ravdin (1994), artificial neural networks are able to deal with these kind of complex interactions, such as protein adsorption.

In this study the application of neural networks to predict the adsorption isotherms of the protein human Immunoglobulin G (IgG) onto a nickel affinity polyethylene vinyl alcohol (PEVA) hollow fiber membrane, prepared using imminodiacetic acid (IDA) as chelating agent, in a Tris-HCl 25 mM pH 7.0 buffer system, is proposed. The adsorption process using Ni(II)-IDA-PEVA hollow fiber membranes is a valuable alternative to the purification of human IgG, as demonstrated by Ribeiro et al. (2008).

2. MATERIAL AND METHODS

2.1 Experimental data

The descriptions of materials and experimental procedures are presented by Ribeiro et al. (2008). The data collection consists of the IgG surface concentrations (Q*, mg g^{-1}) for different

IgG liquid-phase equilibrium concentrations (C*, mg mL^{-1}) at 4ºC (22 points), 15ºC (18 points), 25ºC (19 points) and 37ºC (20 points).

2.2. Artificial neural networks

Artificial neural networks, or simply neural networks, consist of a collection of processing nodes. These nodes, also called neurons, are interconnected and arranged in layers. So, when a stimulus is presented to the ANN, a unidirectional signal is propagated from the input layer to the output layer. The signals that reach each neuron are amplified or suppressed accordingly to a synaptic weight and a bias, processed by means of an activation function and emitted to the next layer. The propagation of the signal takes place until the output layer, where the ANN response to the stimulus is obtained. However, is necessary that the ANN learn to represent adequately the input-output behavior. This is done in the training stage. In this stage a set of input-output patterns are presented to the ANN and, based in the output error, the synaptic weights and bias are adjusted. The ANN obtained after the training must be able to represent the input-output behavior assimilated from the training data and generalize it for unseen data sets.

The effective use of ANN evolves basically the determination of its structure, including the number of layers and the number of neurons on each layer, of the activation function and algorithm of training. The multilayer perceptron is the ANN structure most used for engineering purposes. They are designed with one input layer, one output layer and hidden layers. Their layers are connected in a way that the layer output signal is emitted just for the subsequent layer. The number of neurons in the input and output layers equals the number of inputs and outputs, respectively. The determination of the ideal number of neurons in the hidden layer(s) is a complicated task. Designing an ANN with few neurons in the hidden layers produces an ANN with no sufficient capacity and low precision is obtained. On the other hand, with an excessive number of neurons the capacity of generalization is affected and overfitting can occur. However, the use of generalization improvement techniques such as Bayesian regularization could overcome this problem (MacKay, 1992).

The Bayesian regularization technique could be combined with the Levenberg-Marquardt algorithm, resulting in a efficient training method. The objective function used by this method is a linear combination of the sum of the squares of the synaptic weights and bias (SSW) and of the sum of the squares of the errors (SSE). Therefore, the synaptic weights and bias are enclosed to small values.

The activation functions most used in the hidden layer are nonlinear sigmoid functions (logistic and hyperbolic tangent functions). The nonlinearity imposed by these activation functions leads to local minima in the error surface. Thus, for certain initial sets of synaptic weights a local minimum could be found and the solution attained is not optimal (Demuth et al., 2008).

2.3. Isotherm modelling by means of artificial neural networks

The Mathworks™ neural networks toolbox was used to train the neural networks. The trainings were carried out using the Levenberg-Marquardt algorithm combined with the Bayesian regularization technique. In order to find the best topology neural networks trainings were performed varying the number of neurons in the hidden layer trained (just single hidden layers were considered in this study). The data set was normalized in the range [-1,1] and every different neural network training was repeated fifty times, therefore the chance of obtaining a model that had converged to local minima was reduced. This also reduce the importance of the choice of the transfer function. Thus, only the hyperbolic tangent function was used. After the trainings the neural networks that achieved the smallest sum of squared error was chosen.

3. RESULTS AND DISCUSSION

In the first experiment a neural network was used to predict the adsorption isotherm of human IgG on a Ni(II)-PEVA-IDA membrane at 4ºC. In this case, the neural network have one input, C* and one output, Q*. The data set was divided in three subsets, 14 points were used in the training, 4 in the tests and 4 in the validation.

The training proceed until the neural network convergence, that is, until the training set error becomes constant or the error of validation set begins to increase between an epoch to the next. Also, the number of maximum epochs was set to 200. Trainings were performed for 2 to 15 neurons in the hidden layers and the smaller sum

of squared error achieved was 2018.0 (mg g^{-1})^2 in the 11th training with 9 neurons in the hidden layer, the deviations of all 22 points were considered in this calculation. It was observed that the neural networks had always converged before reach the maximum of epochs.

The 22 points were fitted to the Langmuir isotherm model using the Mathworks™ curve fitting toolbox. Better results were achieved by means of the Levenberg-Marquardt algorithm. For a confidence level of 90%, the fitting resulted the equation (01):

$$Q^* = \frac{Q_m C^*}{K_d + C^*} \qquad (01)$$

where Q_m = 262.5 mg g^{-1} is maximum IgG binding capacity (the confidence bounds were 246.9 mg g^{-1} and 278.0 mg g^{-1}) and K_d = 2.528 mg mL^{-1} is the apparent dissociation constant (the confidence bounds were 1.885 mg mL^{-1} and 3.171 mg mL^{-1}). Equation (01) leads to the coefficient of determination, R^2 = 0.973 and SSE = 4585 (mg g^{-1})^2. The comparison of the results obtained by neural network and by the Langmuir isotherm model is presented in Figure 1.

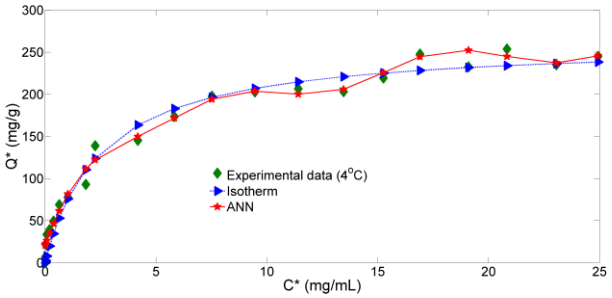

Figure 01. Comparison of adsorption isotherm at 4ºC obtained using Artificial neural network (ANN) and Langmuir isotherm model.

Besides, the maximum deviation obtained by ANN was 20.73 mg g^{-1} against 25.59 mg g^{-1} of the isotherm model. It must be pointed that only 14 of the 22 points were effectively used to prepare the neural model. The R^2 value achieved was 0.988.

In a second experiment, the effect of the temperature was included. Thus, there was two inputs, the IgG liquid-phase equilibrium concentration, C*, and the temperature. In these case, all experimental points obtained at 4ºC and 37ºC were used in the training. The achieved neural model was tested to the interior points, that is, to predict the isotherms at 15ºC and 25ºC. In these case no validation set was considered during the training, so the maximum of epochs has been reached several times.

The performance of the neural networks was measured using the equation 02:

$$P = \min\left\{ \frac{\sum_{T=1}^{2}\left[\sum_{i=1}^{nd}\left(Q^*_{i,T} - Q^*_{N,i,T}\right)^2\right]}{2} \right\} \qquad (02)$$

where P is the performance index, nd is the number of experimental points at temperature set T (nd = 18 for 15ºC, i.e., T=*1* and nd = 19 for 25ºC, i.e., T=*2*) and Q^*_N is the IgG surface concentration calculated by the ANN.

The P value of 3010.0 (mg g^{-1})^2 was obtained for the 26th training with 12 neurons in the hidden layer. The adsorption isotherms at 15ºC and 25ºC obtained using this ANN are illustrated in the Figure 02.

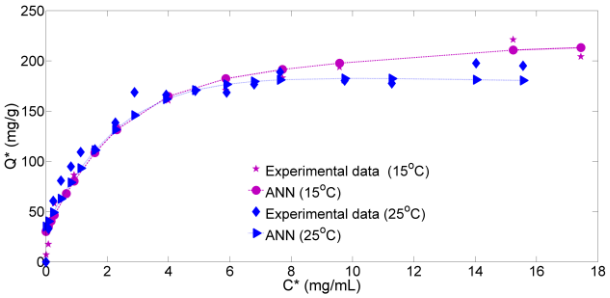

Figure 02. Human IgG surface concentration calculated using the neural model for unseen data.

The correlation coefficients (R) were 0.988 for data set at 15ºC and 0.973 for 25ºC.

In Figure 03 are presented the adsorption isotherms at 4ºC and 37ºC obtained using the neural model. These two sets of data were used in the training. The correlation coefficient (R) achieved for data set at 4ºC was 0.992 and for the data set at 37ºC was 0.961.

It could be observed in Figures 01-03 that ANNs were able to describe the isotherms adequately including the effect of temperature. As expected, the Levenberg-Marquardt algorithm combined with Bayesian regularization technique was able to avoid overfitting problems even for an excessive number of neurons.

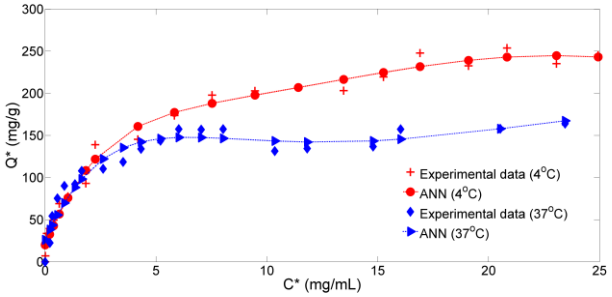

Figure 03. Human IgG surface concentration calculated using the neural model for training data.

These results are in accordance with that presented by Morse et al. (2011). This study could be expanded by including the effect of different chelating agents, pH, or buffer systems in the analysis.

4. CONCLUSIONS

Artificial neural networks were successfully used to predict the adsorption isotherms of human IgG on Ni(II)-IDA-PEVA hollow fiber membranes. The resulting neural network was able to interpolate the behavior of the adsorption process in the temperature range used in the training. The results were similar to that of the traditionally used Langmuir model. However, the interpolation ability of ANNs is an unquestionable advantage.

5. REFERENCES

ÇELEKLI, A.; BOZKURT, H.; GEYIK, F. Use of artificial neural networks and genetic algorithms for prediction of sorption of an azo-metal complex dye onto lentil straw. *Bioresource Technol.*, v. 129, p. 396-404, 2013.

DE LAURENTIIS, M.; RAVDIN, P.M. Survival analysis of censored data: neural networks analysis detection of complex interactions between variables. *Breast Cancer Res. Tr.*, v.32, n. 1., p. 113-118, 1994.

DEMUTH, H.; BEALE, M.; HAGAN, M. *Neural networks toolbox user's guide*. Natick: The Mathworks Inc., 2008.

DUTTA, M.; BASU, J.K. Application of artificial neural network for prediction of Pb(II) adsorption characteristics. *Environ. Sci. Pollut. Res.*, v. 20, p. 3322–3330, 2013.

LABROU, N.; CLONIS, Y. D., The affinity technology in downstream process. *J. Biotechnol.*, v. 36, p. 95-119, 1994.

MACKAY, D.J.C. Bayesian Interpolation. *Neural Comput.*, v. 4, n. 3, p. 415-447, 1992.

MORSE, G.; JONES, R.; THIBAULT, J.; TEZEL, F.H. Neural network modelling of adsorption isotherms. *Adsorption*, v. 17, p. 303-309, 2011.

RAJ, K.R.; KARDAM, A.; ARORA, J.K.; SRIVASTAVA, S.; SRIVASTAVA, M.M. Adsorption behavior of dyes from aqueous solution using agricultural waste: modeling approach. *Clean Techn. Environ. Policy*, v. 15, p. 73-80, 2013.

RIBEIRO, M.B.; VIJAYALAKSHMI, M.; TODOROVA-BALVAY, D., BUENO, S.M.A. Effect of IDA and TREN chelating agents and buffer systems on the purification of human IgG with immobilized nickel affinity membranes. *J. Chromatogr. B*, v. 861, p. 64–73, 2008.

RUTHVEN, D.M. *Principles of adsorption and adsorption processes*. New York: John Wiley & Sons, 1984.

YETILMEZSOY, K.; DEMIREL, S. Artificial neural network (ANN) approach for modeling of Pb(II) adsorption from aqueous solution by Antep pistachio (Pistacia Vera L.) shells. *J. Hazard. Mater.*, v. 153, p. 1288–1300, 2008.