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# Applications of Artificial Neural Networks in Chemical Problems

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## 1. Introduction

In general, chemical problems are composed by complex systems. There are several chemical processes that can be described by different mathematical functions (linear, quadratic, exponential, hyperbolic, logarithmic functions, etc.). There are also thousands of calculated and experimental descriptors/molecular properties that are able to describe the chemical behavior of substances. In several experiments, many variables can influence the chemical desired response [1,2]. Usually, chemometrics (scientific area that employs statistical and mathematical methods to understand chemical problems) is largely used as valuable tool to treat chemical data and to solve complex problems [3-8].

Initially, the use of chemometrics was growing along with the computational capacity. In the 80's, when small computers with relatively high capacity of calculation became popular, the chemometric algorithms and softwares started to be developed and applied [8,9]. Nowadays, there are several softwares and complex algorithms available to commercial and academic use as a result of the technological development. In fact, the interest for robust statistical methodologies for chemical studies also increased. One of the most employed statistical methods is partial least squares (PLS) analysis [10,11]. This technique does not perform a simple regression as multiple linear regression (MLR). PLS method can be employed to a large number of variables because it treats the colinearity of descriptors. Due the complexity of this technique, when compared to other statistical methods, PLS analysis is largely employed to solve chemical problems [10,11].

We can cite some examples of computational packages employed in chemometrics and containing several statistical tools (PLS, MLR, etc.): MATLAB [12], R-Studio [13], Statistica [14] and Pirouette [15]. There are some molecular modeling methodologies as HQSAR [16], CoMFA [17-18], CoMSIA [19] and LTQA-QSAR [20] that also use the PLS analysis to treat their generated descriptors. In general, the PLS method is used to analyse only linear problems. However, when a large number of phenomena and noise are present in the calibration problem, the relationship becomes non-linear [21]. Therefore, artificial neural networks (ANNs) may provide accurate results for very complex and non-linear problems that demand high computational costs [22,23]. One of the most employed learning algorithm is the back-propagation and its main advantage is the use of output information and expected pattern to error corrections [24]. The main advantages of ANN techniques include learning and generalization ability of data, fault tolerance and inherent contextual information processing in addition to fast computation capacity [25]. It is important to mention that since 90's many studies have related advantages of applying ANN techniques when compared to other statistical methods [23,26-31].

Due to the popularization, there is a large interest in ANN techniques, in special in their applications in various chemical fields such as medicinal chemistry, pharmaceutical, theoretical chemistry, analytical chemistry, biochemistry, food research, etc [32-33]. The theory of some ANN methodologies and their applications will be presented as follows.

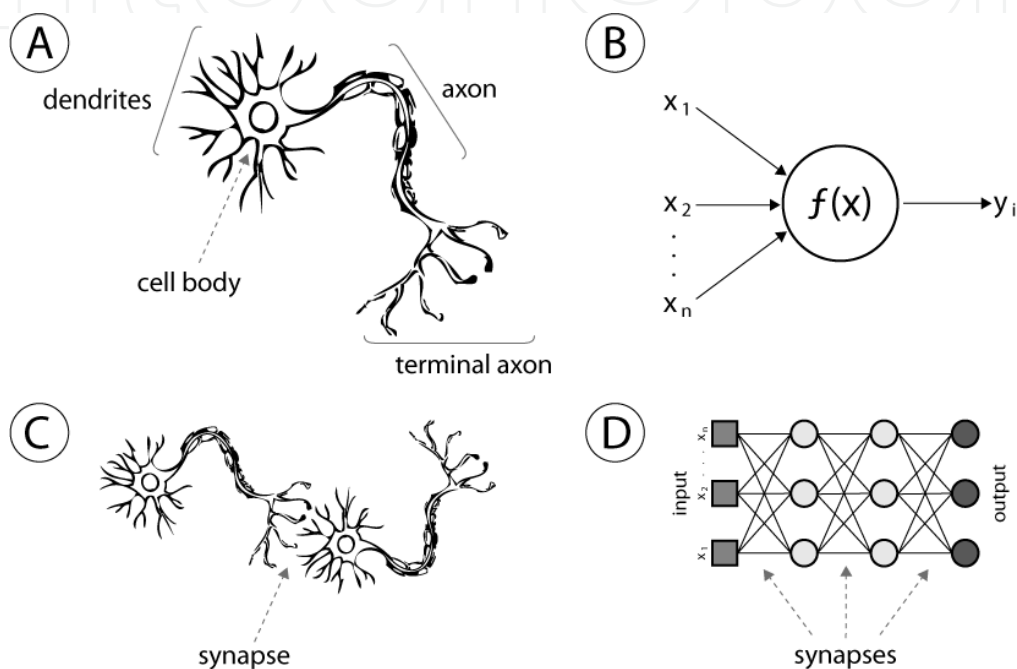
## 2. Artificial Neural Networks (ANNs)

The first studies describing ANNs (also called perceptron network) were performed by McCulloch and Pitts [34,35] and Hebb [36]. The initial idea of neural networks was developed as a model for neurons, their biological counterparts. The first applications of ANNs did not present good results and showed several limitations (such as the treatment of linear correlated data). However, these events stimulated the extension of initial perceptron architecture (a single-layer neural network) to multilayer networks [37,38]. In 1982, Hopfield [39] described a new approach with the introduction of nonlinearity between input and output data and this new architecture of perceptrons yielded a good improvement in the ANN results. In addition to Hopfield's study, Werbos [40] proposed the back-propagation learning algorithm, which helps the ANN popularization.

In few years (1988), one of the first applications of ANNs in chemistry was performed by Hoskins *et al.* [41] that reported the employing of a multilayer feed-forward neural network (described in Session 2.1) to study chemical engineering processes. In the same year, two studies employing ANNs were published with the aim to predict the secondary structure of proteins [42,43].

In general, ANN techniques are a family of mathematical models that are based on the human brain functioning. All ANN methodologies share the concept of "neurons" (also called "hidden units") in their architecture. Each neuron represents a synapse as its biological counterpart. Therefore, each hidden unity is constituted of activation functions that control

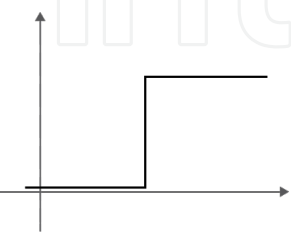
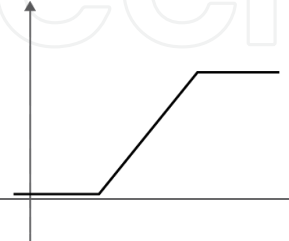
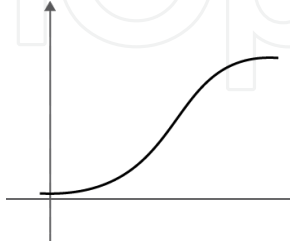

the propagation of neuron signal to the next layer (e.g. positive weights simulate the excitatory stimulus and negative weights simulate the inhibitory ones). A hidden unit is composed by a regression equation that processes the input information into a non-linear output data. Therefore, if more than one neuron is used to compose an ANN, non-linear correlations can be treated. Due to the non-linearity between input and output, some authors compare the hidden unities of ANNs like a “black box” [44-47]. Figure 1 shows a comparison between a human neuron and an ANN neuron.



**Figure 1.** (A) Human neuron; (B) artificial neuron or hidden unity; (C) biological synapse; (D) ANN synapses.

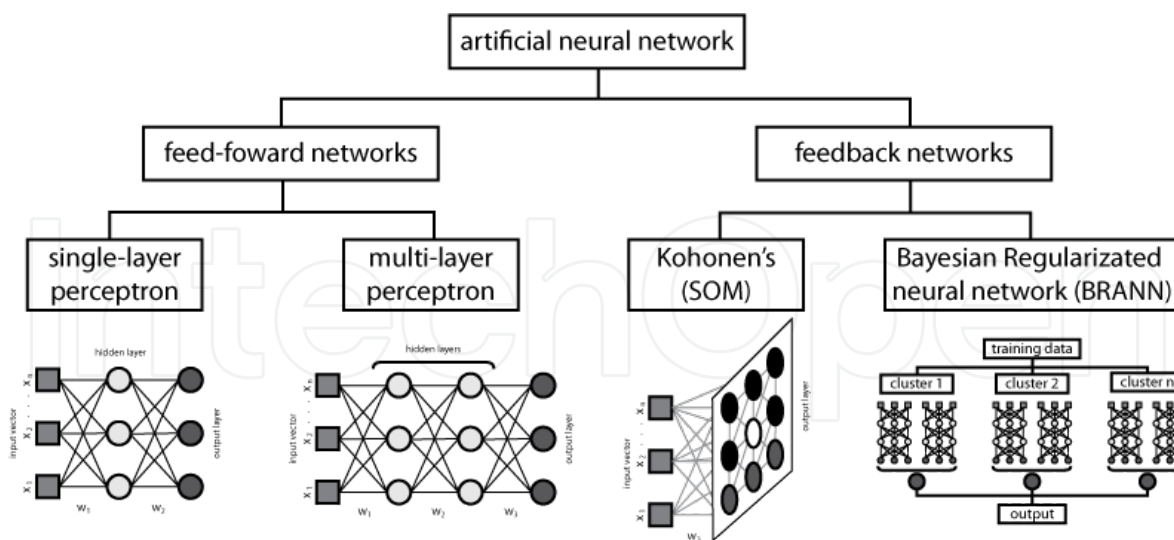
The general purpose of ANN techniques is based on stimulus–response activation functions that accept some input (parameters) and yield some output (response). The difference between the neurons of distinct artificial neural networks consists in the nature of activation function of each neuron. There are several typical activation function used to compose ANNs, as threshold function, linear, sigmoid (e.g. hyperbolic tangent), radial basis function (e.g. gaussian) [25,44-48]. Table 1 illustrates some examples of activation functions.

Different ANN techniques can be classified based on their architecture or neuron connection pattern. The feed-forward networks are composed by unidirectional connections between network layers. In other words, there is a connection flow from the input to output direction. The feedback or recurrent networks are the ANNs where the connections among layers occur in both directions. In this kind of neural network, the connection pattern is characterized by loops due to the feedback behavior. In recurrent networks, when the output signal of a neuron enter in a previous neuron (the feedback connection), the new input data is modified [25,44-47].

threshold	linear	hyperbolic tangent	gaussian
$\varphi(r) = \begin{cases} 1 & \text{if } r \geq 0 \\ 0 & \text{if } r < 0 \end{cases}$	$\varphi(r) = \begin{cases} 1 & r \geq \frac{1}{2} \\ n - \frac{1}{2} & 0 \leq r < \frac{1}{2} \\ 0 & r < -\frac{1}{2} \end{cases}$	$\varphi(r) = \tanh\left(\frac{r}{2}\right) = \frac{1 - \exp(-r)}{1 + \exp(-r)}$	$\varphi(r) = e^{-(\epsilon^v)^2}$
			

**Table 1.** Some activation functions used in ANN studies.

Each ANN architecture has an intrinsic behavior. Therefore, the neural networks can be classified according to their connections pattern, the number of hidden unities, the nature of activation functions and the learning algorithm [44-47]. There are an extensive number of ANN types and Figure 2 exemplifies the general classification of neural networks showing the most common ANN techniques employed in chemistry.



**Figure 2.** The most common neural networks employed in chemistry (adapted from Jain & Mao, 1996 [25]).

According to the previous brief explanation, ANN techniques can be classified based on some features. The next topics explain the most common types of ANN employed in chemical problems.

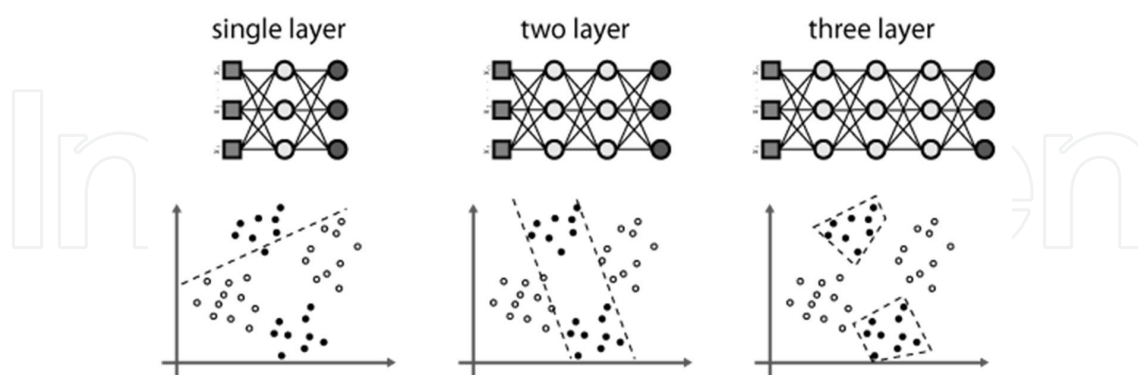
## 2.1. Multilayer perceptrons

Multilayer perceptrons (MLP) is one of the most employed ANN algorithms in chemistry. The term “multilayer” is used because this methodology is composed by several neurons arranged in different layers. Each connection between the input and hidden layers (or two hidden layers) is similar to a synapse (biological counterpart) and the input data is modified by a determined weight. Therefore, a three layer feed-forward network is composed by an input layer, two hidden layers and the output layer [38,48-50].

MLP is also called feed-forward neural networks because the data information flows only in the forward direction. In other words, the produced output of a layer is only used as input for the next layer. An important characteristic of feed-forward networks is the supervised learning [38,48-50].

The crucial task in the MLP methodology is the training step. The training or learning step is a search process for a set of weight values with the objective of reducing/minimizing the squared errors of prediction (experimental  $\times$  estimated data). This phase is the slowest one and there is no guarantee of minimum global achievement. There are several learning algorithms for MLP such as conjugate gradient descent, quasi-Newton, Levenberg-Marquardt, etc., but the most employed one is the back-propagation algorithm. This algorithm uses the error values of the output layer (prediction) to adjust the weight of layer connections. Therefore, this algorithm provides a guarantee of minimum (local or global) convergence [38,48-50].

The main challenge of MLP is the choice of the most suitable architecture. The speed and the performance of the MLP learning are strongly affected by the number of layers and the number of hidden unities in each layer [38,48-50]. Figure 3 displays the influence of number of layers on the pattern recognition ability of neural network.



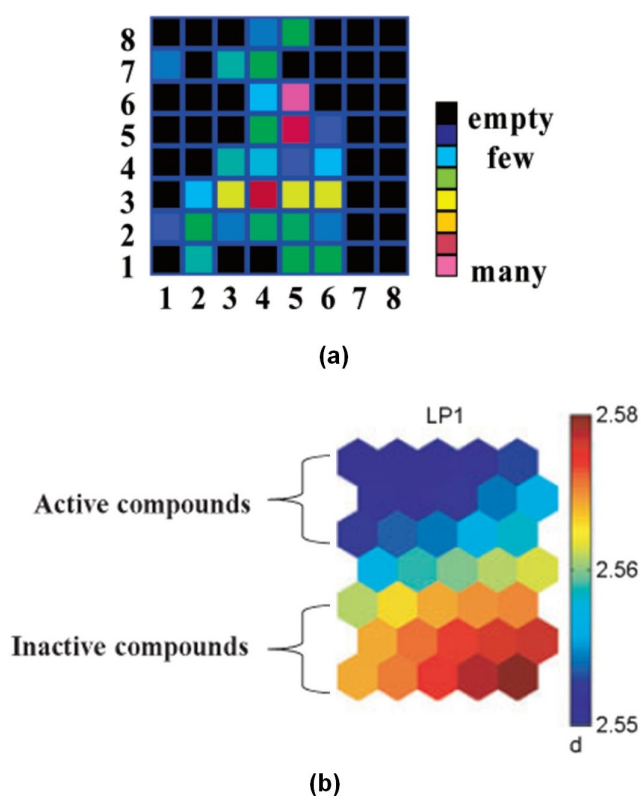
**Figure 3.** Influence of the number of layers on the pattern recognition ability of MLP (adapted from Jain & Mao, 1996 [25]).

The increase in the number of layers in a MLP algorithm is proportional to the increase of complexity of the problem to be solved. The higher the number of hidden layers, the higher the complexity of the pattern recognition of the neural network.



## 2.2. Self-organizing map or Kohonen neural network

Self-organizing map (SOM), also called Kohonen neural network (KNN), is an unsupervised neural network designed to perform a non-linear mapping of a high-dimensionality data space transforming it in a low-dimensional space, usually a bidimensional space. The visualization of the output data is performed from the distance/proximity of neurons in the output 2D-layer. In other words, the SOM technique is employed to cluster and extrapolate the data set keeping the original topology. The SOM output neurons are only connected to its nearest neighbors. The neighborhood represents a similar pattern represented by an output neuron. In general, the neighborhood of an output neuron is defined as square or hexagonal and this means that each neuron has 4 or 6 nearest neighbors, respectively [51-53]. Figure 4 exemplifies the output layers of a SOM model using square and hexagonal neurons for a combinatorial design of purinergic receptor antagonists [54] and cannabinoid compounds [30], respectively.



**Figure 4.** Example of output layers of SOM models using square and hexagonal neurons for the combinatorial design of (a) purinergic receptor antagonists [54] and (b) cannabinoid compounds [30], respectively.

The SOM technique could be considered a competitive neural network due to its learning algorithm. The competitive learning means that only the neuron in the output layer is selected if its weight is the most similar to the input pattern than the other input neurons. Finally, the learning rate for the neighborhood is scaled down proportional to the distance of the winner output neuron [51-53].

### 2.3. Bayesian regularized artificial neural networks

Different from the usual back-propagation learning algorithm, the Bayesian method considers all possible values of weights of a neural network weighted by the probability of each set of weights. This kind of neural network is called Bayesian regularized artificial neural (BRANN) networks because the probability of distribution of each neural network, which provides the weights, can be determined by Bayes's theorem [55]. Therefore, the Bayesian method can estimate the number of effective parameters to predict an output data, practically independent from the ANN architecture. As well as the MLP technique, the choice of the network architecture is a very important step for the learning of BRANN. A complete review of the BRANN technique can be found in other studies [56-59].

### 2.4. Other important neural networks

Adaptative resonance theory (ART) neural networks [60,61] constitute other mathematical models designed to describe the biological brain behavior. One of the most important characteristic of this technique is the capacity of knowledge without disturbing or destroying the stored knowledge. A simple variation of this technique, the ART-2a model, has a simple learning algorithm and it is practically inexpensive compared to other ART models [60-63]. The ART-2a method consists in constructing a weight matrix that describes the centroid nature of a predicted class [62,63]. In the literature, there are several chemical studies that employ the ART-based neural networks [64-73].

The neural network known as radial basis function (RBF) [74] typically has the input layer, a hidden layer with a RBF as the activation function and the output layer. This network was developed to treat irregular topographic contours of geographical data [75-76] but due to its capacity of solving complex problems (non-linear specially), the RBF networks have been successfully employed to chemical problems. There are several studies comparing the robustness of prediction (prediction coefficients,  $r^2$ , pattern recognition rates and errors) of RBF-based networks and other methods [77-80].

The Hopfield neural network [81-82] is a model that uses a binary  $n \times n$  matrix (presented as  $n \times n$  pixel image) as a weight matrix for  $n$  input signals. The activation function treats the activation signal only as 1 or -1. Besides, the algorithm treats black and white pixels as 0 and 1 binary digits, respectively, and there is a transformation of the matrix data to enlarge the interval from 0 – 1 to (-1) – (+1). The complete description of this technique can be found in reference [47]. In chemistry research, we can find some studies employing the Hopfield model to obtain molecular alignments [83], to calculate the intermolecular potential energy function from the second virial coefficient [84] and other purposes [85-86].

## 3. Applications

Following, we will present a brief description of some studies that apply ANN techniques as important tools to solve chemical problems.



### 3.1. Medicinal Chemistry and Pharmaceutical Research

The drug design research involves the use of several experimental and computational strategies with different purposes, such as biological affinity, pharmacokinetic and toxicological studies, as well as quantitative structure-activity relationship (QSAR) models [87-95]. Another important approach to design new potential drugs is virtual screening (VS), which can maximize the effectiveness of rational drug development employing computational assays to classify or filter a compound database as potent drug candidates [96-100]. Besides, various ANN methodologies have been largely applied to control the process of the pharmaceutical production [101-104].

Fanny *et al.* [105] constructed a SOM model to perform VS experiments and tested an external database of 160,000 compounds. The use of SOM methodology accelerated the similarity searches by using several pharmacophore descriptors. The best result indicated a map that retrieves 90% of relevant neighbors (output neurons) in the similarity search for virtual hits.

### 3.2. Theoretical and Computational Chemistry

In theoretical/computational chemistry, we can obtain some applications of ANN techniques such as the prediction of ionization potential [106], lipophilicity of chemicals [107, 108], chemical/physical/mechanical properties of polymer employing topological indices [109] and relative permittivity and oxygen diffusion of ceramic materials [110].

Stojković *et al.* [111] also constructed a quantitative structure-property relationship (QSPR) model to predict  $pK_{BH^+}$  for 92 amines. To construct the regression model, the authors calculated some topological and quantum chemical descriptors. The counter-propagation neural network was employed as a modeling tool and the Kohonen self-organizing map was employed to graphically visualize the results. The authors could clearly explain how the input descriptors influenced the  $pK_{BH^+}$  behavior, in special the presence of halogens atoms in the amines structure.

### 3.3. Analytical Chemistry

There are several studies in analytical chemistry employing ANN techniques with the aim to obtain multivariate calibration and analysis of spectroscopy data [112-117], as well as to model the HPLC retention behavior [118] and reaction kinetics [119].

Fatemi [120] constructed a QSPR model employing the ANN technique with back-propagation algorithm to predict the ozone tropospheric degradation rate constant of organic compounds. The data set was composed of 137 organic compounds divided into training, test and validation sets. The author also compared the ANN results with those obtained from the MLR method. The correlation coefficients obtained with ANN/MLR were 0.99/0.88, 0.96/0.86 and 0.96/0.74 for the training, test and validation sets, respectively. These results showed the best efficacy of the ANN methodology in this case.

### 3.4. Biochemistry

Neural networks have been largely employed in biochemistry and correlated research fields such as protein, DNA/RNA and molecular biology sciences [121-127].

Petritis *et al.* [128] employed a three layer neural network with back-propagation algorithm to predict the reverse-phase liquid chromatography retention time of peptides enzymatically digested from proteomes. In the training set, the authors used 7000 known peptides from *D. radiodurans*. The constructed ANN model was employed to predict a set with 5200 peptides from *S. oneidensis*. The used neural network generated some weights for the chromatographic retention time for each aminoacid in agreement to results obtained by other authors. The obtained ANN model could predict a peptide sequence containing 41 aminoacids with an error less than 0.03. Half of the test set was predicted with less than 3% of error and more than 95% of this set was predicted with an error around 10%. These results showed that the ANN methodology is a good tool to predict the peptide retention time from liquid chromatography.

Huang *et al.* [129] introduced a novel ANN approach combining aspects of QSAR and ANN and they called this approach of physics and chemistry-driven ANN (Phys-Chem ANN). This methodology has the parameters and coefficients clearly based on physicochemical insights. In this study, the authors employed the Phys-Chem ANN methodology to predict the stability of human lysozyme. The data set was composed by 50 types of mutated lysozymes (including the wild type) and the experimental property used in the modeling was the change in the unfolding Gibbs free energy ( $\text{kJ}^{-1} \text{mol}$ ). This study resulted in significant coefficients of calibration and validation ( $r^2=0.95$  and  $q^2=0.92$ , respectively). The proposed methodology provided good prediction of biological activity, as well as structural information and physical explanations to understand the stability of human lysozyme.

### 3.5. Food Research

ANNs have also been widely employed in food research. Some examples of application of ANNs in this area include vegetable oil studies [130-138], beers [139], wines [140], honeys [141-142] and water [143-144].

Bos *et al.* [145] employed several ANN techniques to predict the water percentage in cheese samples. The authors tested several different architecture of neurons (some functions were employed to simulate different learning behaviors) and analyzed the prediction errors to assess the ANN performance. The best result was obtained employing a radial basis function neural network.

Cimpoi *et al.* [146] used the multi-layer perceptron with the back-propagation algorithm to model the antioxidant activity of some classes of tea such as black, express black and green teas. The authors obtained a correlation of 99.9% between experimental and predicted antioxidant activity. A classification of samples was also performed using an ANN technique with a radial basis layer followed by a competitive layer with a perfect match between real and predicted classes.

## 4. Conclusions

Artificial Neural Networks (ANNs) were originally developed to mimic the learning process of human brain and the knowledge storage functions. The basic unities of ANNs are called neurons and are designed to transform the input data as well as propagating the signal with the aim to perform a non-linear correlation between experimental and predicted data. As the human brain is not completely understood, there are several different architectures of artificial neural networks presenting different performances. The most common ANNs applied to chemistry are MLP, SOM, BRANN, ART, Hopfield and RBF neural networks. There are several studies in the literature that compare ANN approaches with other chemometric tools (e.g. MLR and PLS), and these studies have shown that ANNs have the best performance in many cases. Due to the robustness and efficacy of ANNs to solve complex problems, these methods have been widely employed in several research fields such as medicinal chemistry, pharmaceutical research, theoretical and computational chemistry, analytical chemistry, biochemistry, food research, etc. Therefore, ANN techniques can be considered valuable tools to understand the main mechanisms involved in chemical problems.

## Notes

Techniques related to artificial neural networks (ANNs) have been increasingly used in chemical studies for data analysis in the last decades. Some areas of ANN applications involve pattern identification, modeling of relationships between structure and biological activity, classification of compound classes, identification of drug targets, prediction of several physicochemical properties and others. Actually, the main purpose of ANN techniques in chemical problems is to create models for complex input–output relationships based on learning from examples and, consequently, these models can be used in prediction studies. It is interesting to note that ANN methodologies have shown their power and robustness in the creation of useful models to help chemists in research projects in academy and industry. Nowadays, the evolution of computer science (software and hardware) has allowed the development of many computational methods used to understand and simulate the behavior of complex systems. In this way, the integration of technological and scientific innovation has helped the treatment of large databases of chemical compounds in order to identify possible patterns. However, people that can use computational techniques must be prepared to understand the limits of applicability of any computational method and to distinguish between those opportunities which are appropriate to apply ANN methodologies to solve chemical problems. The evolution of ANN theory has resulted in an increase in the number of successful applications. So, the main contribution of this book chapter will be briefly outline our view on the present scope and future advances of ANNs based on some applications from recent research projects with emphasis in the generation of predictive ANN models.

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## References

- [1] Teófilo, R. F., & Ferreira, M. M. C. (2006). Quimiometria II: Planilhas Eletrônicas para Cálculos de Planejamento Experimental um Tutorial. *Quim. Nova*, 29, 338-350.
- [2] Lundstedt, T., Seifert, E., Abramo, L., Theilin, B., Nyström, A., Pettersen, J., & Bergman, R. (1998). Experimental design and optimization. *Chemom. Intell. Lab.*, 42, 3-40.
- [3] Kowalski, B. R. J. (1957). Chemometrics: Views and Propositions. *J. Chem. Inf. Comp. Sci.*, 15, 201-203.
- [4] Wold, S. (1976). Pattern recognition by means of disjoint principal component models. *Pattern Recognition*, 8, 127-139.
- [5] Vandeginste, B. G. M. (1987). Chemometrics- General Introduction and Historical Development. *Top. Curr. Chem.*, 141, 1-42.
- [6] Wold, S., & Sjöström, M. (1998). Chemometrics present and future success. *Chemom. Intell. Lab.*, 44, 3-14.
- [7] Ferreira, M. M. C., Antunes, A. M., Melgo, M. S., & Volpe, P. L. O. (1999). Quimiometria I: calibração multivariada um tutorial. *Quím. Nova*, 22, 724-731.
- [8] Neto, B. B., Scarminio, I. S., & Bruns, R. E. (2006). Anos de Quimiometria no Brasil. *Quim. Nova*, 29, 1401-1406.
- [9] Hopke, P. K. (2003). The evolution of chemometrics. *Anal. Chim. Acta*, 500, 365-377.
- [10] Wold, S., Ruhe, A., Wold, H., & Dunn, W. (1984). The collinearity problem in linear regression: The partial least squares approach to generalized inverses. *SIAM J. Sci. Stat. Comput.*, 5, 753-743.
- [11] Wold, S., Sjöström, M., & Eriksson, L. (2001). PLS-regression: a basic tool of chemometrics. *Chemom. Intell. Lab.*, 58, 109-130.

- [12] MATLAB r. (2011). *MathWorks Inc.*
- [13] RStudioTM 3. (2012). *RStudio Inc.*
- [14] Statistica. (2011). *Data Analysis Software System.*
- [15] Pirouette. (2001). *Infometrix Inc.*
- [16] HQSAR<sup>TM</sup>. (2007). *Manual Release in Sybyl 7.3. Tripos Inc.*
- [17] Cramer, R. D., Patterson, D. E., & Bunce, J. D. (1988). Comparative molecular field analysis (CoMFA). 1. Effect of shape on binding of steroids to carrier proteins. *J. Am. Chem. Soc.*, 110, 5959-5967.
- [18] Cramer, R. D., Patterson, D. E., & Bunce, J. D. (1989). *Recent advances in comparative molecular field analysis (CoMFA)*, *Prog. Clin. Biol. Res.*, 291, 161-165.
- [19] Klebe, G., Abraham, U., & Mietzner, T. (1994). Molecular Similarity Indices in a Comparative Analysis (CoMSIA) of Drug Molecules to Correlate and Predict Their Biological Activity. *J. Med. Chem.*, 37, 4130-4146.
- [20] Martins, J. P. A., Barbosa, E. G., Pasqualoto, K. F. M., & Ferreira, M. M. C. (2009). LQTA-QSAR: A New 4D-QSAR Methodology. *J. Chem. Inf. Model.*, 49, 1428-1436.
- [21] Long, J. R., Gregoriou, V. G., & Gemperline, P. J. (1990). Spectroscopic calibration and quantitation using artificial neural networks. *Anal. Chem.*, 62, 1791-1797.
- [22] Cerqueira, E. O., Andrade, J. C., & Poppi, R. J. (2001). Redes neurais e suas aplicações em calibração multivariada. *Quím. Nova*, 24, 864-873.
- [23] Sigman, M. E., & Rives, S. S. (1994). Prediction of Atomic Ionization Potentials I-III Using an Artificial Neural Network. *J. Chem. Inf. Comput. Sci.*, 34, 617-620.
- [24] Hsiao, T., Lin, C., Zeng, M., & Chiang, H. K. (1998). The Implementation of Partial Least Squares with Artificial Neural Network Architecture. *Proceedings of the 20th Annual International Conference of the IEEE Engineering in Medicine and Biology Society*, 20, 1341-1343.
- [25] Jain, A. K., Mao, J., & Mohiuddin, K. M. (1996). Artificial Neural Networks: A Tutorial. *IEEE Computer*, 29, 31-44.
- [26] Borggaard, C., & Thodberg, H. H. (1992). Optimal minimal neural interpretation of spectra. *Anal. Chem.*, 64, 545-551.
- [27] Zheng, F., Zheng, G., Deaciuc, A. G., Zhan, C. G., Dwoskin, L. P., & Crooks, P. A. (2007). Computational neural network analysis of the affinity of lobeline and tetrabenazine analogs for the vesicular monoamine transporter-2. *Bioorg. Med. Chem.*, 15, 2975-2992.
- [28] Louis, B., Agrawal, V. K., & Khadikar, P. V. (2010). Prediction of intrinsic solubility of generic drugs using mlr, ann and svm analyses. *Eur. J. Med. Chem.*, 45, 4018-4025.



- [29] Fatemi, M. H., Heidari, A., & Ghorbanzade, M. (2010). Prediction of aqueous solubility of drug-like compounds by using an artificial neural network and least-squares support vector machine. *Bull. Chem. Soc. Jpn.*, 83, 1338-1345.
- [30] Honório, K. M., de Lima, E. F., Quiles, M. G., Romero, R. A. F., Molfetta, F. A., & da, Silva. A. B. F. (2010). Artificial Neural Networks and the Study of the Psychoactivity of Cannabinoid Compounds. *Chem. Biol. Drug. Des.*, 75, 632-640.
- [31] Qin, Y., Deng, H., Yan, H., & Zhong, R. (2011). An accurate nonlinear QSAR model for the antitumor activities of chloroethylnitrosoureas using neural networks. *J. Mol. Graph. Model.*, 29, 826-833.
- [32] Himmelblau, D. M. (2000). Applications of artificial neural networks in chemical engineering. *Korean J. Chem. Eng.*, 17, 373-392.
- [33] Marini, F., Bucci, R., Magri, A. L., & Magri, A. D. (2008). Artificial neural networks in chemometrics: History examples and perspectives. *Microchem. J.*, 88, 178-185.
- [34] Mc Cutloch, W. S., & Pttts, W. (1943). A logical calculus of the Ideas imminent in nervous activity. *Bull. Math. Biophys.*, 5, 115-133.
- [35] Pitts, W., & Mc Culloch, W. S. (1947). How we know universals: the perception of auditory and visual forms. *Bull. Math. Biophys.*, 9, 127-147.
- [36] Hebb, D. O. (1949). *The Organization of Behavior*, New York, Wiley.
- [37] Zupan, J., & Gasteiger, J. (1991). Neural networks: A new method for solving chemical problems or just a passing phase? *Anal. Chim. Acta*, 248, 1-30.
- [38] Smits, J. R. M., Melssen, W. J., Buydens, L. M. C., & Kateman, G. (1994). Using artificial neural networks for solving chemical problems. Part I. Multi-layer feed-forward networks. *Chemom. Intell. Lab.*, 22, 165-189.
- [39] Hopfield, J. J. (1982). Neural networks and physical systems with emergent collective computational abilities. *Proc. Nat. Acad. Set.*, 79, 2554-2558.
- [40] Werbos, P. (1974). Beyond Regression: New Tools for Prediction and Analysis in the Behavioral Sciences. *PhD thesis*, Harvard University Cambridge.
- [41] Hoskins, J. C., & Himmelbau, D. M. (1988). Artificial Neural Network Models of Knowledge Representation in Chemical Engineering. *Comput. Chem. Eng.*, 12, 881-890.
- [42] Qian, N., & Sejnowski, T. J. (1988). Predicting the Secondary Structure of Globular Proteins Using Neural Network Models. *J. Mol. Biol.*, 202, 865-884.
- [43] Bohr, H., Bohr, J., Brunak, S., Cotterill, R., Lautrup, B., Nørskov, L., Olsen, O., & Petersen, S. (1988). Protein Secondary Structure and Homology by Neural Networks. *FEBS Lett.*, 241, 223-228.
- [44] Hassoun, M. H. (2003). *Fundamentals of Artificial Neural Networks. A Bradford Book*.



- [45] Zurada, J. M. (1992). *Introduction to Artificial Neural Systems*, Boston, PWS Publishing Company.
- [46] Zupan, J., & Gasteiger, J. (1999). *Neural Networks in Chemistry and Drug Design* (2 ed.), Wiley-VCH.
- [47] Gasteiger, J., & Zupan, J. (1993). Neural Networks in Chemistry. *Angew. Chem. Int. Edit.*, 32, 503-527.
- [48] Marini, F. (2009). Artificial neural networks in foodstuff analyses: Trends and perspectives. *A review. Anal. Chim. Acta*, 635, 121-131.
- [49] Miller, F. P., Vandome, A. F., & Mc Brewster, J. (2011). *Multilayer Perceptron*, Alpha-script Publishing.
- [50] Widrow, B., & Lehr, M. A. (1990). 30 years of Adaptive Neural Networks: Perceptron Madaline and Backpropagation. *Proc. IEEE*, 78, 1415-1442.
- [51] Kohonen, T. (2001). *Self Organizing Maps* (3 ed.), New York, Springer.
- [52] Zupan, J., Noviča, M., & Ruisánchez, I. (1997). Kohonen and counterpropagation artificial neural networks in analytical chemistry. *Chemom. Intell. Lab.*, 38, 1-23.
- [53] Smits, J. R. M., Melssen, W. J., Buydens, L. M. C., & Kateman, G. (1994). Using artificial neural networks for solving chemical problems. Part II. Kohonen self-organising feature maps and Hopfield networks. *Chemom. Intell. Lab.*, 23, 267-291.
- [54] Schneider, G., & Nettekoven, M. (2003). Ligand-based combinatorial design of selective purinergic receptor (a2a) antagonists using self-organizing maps. *J. Comb. Chem.*, 5-233.
- [55] Bayes, T. (1764). An Essay toward solving a problem in the doctrine of chances. *Philosophical Transactions of the Royal Society of London*, 53, 370-418.
- [56] Mackay, D. J. C. (1995). Probable Networks and Plausible Predictions- a Review of Practical Bayesian Methods for Supervised Neural Networks. *Comput. Neural Sys.*, 6, 469-505.
- [57] Mackay, D. J. C. (1992). Bayesian Interpolation. *Neural Comput.*, 4, 415-447.
- [58] Buntine, W. L., & Weigend, A. S. (1991). Bayesian Back-Propagation. *Complex. Sys.*, 5, 603-643.
- [59] de Freitas, J. F. G. (2003). Bayesian Methods for Neural Networks. *PhD thesis*, University Engineering Dept Cambridge.
- [60] Grossberg, S. (1976). Adaptive pattern classification and universal recoding I. Parallel development and coding of neural feature detectors. *Biol. Cybern.*, 23, 121-134.
- [61] Grossberg, S. (1976). Adaptive pattern classification and universal recoding II. Feed-back expectation olfaction and illusions. *Biol. Cybern.*, 23, 187-203.

- [62] Carpenter, G. A., Grossberg, S., & Rosen, D. B. (1991). ART-2a-an adaptive resonance algorithm for rapid category learning and recognition. *Neural Networks*, 4, 493-504.
- [63] Wienke, D., & Buydens, L. (1995). Adaptive resonance theory based neural networks-the 'ART' of real-time pattern recognition in chemical process monitoring? *TrAC Trend. Anal. Chem.*, 14, 398-406.
- [64] Lin, C. C., & Wang, H. P. (1993). Classification of autoregressive spectral estimated signal patterns using an adaptive resonance theory neural network. *Comput. Ind.*, 22, 143-157.
- [65] Whiteley, J. R., & Davis, J. F. (1994). A similarity-based approach to interpretation of sensor data using adaptive resonance theory. *Comput. Chem. Eng.*, 18, 637-661.
- [66] Whiteley, J. R., & Davis, J. F. (1993). Qualitative interpretation of sensor patterns. *IEEE Expert*, 4, 54-63.
- [67] Wienke, D., & Kateman, G. (1994). Adaptive resonance theory based artificial neural networks for treatment of open-category problems in chemical pattern recognition-application to UV-Vis and IR spectroscopy. *Chemom. Intell. Lab.*, 23, 309-329.
- [68] Wienke, D., Xie, Y., & Hopke, P. K. (1994). An adaptive resonance theory based artificial neural network (ART-2a) for rapid identification of airborne particle shapes from their scanning electron microscopy images. *Intell. Lab.*, 26, 367-387.
- [69] Xie, Y., Hopke, P. K., & Wienke, D. (1994). Airborne particle classification with a combination of chemical composition and shape index utilizing an adaptive resonance artificial neural network. *Environ. Sci. Technol.*, 28, 1921-1928.
- [70] Wienke, D., van den, Broek. W., Melssen, W., Buydens, L., Feldhoff, R., Huth-Fehre, T., Kantimm, T., Quick, L., Winter, F., & Cammann, K. (1995). Comparison of an adaptive resonance theory based neural network (ART-2a) against other classifiers for rapid sorting of post consumer plastics by remote near-infrared spectroscopic sensing using an InGaAs diode array. *Anal. Chim. Acta*, 317, 1-16.
- [71] Domine, D., Devillers, J., Wienke, D., & Buydens, L. (1997). ART 2-A for Optimal Test Series Design in QSAR. *J. Chem. Inf. Comput. Sci.*, 37, 10-17.
- [72] Wienke, D., & Buydens, L. (1996). Adaptive resonance theory based neural network for supervised chemical pattern recognition (FuzzyARTMAP). Part 1: Theory and network properties. *Chemom. Intell. Lab.*, 32, 151-164.
- [73] Wienke, D., van den, Broek. W., Buydens, L., Huth-Fehre, T., Feldhoff, R., Kantimm, T., & Cammann, K. (1996). Adaptive resonance theory based neural network for supervised chemical pattern recognition (FuzzyARTMAP). Part 2: Classification of post-consumer plastics by remote NIR spectroscopy using an InGaAs diode array. *Chemom. Intell. Lab.*, 32, 165-176.
- [74] Buhmann, M. D. (2003). *Radial Basis Functions: Theory and Implementations*, Cambridge University.

- [75] Lingireddy, S., & Ormsbee, L. E. (1998). Neural Networks in Optimal Calibration of Water Distribution Systems. In: Flood I, Kartam N. (eds.) *Artificial Neural Networks for Civil Engineers: Advanced Features and Applications*. Amer. Society of Civil Engineers, 53-76.
- [76] Shahsavand, A., & Ahmadpour, A. (2005). Application of Optimal Rbf Neural Networks for Optimization and Characterization of Porous Materials. *Comput. Chem. Eng.*, 29, 2134-2143.
- [77] Regis, R. G., & Shoemaker, C. (2005). A Constrained Global Optimization of Expensive Black Box Functions Using Radial Basis Functions. *J. Global. Optim.*, 31, 153-171.
- [78] Han, H., Chen, Q., & Qiao, J. (2011). An efficient self-organizing RBF neural network for water quality prediction. *Neural Networks*, 24, 717-725.
- [79] Fidêncio, P. H., Poppi, R. J., Andrade, J. C., & Abreu, M. F. (2008). Use of Radial Basis Function Networks and Near-Infrared Spectroscopy for the Determination of Total Nitrogen Content in Soils from Sao Paulo State. *Anal. Sci.*, 24, 945-948.
- [80] Yao, X., Liu, M., Zhang, X., Zhang, R., Hu, Z., & Fan, B. (2002). Radial Basis Function Neural Networks Based QSPR for the Prediction of log P. *Chinese J. Chem.*, 20, 722-730.
- [81] Hopfield, J. J. (1982). Neural networks and physical systems with emergent collective computational abilities. *Proc. Natl. Acad. Sci., USA*, 79, 2554-2558.
- [82] Hopfield, J. J. (1984). Neurons with graded response have collective computational properties like those of two-state neurons. *Proc. Natl. Acad. Sci., USA*, 81, 3088-3092.
- [83] Arakawa, M., Hasegawa, K., & Funatsu, K. (2003). Application of the Novel Molecular Alignment Method Using the Hopfield Neural Network to 3D-QSAR. *J. Chem. Inf. Comput. Sci.*, 43, 1396-1402.
- [84] Braga, J. P., Almeida, M. B., Braga, A. P., & Belchior, J. C. (2000). Hopfield neural network model for calculating the potential energy function from second virial data. *Chem. Phys.*, 260, 347-352.
- [85] Hjelmfelt, A., & Ross, J. (1992). Chemical implementation and thermodynamics of collective neural networks. *PNAS*, 89, 388-391.
- [86] Hjelmfelt, A., Schneider, F. W., & Ross, J. (1993). Pattern Recognition in Coupled Chemical Kinetic Systems. *Science*, 260, 335-337.
- [87] Vracko, M. (2005). Kohonen Artificial Neural Network and Counter Propagation Neural Network in Molecular Structure-Toxicity Studies. *Curr. Comput-Aid. Drug*, 1, 73-78.
- [88] Guha, R., Serra, J. R., & Jurs, P. C. (2004). Generation of QSAR sets with a self-organizing map. *J. Mol. Graph. Model.*, 23, 1-14.

- [89] Hoshi, K., Kawakami, J., Kumagai, M., Kasahara, S., Nishimura, N., Nakamura, H., & Sato, K. (2005). An analysis of thyroid function diagnosis using Bayesian-type and SOM-type neural networks. *Chem. Pharm. Bull.*, 53, 1570-1574.
- [90] Nandi, S., Vracko, M., & Bagchi, M. C. (2007). Anticancer activity of selected phenolic compounds: QSAR studies using ridge regression and neural networks. *Chem. Biol. Drug Des.*, 70, 424-436.
- [91] Xiao, Y. D., Clauset, A., Harris, R., Bayram, E., Santago, P., & Schmitt, . (2005). Supervised self-organizing maps in drug discovery. 1. Robust behavior with overdetermined data sets. *J. Chem. Inf. Model.*, 45, 1749-1758.
- [92] Molfetta, F. A., Angelotti, W. F. D., Romero, R. A. F., Montanari, C. A., & da, Silva. A. B. F. (2008). A neural networks study of quinone compounds with trypanocidal activity. *J. Mol. Model.*, 14, 975-985.
- [93] Zheng, F., Zheng, G., Deaciuc, A. G., Zhan, C. G., Dwoskin, L. P., & Crooks, P. A. (2007). Computational neural network analysis of the affinity of lobeline and tetrabenazine analogs for the vesicular monoamine transporter-2. *Bioorg. Med. Chem.*, 15, 2975-2992.
- [94] Caballero, J., Fernandez, M., & Gonzalez-Nilo, F. D. (2008). Structural requirements of pyrido[2,3-d]pyrimidin-7-one as CDK4/D inhibitors: 2D autocorrelation CoMFA and CoMSIA analyses. *Bioorg. Med. Chem.*, 16, 6103-6115.
- [95] Schneider, G., Coassolo, P., & Lavé, T. (1999). Combining in vitro and in vivo pharmacokinetic data for prediction of hepatic drug clearance in humans by artificial neural networks and multivariate statistical techniques. *J. Med. Chem.*, 42, 5072-5076.
- [96] Hu, L., Chen, G., & Chau, R. M. W. (2006). A neural networks-based drug discovery approach and its application for designing aldose reductase inhibitors. *J. Mol. Graph. Model.*, 24, 244-253.
- [97] Afantitis, A., Melagraki, G., Koutentis, P. A., Sarimveis, H., & Kollias, G. (2011). Ligand-based virtual screening procedure for the prediction and the identification of novel  $\beta$ -amyloid aggregation inhibitors using Kohonen maps and Counterpropagation Artificial Neural Networks. *Eur. J. Med. Chem.*, 46, 497-508.
- [98] Noeske, T., Trifanova, D., Kaus, V., Renner, S., Parsons, C. G., Schneider, G., & Weil, T. (2009). Synergism of virtual screening and medicinal chemistry: Identification and optimization of allosteric antagonists of metabotropic glutamate receptor 1. *Bioorg. Med. Chem.*, 17, 5708-5715.
- [99] Karpov, P. V., Osolodkin, D. I., Baskin, I. I., Palyulin, V. A., & Zefirov, N. S. (2011). One-class classification as a novel method of ligand-based virtual screening: The case of glycogen synthase kinase 3 $\beta$  inhibitors. *Bioorg. Med. Chem. Lett.*, 21, 6728-6731.
- [100] Molnar, L., & Keseru, G. M. (2002). A neural network based virtual screening of cytochrome p450a4 inhibitors. *Bioorg. Med. Chem. Lett.*, 12, 419-421.

- [101] Di Massimo, C., Montague, G. A., Willis, M. T., & Morris, A. J. (1992). Towards improved penicillin fermentation via artificial neural networks. *Comput. Chem. Eng.*, 16, 283-291.
- [102] Palancar, M. C., Aragón, J. M., & Torrecilla, J. S. (1998). pH-Control System Based on Artificial Neural Networks. *Ind. Eng. Chem. Res.*, 37, 2729-2740.
- [103] Takayama, K., Fujikawa, M., & Nagai, T. (1999). Artificial Neural Network as a Novel Method to Optimize Pharmaceutical Formulations. *Pharm. Res.*, 16, 1-6.
- [104] Takayama, K., Morva, A., Fujikawa, M., Hattori, Y., Obata, Y., & Nagai, T. (2000). Formula optimization of theophylline controlled-release tablet based on artificial neural networks. *J. Control. Release*, 68, 175-186.
- [105] Fanny, B., Gilles, M., Natalia, K., Alexandre, V., & Dragos, H. Using Self-Organizing Maps to Accelerate Similarity Search. *Bioorg. Med. Chem.*, In Press, <http://dxdoi.org/101016/jbmc201204024>.
- [106] Sigman, M. E., & Rives, S. S. (1994). Prediction of Atomic Ionization Potentials I-III Using an Artificial Neural Network. *J. Chem. Inf. Comput. Sci.*, 34, 617-620.
- [107] Tetko, I. V., & Tanchuk, V. Y. (2002). Application of Associative Neural Networks for Prediction of Lipophilicity in ALOGPS 2.1 Program. *J. Chem. Inf. Comput. Sci.*, 42, 1136-1145.
- [108] Tetko, I. V., Tanchuk, V. Y., & Villa, A. E. P. (2001). Prediction of n-Octanol/Water Partition Coefficients from PHYSPROP Database Using Artificial Neural Networks and E-State Indices. *J. Chem. Inf. Comput. Sci.*, 41, 1407-1421.
- [109] Sumpter, B. G., & Noid, D. W. (1994). Neural networks and graph theory as computational tools for predicting polymer properties. *Macromol. Theor. Simul.*, 3, 363-378.
- [110] Scotta, D. J., Coveney, P. V., Kilnerb, J. A., Rossinyb, J. C. H., & Alford, N. M. N. (2007). Prediction of the functional properties of ceramic materials from composition using artificial neural networks. *J. Eur. Ceram. Soc.*, 27, 4425-4435.
- [111] Stojković, G., Noviĉ, M., & Kuzmanovski, I. (2010). Counter-propagation artificial neural networks as a tool for prediction of pK<sub>BH</sub><sup>+</sup> for series of amides. *Chemom. Intell. Lab.*, 102, 123-129.
- [112] Næs, T., Kvaal, K., Isaksson, T., & Miller, C. (1993). Artificial neural networks in multivariate calibration. *J. Near. Infrared Spectrosc.*, 1, 1-11.
- [113] Munk, M. E., Madison, M. S., & Robb, E. W. (1991). Neural-network models for infrared-spectrum interpretation. *Mikrochim. Acta*, 2, 505-524.
- [114] Meyer, M., & Weigelt, T. (1992). Interpretation of infrared spectra by artificial neural networks. *Anal. Chim. Acta*, 265, 183-190.



- [115] Smits, J. R. M., Schoenmakers, P., Stehmann, A., Sijstermans, F., & Chemom, Kate-man G. (1993). Interpretation of infrared spectra with modular neural-network sys-tems. *Intell. Lab.*, 18, 27-39.
- [116] Goodacre, R., Neal, M. J., & Kell, D. B. (1994). Rapid and Quantitative Analysis of the Pyrolysis Mass Spectra of Complex Binary and Tertiary Mixtures Using Multivariate Calibration and Artificial Neural Networks. *Anal. Chem.*, 66, 1070-1085.
- [117] Cirovic, D. (1997). Feed-forward artificial neural networks: applications to spectro-scopy. *TrAC Trend. Anal. Chem.*, 16, 148-155.
- [118] Zhao, R. H., Yue, B. F., Ni, J. Y., Zhou, H. F., & Zhang, Y. K. (1999). Application of an artificial neural network in chromatography-retention behavior prediction and pat-tern recognition. *Chemom. Intell. Lab.*, 45, 163-170.
- [119] Blanco, M., Coello, J., Iturriaga, H., Maspoch, S., & Redon, M. (1995). Artificial Neural Networks for Multicomponent Kinetic Determinations. *Anal. Chem.*, 67, 4477-4483.
- [120] Fatemi, M. H. (2006). Prediction of ozone tropospheric degradation rate constant of organic compounds by using artificial neural networks. *Anal. Chim. Acta*, 556, 355-363.
- [121] Diederichs, K., Freigang, J., Umhau, S., Zeth, K., & Breed, J. (1998). Prediction by a neural network of outer membrane {beta}-strand protein topology. *Protein Sci.*, 7, 2413-2420.
- [122] Meiler, J. (2003). PROSHIFT: Protein chemical shift prediction using artificial neural networks. *J. Biomol. NMR*, 26, 25-37.
- [123] Lohmann, R., Schneider, G., Behrens, D., & Wrede, P. A. (1994). Neural network model for the prediction of membrane-spanning amino acid sequences. *Protein Sci.*, 3, 1597-1601.
- [124] Dombi, G. W., & Lawrence, J. (1994). Analysis of protein transmembrane helical re-gions by a neural network. *Protein Sci.*, 3, 557-566.
- [125] Wang, S. Q., Yang, J., & Chou, K. C. (2006). Using stacked generalization to predict membrane protein types based on pseudo-amino acid composition. *J. Theor. Biol.*, 242, 941-946.
- [126] Ma, L., Cheng, C., Liu, X., Zhao, Y., Wang, A., & Herdewijn, P. (2004). A neural net-work for predicting the stability of RNA/DNA hybrid duplexes. *Chemom. Intell. Lab.*, 70, 123-128.
- [127] Ferran, E. A., Pflugelaer, B., & Ferrara, P. (1994). Self-organized neural maps of hu-man protein sequences. *Protein Sci.*, 3, 507-521.
- [128] Petritis, K., Kangas, L. J., Ferguson, P. L., Anderson, G. A., Paša-Tolić, L., Lipton, M. S., Auberry, K. J., Strittmatter, E. F., Shen, Y., Zhao, R., & Smith, R. D. (2003). Use of Artificial Neural Networks for the Accurate Prediction of Peptide Liquid Chromatog-raphy Elution Times in Proteome Analyses. *Anal. Chem.*, 75, 1039-1048.



- [129] Huang, R., Du, Q., Wei, Y., Pang, Z., Wei, H., & Chou, K. (2009). Physics and chemistry-driven artificial neural network for predicting bioactivity of peptides and proteins and their design. *J. Theor. Biol.*, 256, 428-435.
- [130] Martin, Y. G., Oliveros, M. C. C., Pavon, J. L. P., Pinto, C. G., & Cordero, B. M. (2001). Electronic nose based on metal oxide semiconductor sensors and pattern recognition techniques: characterisation of vegetable oils. *Anal. Chim. Acta*, 449, 69-80.
- [131] Brodnjak-Voncina, D., Kodba, Z. C., & Novic, M. (2005). Multivariate data analysis in classification of vegetable oils characterized by the content of fatty acids. *Chemom. Intell. Lab.*, 75, 31-43.
- [132] Zhang, G. W., Ni, Y. N., Churchill, J., & Kokot, S. (2006). Authentication of vegetable oils on the basis of their physico-chemical properties with the aid of chemometrics. *Talanta*, 70, 293-300.
- [133] Goodacre, R., Kell, D. B., & Bianchi, G. (1993). Rapid assessment of the adulteration of virgin olive oils by other seed oils using pyrolysis mass spectrometry and artificial neural networks. *J. Sci. Food Agr.*, 63, 297-307.
- [134] Bianchi, G., Giansante, L., Shaw, A., & Kell, D. B. (2001). Chemometric criteria for the characterisation of Italian DOP olive oils from their metabolic profiles. *Eur. J. Lipid. Sci. Tech.*, 103, 141-150.
- [135] Bucci, R., Magri, A. D., Magri, A. L., Marini, D., & Marini, F. (2002). Chemical Authentication of Extra Virgin Olive Oil Varieties by Supervised Chemometric Procedures. *J. Agric. Food Chem.*, 50, 413-418.
- [136] Marini, F., Balestrieri, F., Bucci, R., Magri, A. D., Magri, A. L., & Marini, D. (2004). Supervised pattern recognition to authenticate Italian extra virgin olive oil varieties. *Chemom. Intell. Lab.*, 73, 85-93.
- [137] Marini, F., Balestrieri, F., Bucci, R., Magri, A. L., & Marini, D. (2003). Supervised pattern recognition to discriminate the geographical origin of rice bran oils: a first study. *Microch. J.*, 74, 239-248.
- [138] Marini, F., Magri, A. L., Marini, D., & Balestrieri, F. (2003). Characterization of the lipid fraction of Niger seeds (*Guizotia abyssinica* cass) from different regions of Ethiopia and India and chemometric authentication of their geographical origin. *Eur. J. Lipid. Sci. Tech.*, 105, 697-704.
- [139] Alexander, P. W., Di Benedetto, L. T., & Hibbert, D. B. (1998). A field-portable gas analyzer with an array of six semiconductor sensors. Part 2: Identification of beer samples using artificial neural networks. *Field. Anal. Chem. Tech.*, 2, 145-153.
- [140] Penza, M., & Cassano, G. (2004). Chemometric characterization of Italian wines by thin-film multisensors array and artificial neural networks. *Food Chem.*, 86, 283-296.

- [141] Latorre, Pena. R., Garcia, S., & Herrero, C. (2000). Authentication of Galician (NW Spain) honeys by multivariate techniques based on metal content data. *Analyst.*, 125, 307-312.
- [142] Cordella, C. B. Y., Militao, J. S. L. T., & Clement, M. C. (2003). Cabrol-Bass D Honey Characterization and Adulteration Detection by Pattern Recognition Applied on HPAEC-PAD Profiles. 1. Honey Floral Species Characterization. *J. Agric. Food Chem.*, 51, 3234-3242.
- [143] Brodnjak-Voncina, D., Dobcnik, D., Novic, M., & Zupan, J. (2002). Chemometrics characterisation of the quality of river water. *Anal. Chim. Acta*, 462, 87-100.
- [144] Voncina, E., Brodnjak-Voncina, D., Sovic, N., & Novic, M. (2007). Chemometric characterisation of the Quality of Ground Waters from Different wells in Slovenia. *Acta Chim. Slov.*, 54, 119-125.
- [145] Bos, A., Bos, M., & van der Linden, W. E. (1992). Artificial neural networks as a tool for soft-modelling in quantitative analytical chemistry: the prediction of the water content of cheese. *Anal. Chim. Acta*, 256, 133-144.
- [146] Cimpoi, C., Cristea, V., Hosu, A., Sandru, M., & Seserman, L. (2011). Antioxidant activity prediction and classification of some teas using artificial neural networks. *Food Chem.*, 127, 1323-1328.

