Prediction of Selectivity Coefficients of Medicine Electrode Using Artificial Neural Networks and Partial Least Squares

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In this paper, the selectivity coefficient of ion selective electrode is first predicted by artificial neural networks (ANN) and partial least squares (PLS), with topological indices of the interference taken as inputs for these two chemometric techniques. The prediction results for ANN were better than that for PLS.

The problem of the selectivity of ion selective electrode has been exploring by many chemists since it was invented. The development in theory is far inferior to that in applications. There are many factors affecting the selectivity of electrodes. For example, for the PVC membrane medicine electrode studied in this paper, the active matter was obtained by mixing sodium tetraphenylboron and berberinum hydrochloride to produce ion association compound. The selectivity of the electrode coated by this active matter for the analytes is affected by many factors, such as solvent, the property of the active matter and the property of the interference ions.[1] Discussion about the relationship between the structural descriptors and their selectivity coefficients when the solvent and component of active matter and other conditions are controlled to be constant will be beneficial to the study of reactions at electrodes.

In this study, the application of both ANN and PLS are investigated. The ANN approach is selected because of its adaptability to almost any mathematical function.[2] It is much better at many directions than conventional multivariate methods, e. g. partial least squares (PLS) which has been shown in this paper.

ANNs have been applied to the area of QSAR in recent years. Reports were either about prediction of retention performance of chromatography,[3-5] chemical activity or physical property.[6] However, studies about prediction of selectivity coefficient of electrode has never been reported. As we know, ANN is not very suitable for prediction of very accuracy data,[7] and selectivity coefficient is just a kind of reference experiment data which may fluctuate with experiment conditions such as electrode performance, purity of the interference, speed of stirring, etc. The accuracy requirement for selectivity coefficient is not very strict. So it is suitable to use ANN for prediction of its value.

A two-layer back-propagation network was used in our experiment which has nine inputs (topological indices) in the input layer, an arbitrary number of artificial neurons in the hidden layer (5) and one neuron in the output layer (selectivity coefficient). In our study, a sigmoid activation function was used. In the experiment, learning rate in the network training was set as 0.5, the momentum coefficient, 0.8.

Table 1. Topological indices of interference

interference	$N_{C=C}$	$N_{OH(1)}$	$N_{OH(2)}$	T	$N_{N(1)}$	$N_{N(2)}$	$N_{N(3)}$	$N_{C=O}$	$N_{(RO)}$
1. 5,6-dihydro-2,3.9,10-tetra-methoxy hydrochloride	7	0	1	9	0	0	1	0	3
2. 5,6-dihydro-3-hydroxy-2,9,10-trimethoxy hydrochloride	7	0	0	9	0	0	1	0	4
3. crystal violet	9	0	0	7	0	0	3	0	0
4. pilocarpine hydrochloride	1	0	0	1	0	0	2	1	1
5. tetrabutylammonium bromide	0	0	0	0	0	0	1	0	0
6. ephedrine hydrochloride	3	0	1	3	0	1	0	0	0
7. triethanolamine	0	3	0	0	0	0	1	0	0
8. strynine	4	0	0	5	0	0	2	1	1
9. caffeine	1	0	0	4	0	0	4	0	2
10. atropine sulfate	3	1	0	1	0	0	1	1	1
11. acridine yellow	6	0	0	7	1	4	0	0	0
12. urea	0	0	0	1	2	0	0	1	0
13. tartaric acid	0	0	1	3	0	0	0	2	0
14. vitamin B_6	0	2	1	1	0	0	1	0	0
15. brucine	4	0	0	7	0	0	2	1	3
16. diphenhydramine hydrochloride	6	0	0	0	0	0	1	0	1
17. quinine	5	0	1	4	0	0	2	0	1
18. hexadecyltrimethylammonium bromide	0	0	0	0	0	0	1	0	0
19. scopoamine hydrobromide	3	1	1	1	0	0	1	1	1
20. benzyltrimethylammonium chloride	3	0	0	1	0	0	1	0	0
21. procaine hydrochloride[a]	3	0	0	3	1	0	1	1	1
22. colchicine[a]	6	0	0	9	0	1	0	2	4
23. tetramethylammonium chloride[a]	0	0	0	0	0	0	1	0	0
24. ethyl violet[a]	6	0	0	7	0	0	3	0	0

[a] Test sample.

Table2. Correspondence between the ideal output of ANN and selectivity coefficients of electrode

K_{ij}[a]	>0.5	0.1-0.5	0.05-0.09	0.01-0.05	0.005-0.009	0.001-0.005	<0.001
O[b]	0.90	0.75	0.60	0.45	0.30	0.15	0.01

[a]Selectivity coefficients of electrode. [b]ANN ideal output.

Table3. Selectivity coefficients prediction results for ANN and PLS

Sample No	Ideal output	ANN predicted output	PLS predicted output
21	0.45	0.381	0.511
22	0.30	0.351	0.967[a]
23	0.60	0.570	0.106[a]
24	0.75	0.749	0.768

[a]Predicted mistake.

It is very important to choose appropriate structural descriptors for successful prediction of physical or chemical property. One of the advantages of ANN is that it does not require linear relationship between input variables and aim functions and linear irrelevance between input variables. So the topological indices were chosen,[8] which can be obtained from molecular structural figure and does not depend on experiment data as well as complex computation. Following topological indices were used in our experiment.

1. number of double bonds between carbon atoms in the molecular
2. number of hydroxy group in primary alcohol
3. number of hydroxy group in secondary and tertiary alcohol
4. number of quaterary carbon atoms
5. number of amidogen in primary amine
6. number of amidogen in secondary amine
7. number of amidogen in tetraamine
8. number of ketonic oxygen
9. number of alkoxy group

The principle for choosing these parameters is that they can reflect the characteristic of molecules and their degeneracy should be low. Table 1 shows the topological indices.

Medicine berberinum selective electrode was made according to Ref. [9]. The detection limit of it arrived 10^{-6} mol/l. In the range of 10^{-6} to 10^{-2} mol/l, the response of the electrode for berberinum accord with Nernst equation. The slope was 56-59 mV. More than twenty interference's selectivity coefficients were detected using mixing solution and respective solution methods respectively. Since it is not suitable to give the selectivity coefficient a accuracy and fixed value, we divided them into seven grades from the lowest to the highest. Every grade range corresponds to a ideal output centre value for ANN so as to train the network. The derivation of prediction data from the centre value in each grade less than 0.075 was considered qualified or converged. The corresponding relationship between K_{ij} and the output value of ANN is shown in Table 2.

The two chemometric techniques used in this paper are ANN and PLS. The calibration set consisted of 20 interference for these two methods was the same given in Table1. The test set consisted of four interference which were not included in the calibration set. It can be seen from Table 3 that the selectivity coefficient prediction results for ANN were better than that for PLS. For ANN, the output values for the four interference all fell to the qualified range, in contrast, there were two prediction mistakes for PLS, and the error values are relatively large. The increase in prediction capacity for ANN is due to its advantageous ability to treat nonlinear problem. In contrast, PLS is good at dealing with linear problem, so it gave larger relative errors of prediction.

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