South African Journal of Chemical Engineering, vol. 20, 2015, no. 2, pp. 1-17

Application of Neural Network in Chemical and Non-Chemical Engineering Problems

M. Chetty[1], M. Carsky[1,2], and E. Kormuth[2]
[1]Department of Chemical Engineering, Durban University of Technology, Durban, South Africa
[2] College of Agriculture, Engineering, and Science. University of KwaZulu Natal, Durban, South Africa

Abstract

Use of a neural network approach to the solution of complex tasks is demonstrated on first, the identification of a food chemical specification ("Chemical Engineering case") and second, the prediction of survival and prognosis for leukaemia patients ("Non-Chemical Engineering case").

In the first case product colour was identified as an important quality feature, which significantly affects marketing of food grade antioxidants used for preservation of edible oils. The product quality is specified in terms of the "Lovibond colour index". Production of phenolic antioxidant in a well-established operation exhibited for an extended period of time a variation of the product colour. Due to the complexity of the technological process it is impossible to pinpoint a simple reason for variations. The product is synthesised in a batch reactor, the crude product is then recovered from post-reaction batch via crystallisation and refined in a complex purification process to get the final product, which meets specification. It is unclear, whether the undesirable colour is formed during the synthesis itself or results from underperformance of the purification process. Data from the manufacturing process were collected over 140 batches, where the impurity profile of crude product was recorded along with some other purification parameters. Impurity profile included an occurrence of 32 different compounds, some of them occurring on a random basis. The neural network model predicts the final product quality on the basis of a crude product impurity profile. Thus the process management decision to premeditate the product can be made well in advance during the process. Should the prediction show that the final product would not meet the required specification, corrective measures can be implemented well in advance to rescue the final product.

In the second case the neural network model attempts to predict survival rate of leukaemia patients over two and three year periods based on 38 medical factors of patients and treatment procedures chosen, Which make it possible to apply the right treatment at an early stage.

[2] Professor Emeritus at University of KwaZulu-Natal, School of Engineering, Durban, RSA

Introduction

Artificial neural networks are classified as "black box" mathematical non-linear regression tools. They learn and identify correlative patterns between sets of input data and corresponding outputs. As in the human brain, learning starts with known data and eventually the brain is trained to adapt to changing environments but the basis is always what was learnt during the training period. As the saying goes "good judgment comes from experience, experience comes from bad judgment," so the neural network needs "experience" to learn to make "good judgments". This experience comes from training it with rich characteristic data of the system under consideration. The training of these neural networks is a form of non-linear regression and has developed into a tried and tested technique.

An artificial neural network is typically a massive parallel-interconnected network of "artificial neurons" (also called Processing Elements, Nodes or Units). The way in which these processing elements are mutually interconnected determines the network architecture. Over 50 different types of network architecture can be found in the literature (Morris et. all, 1994), (Bulsari, 1995). In this paper we have used the most common type of a neural network architecture called the feedforward or backpropagation network. A feedforward neural network is made up of layers of processing elements. An example of the structure of a feedforward neural network with one input layer, one hidden and one output layer is illustrated in Fig. 1. The data from the input layer are propagated through the network via the interconnections to processing elements in the first hidden layer where they are combined and modified by activation functions. The signals proceed in this way from layer to layer until they reach the output layer. The output from any processing element of the hidden layer is given by

$$y_j = f\left(\sum_{i=1}^{l} w^0_{ji} x_i\right), \quad \text{j} = 1,...,m \tag{1}$$

where m is the number of processing elements in the hidden layer and w^0_{ji} is a weight associated with a connection between the ith processing element in the input layer and the jth processing element in the hidden layer. The formula for the output nodes of the neural network is similar to that of eq.1:

$$z_k = f\left(\sum_{j=1}^{m} w^1_{kj} y_j\right), \qquad \text{k} = 1,...,n \tag{2}$$

n is the number of output neurons, and w^1_{kj} is weight associated with a connection between the jth processing element in the hidden layer and the kth processing element in the output layer. The activation functions chosen for output and hidden layer processing elements are a sigmoidal function $f(x) = 1/(1+e^{-x})$ and a symmetric sigmoidal function $f(x) = \tanh(x)$, respectively.

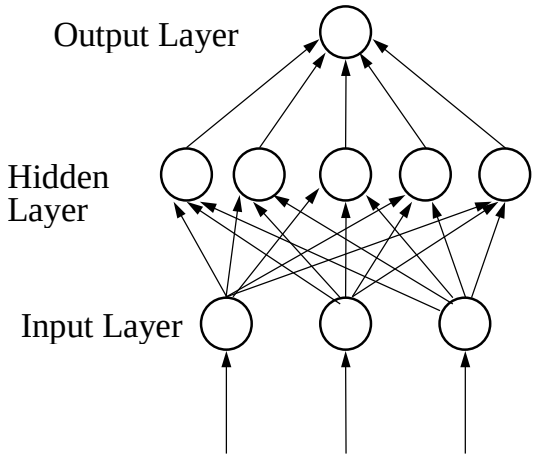

Fig. 1. An example of a 3-5-1 feedforward neural network.

Mathematical modelling of the neuron is based on neurophysiology of biological neurons. The mathematics of a typical artificial neuron may be represented by Figure 2 (Haykin, 1994). The effects of the synaptic gap on activation of the neuron are modelled by weights (w_{kp}) which are multiplied by frequencies (x_i). The "weighted" neurons are then summed up to form the internal activity (u_k) of the neuron. The result is processed by a transfer function to produce the outputs.

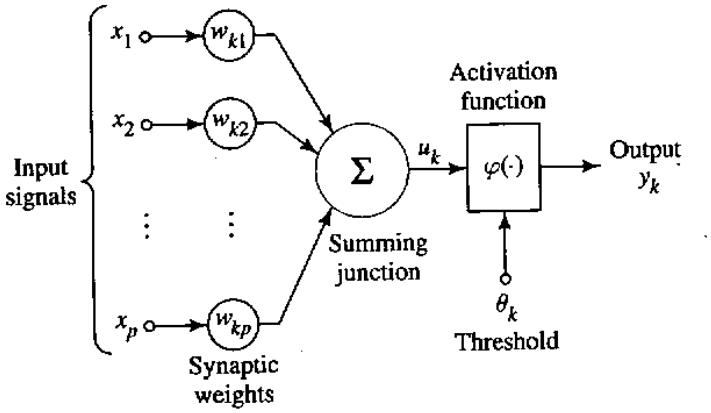

Fig. 2 Non-linear model of a neuron

Neural network modelling

The neural network package "*Predict*" was used for the simulation in both cases (NeuralWorks Predict, 1995). *Predict* uses one hidden layer only. Otherwise, the network architecture is not fully determined in advance. The number of nodes in an output layer is given by a number of model output variables. For a hidden layer, *Predict* uses a method called "Cascade Learning"

(Fahlmann and Lebiere, 1988) in order to determine a suitable number of hidden nodes. The number of input nodes may correspond to the number of input variables chosen. Or, alternatively, *Predict* can employ its genetic algorithm to analyse input variables and to find the most advantageous set of them for neural network modelling. Every input variable may be used more times in different transformations. The genetic algorithm may identify principal process variables, which have the most significant effect on model outputs, and it may also disregard input variables that show small or negligible effect on the process under consideration.

Case 1

Phenolic antioxidant is synthesized in a batch reactor by alkylation of phenolic precursor slurried in an organic solvent using alcohol as an alkylating agent. The reaction proceeds in the presence of mineral acid as a catalyst. After alkylation an acid phase is decanted and re-used in the next batch, while crude product is crystallised from the solvent and after separation subjected to the purification process.

The final product quality is only established after the product exits the purification process and enters the packaging line. The product is analysed for all specification features based on FCC specification as well as the features required by specific customers. Of the features important for some of the customers is colour in solution, which is measured on the product dissolved in propylene glycol. During the test the colour components, which is otherwise impossible to identify by the naked eye are quantified using the Lovibond colour index.

The manufacturing process itself features an extended batch time, whereby it takes about 60 hours on average from the time the molecule of the phenolic precursor enters the process to the time, the respective molecule of product exits the process and is transferred from the operation into a warehouse. Significant value is being added during the process and the final result is only found once all the process steps are completed.

An in-process-control system caters for regular sampling of all raw materials, crude, post-reaction product and an intermediate during the purification of crude material. Analysis of crude post-reaction product is conducted on GC and only three of many of peaks at the chromatogram are regularly evaluated in order to establish conversion and selectivity of the reaction. In addition the chromatogram provides an impurities profile, which was not evaluated due to the complexity of the component matrix.

An attempt was made to link the impurities profile to the final colour of the product and thus to test whether it is possible to predict the final colour based on the chromatogram obtained from the crude product analysis. This will bring a significant benefit to the operation in two main factors. Firstly the important feature of the final product will be known after 8 hours from the beginning of manufacturing process instead of 60 hours. Secondly, it can clearly show, whether the colour index is pre-determined in a synthesis process or only during downstream processing.

Early knowledge of the final product quality enables corrective measures to be conducted timeously, particularly by means of discarding recycled raw materials where the impurity build-up was impossible to identify by the direct analysis.

Chromatographic record revealed the presence of as many as 32 peaks representing various product impurities. It is anticipated that these impurities have a decisive effect on the colour of the final product. However the complexity of the problem does not allow any direct determination of this effect. In such a case it is advantageous to employ neural network modelling in order to find a correlation between multiple input variables (here chromatographic data) and output variable(s) (here product colour characterised by Lovibond colour index). This correlation is expected to exist but in a way that is not quite clear.

Data processing

The data used for neural network prediction of the Lovibond colour index of the final product were taken from a GC analysis of crude, post-reaction product. The chromatogram revealed in total of 32 peaks thus providing a so called "crude product impurity profile". Each peak was characterised numerically by an "area count", which indicates the amount of a particular component present. These values of area counts were taken as input variables for the neural network model. The only output variable was the colour of the final product characterised by "Lovibond colour index", which was determined by a standard procedure. The ultimate goal of the neural network simulation was finding a mathematical model correlating the input variables (chromatographic data) with the product colour index.

Results and discussion

The weights ($\boldsymbol{w^0}$ and $\boldsymbol{w^1}$) between processing elements in the input and hidden layer and between the hidden and output layer are established so as to minimise the differences between network outputs and the experimental values. This phase is called "neural network training". An objective function is specified which is a measure of how closely the outputs of the network match the target values from the training set of data. Experimental data stated above was used to find a relation between input variables and the final product colour.

All experimental data collected in the process, i.e. 140 impurity profiles (items) collected on 140 batches were used in developing (building and training) the neural network model. All the data were split randomly into the training set (80%) and test set (20%). Then the neural net was trained and the root mean square error was evaluated on the test set predictions. The training was repeated several times for different data partitioning into the training and test sets and predictions for each test set were calculated. Because the input-output relationship represented by a network did not depend on the way of splitting the experimental data into training and test sets, the training could be regarded as stable. Each item of data consisted of as many as 32 input variables to the model and one output (product colour). Several neural network models were constructed using different combinations of input variables (including the whole set). The decision, which model was the best one was made on the basis of a minimal value of a root mean square error (RMSE) chosen as an optimisation criterion. According to that criterion a model with 11 input variables, corresponding to 12 input transformations, 9 hidden and 1 output nodes (nn model 12-9-1) was chosen finally. In the development of this model 21 variables were identified as having no or negligible effect on the product colour and were rejected. Table 1 shows details of the resulting neural network architecture, and the active (i.e. not rejected) variables and their transformations.

The predicted values of Lovibond colour index of the final product are plotted against the experimental values in Fig. 3 for all data, with an indication of a 95%-confidence interval. The limiting value of the Lovibond colour index according to the product specification is 0.7. If this value is exceeded then the product does not meet the specifications and cannot be sold (see Fig. 3). The results show that a single neural network model has not correlated the whole range of experimental data very well, for index values greater than 0.7 especially. The lower accuracy of model predictions, for off-spec colour index values in particular is also indicated by the 95%-confidence interval and the root mean square error (see Table 2).

In eleven cases, when the real colour index was above the limiting value of 0.7 the neural network model provided underestimated predictions (see the bottom marked area in Fig.3). This would lead in practice to production of an off-spec product. On the other hand, in four cases the real index value well below the limit was overestimated (see the upper marked area in Fig.3). On the basis of these predictions the crude product would be re-processed, although that was in fact not necessary.

TABLE 1. All data: Neural network architecture, model variables and their transformations.

Variable	Transformation(s)	Input/Output
Peak no.2	Hyperbolic tangent function	Input
Peak no.5	Natural logarithm function	Input
Peak no.7	Fuzzy centre function	Input
Peak no.8	Inverse function	Input
Peak no.13	Hyperbolic tangent function	Input
Peak no.16	Fuzzy centre function	Input
Peak no.18	Fuzzy centre function	Input
Peak no.20	Linear function Hyperbolic tangent function	Input
Peak no.26	Natural logarithm function	Input
Peak no.30	Hyperbolic tangent function	Input
Peak no.32	Linear function	Input
Lovibond colour index	Inverse square function	Output
Nodes in input layer*	12	
Nodes in hidden layer	9	
Nodes in output layer**	1	

* Number of nodes in input layer = number of transformations of input variables

** Number of nodes in output layer = number of output variables

TABLE 2. Root mean square errors and limits of 95% confidence intervals of neural network models.

Model	All data	Index < 1
Limits for 95% Confidence Interval	±0.633	±0.283
Root Mean Square Error in prediction	0.309	0.137

$$\text{Root Mean Square Error} = \sqrt{\frac{1}{n}\sum_{i=1}^{n}(z_{i,\text{model}} - z_{i,\text{exp}})^2}$$

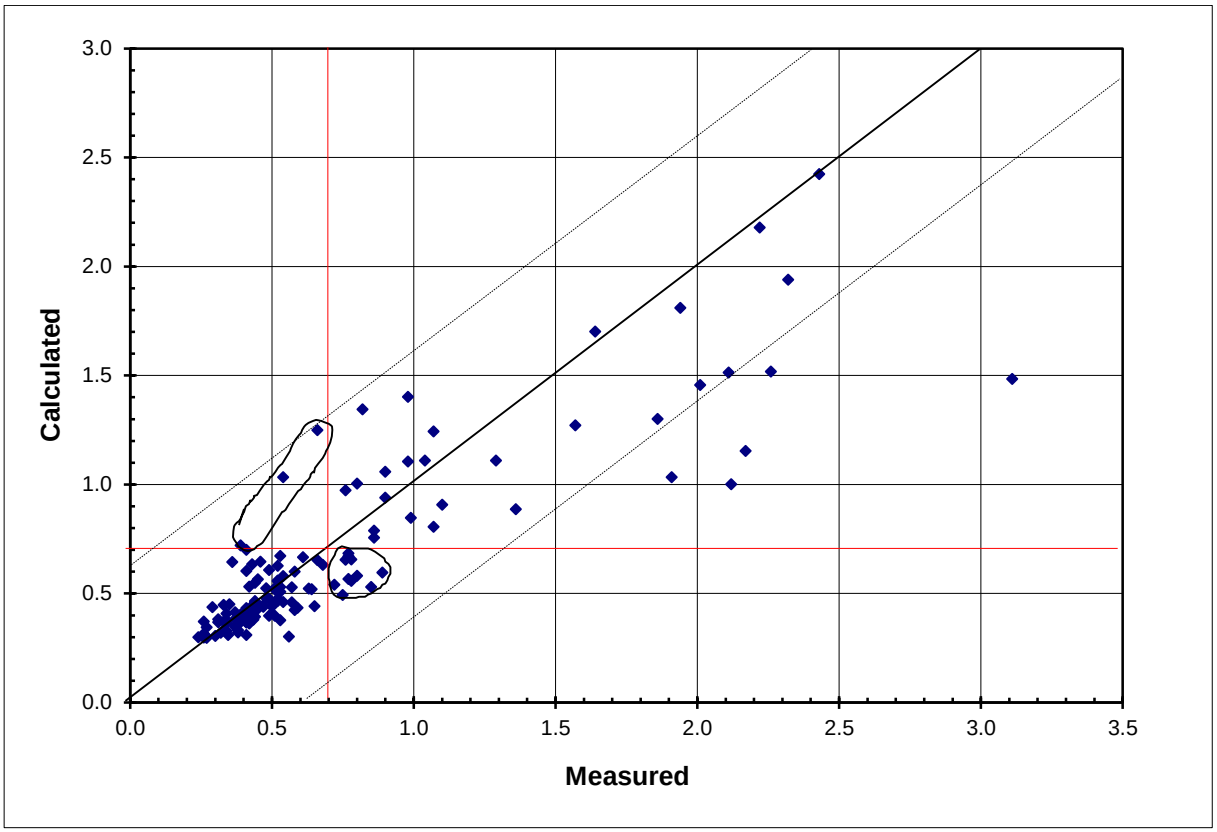

Fig.3. Calculated vs. measured Lovibond colour index. (All data).

The model based on the whole range of data can nevertheless give a rough indication of the final product colour. Then, in 2nd step the colour may be predicted with a higher accuracy. The experimental data was thus divided according to the value of the colour index, and a neural network model was developed for colour index smaller than 1. 117 items of data were used in developing (building and training) the neural network model. Again, the data were split randomly into the training set (80%) and test set (20%). A model with 13 input variables, corresponding to 17 input transformations, 3 hidden and 1 output nodes (nn model 17-3-1) was chosen finally. In the development of this model 15 variables were identified as having no or negligible effect on the product colour and were rejected (see Table 3 for details).

The predicted values of Lovibond colour index of the final product are plotted against the experimental values in Fig. 4, with an indication of a 95%-confidence interval and the limiting value of the Lovibond colour index (0.7). As can be seen in the figure the accuracy of model predictions has increased substantially. This improvement is also demonstrated in Table 2 by the values of the 95%-confidence interval and the root mean square error. While the number of underestimated predictions for off-spec product dropped only marginally from 11 to 10 (see the marked area in Fig.4) no overshot predictions for a good quality product have occurred.

TABLE 3. Colour index smaller than 1: Neural network architecture, model variables and their transformations.

Variable	Transformation(s)	Input/Output
Peak no.2	Linear function Fuzzy centre function	Input
Peak no.3	Fuzzy centre function	Input
Peak no.5	Fuzzy centre function	Input
Peak no.8	Inverse function Linear function	Input
Peak no.16	Linear function Fuzzy centre function	Input
Peak no.20	Linear function	Input
Peak no.21	Hyperbolic tangent function	Input
Peak no.24	Hyperbolic tangent function	Input
Peak no.26	Natural logarithm function	Input
Peak no.28	Hyperbolic tangent function	
Peak no.29	Linear function Fuzzy centre function	
Peak no.30	Hyperbolic tangent function	Input
Peak no.32	Linear function	Input
Lovibond colour index	Inverse function	Output
Nodes in input layer*	17	
Nodes in hidden layer	3	
Nodes in output layer**	1	

* Number of nodes in input layer = number of transformations of input variables

** Number of nodes in output layer = number of output variables

Once the product is rejected because of the value of Lovibond colour index exceeding 0.7 there is no practical need to determine its value with a high accuracy.

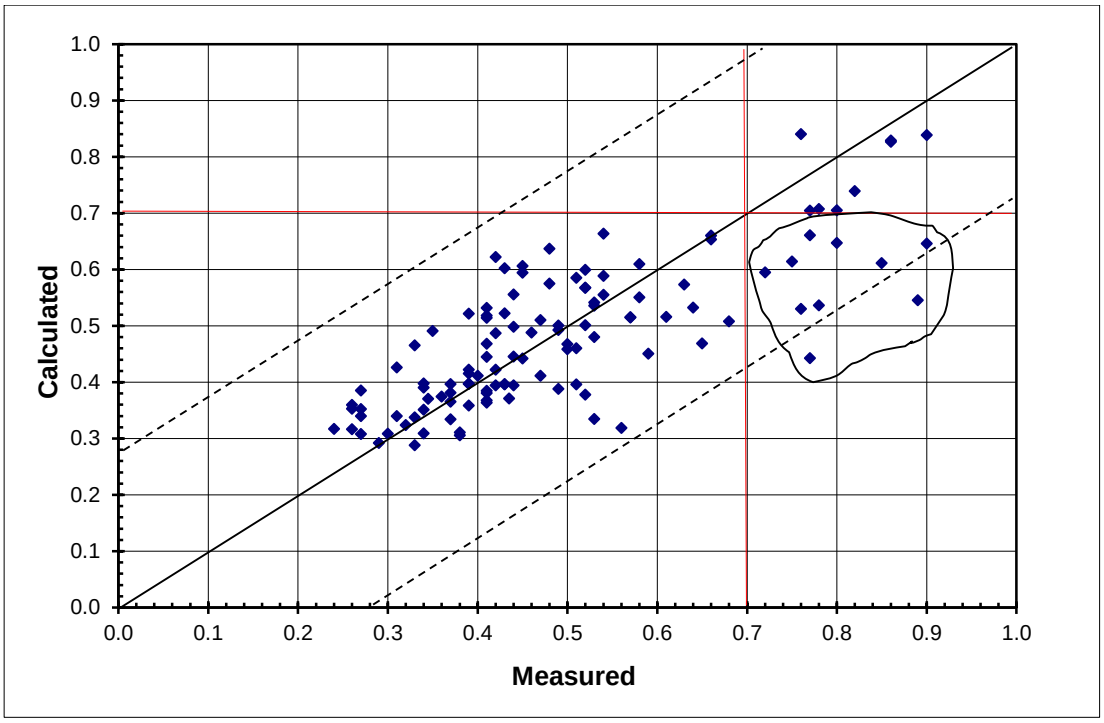

Fig.4. Calculated vs. measured Lovibond colour index. (Range 0 - 1).

Case 2

The aim of this study was to determine the survival rate of leukaemia patients and the prognostic factors that affects this outcome. A retrospective study was carried out on leukaemia patients from the Haematology Department at Inkosi Albert Luthuli Hospital (IALH), Durban. Patient confidentiality was maintained by using coded values. Data was obtained for the period from 2002 to 2008, but some patients had records from previous years in their files.

Leukaemia is a serious illness ending often in patients' death. Different kinds of leukaemia are believed to have different causes. The four main types of leukaemia are: acute lymphoblastic leukaemia (ALL), acute myeloid leukaemia (AML), chronic lymphocytic leukaemia (CLL) and chronic myeloid leukaemia (CML). Some causes of leukaemia are known (exposure to ionizing radiation, some chemicals); influence of factors like age, race, gender, and other medical conditions is not known. Standard nomenclature for the human leukocyte differentiation antigen termed "cluster differentiation (CD) nomenclature. The CD status has also been used as a parameter to model the survival of patients. The cluster of differentiation is a protocol used for the identification and investigation of cell surface molecules providing targets for immunophenotyping of cells. It allows cells to be defined based on what molecules are present on their surface. These markers are often used to associate cells with certain immune functions. It is an important marker which is used to determine the type of leukaemia. It is also used during the course of the treatment for the patient's prognosis. CD for humans is numbered up to 364. The number indicates the characterisation of the cells and its disease status. The combination of CD numbers indicates the type of disease and the stage of the disease. This paper attempts to predict a the survival rate over two and three year periods based on medical factors of patients and treatment procedures chosen.
The following models have been proposed based on an analysis of the patient data:

- Case study 2a: patients who survived at least 24 months. Some had died and some have survived beyond the 24 months.
- Case study 2b: patients who survived at least 36 months. Some had died and some have survived beyond the 36 months.

Data Processing

The following parameters were recorded for all patients included in this study: date of birth, age, gender, race, leukaemia type, date of diagnosis or tests, full blood count (10 parameters), differential count (4 parameters), flow cytometry (21 parameters), cytogenetics, and their survival status (months alive). A final input of 38 variables was used in building the neural network. Data was categorised into ranges and coded for input into the software for the building of the neural networks. The coded system for some variables is shown in Table 4.

Table 4. Examples of coding of variables

Variable	Ranges	Codes
Age (years)	0-20 20-40 40-60 60-80 > 80	0 1 2 3 4
Gender	female male	0 1
Race	black Indian coloured white	0 1 2 3
Type of leukaemia	all aml cll cml	0 1 2 3
Red cell count (rcc)	0-1.99 2-2.99 3-3.99 4-4.99 5-5.99	1 2 3 4 5
Haemoglobin (gd/L) (hmb)	0-5 5-10 10-15	0 1 2
Haematocrit (%) (hmr)	1-10 10-20 20-30 30-40 40-50	0 1 2 3 4
Mean cell volume (fL) (mcv)	< 70 70-80 80-90 90-100	0 1 2 3

Each transform function in the data analysis table is identified by its continuous function *f* which can be any one of the following shown in Table 5.

Table 5. Transform functions

Transformation	Definition
linear	linear function
log	natural logarithm function
exp	exponential
pwr2	square power function
rt2	square root function
inv	inverse function
tanh	hyperbolic tangent function
logical	logical function (0/1)
rlogical	reverse logical function (0/1)

Results and discussion

In an initial analysis of all patient data there were 77 deaths in the 2 year patient group (see Table 6). The general trend is that if a patient survives at least two years with treatment then the likelihood of remission and or a survival rate beyond 5 years is much greater. The neural network model was applied to predict the survival for the particular group of patients.

Table 6. Statistics for patient data

Variables	Parameter	2-year Case study	3-year Case study
gender	% males	58	60
	% females	42	40
race	% blacks	67	63
	% indians	23	27
	% coloureds	2	1
	% whites	8	9
type	% ALL	43	47
	% AML	37	34
	% CLL	18	17
	% CML	2	2
age	% 0-20	41	44
	% 20-40	28	26
	% 40-60	20	20
	% 60-80	10	9
	% > 80	1	1

Variables that were prognostically insignificant were rejected during the training phase. Accepted variables were rated according to the frequency, a value between 0 and 1 (1 corresponding to 100%), indicating the importance of the variable in the neural network model building process. Final models were built based on a unique set of accepted variables that were then transformed to produce the required output. There is one output for each model and that

is "survival time". "Actual survival data is compared to the survival predicted by the neural network models. The dashed lines represent the 95% confidence interval range i.e. 95% of the predicted data lies within the confidence interval represented by the dashed lines bordering the 45^0 line on the graphs.

Case 2a - ALL leukaemia type

Cytogenetics is a critical component that is essential in the assessment of newly diagnosed leukaemia patients. Chromosome abnormalities in ALL are divided into those that have a poor or good prognosis but other blood results and expression of specific markers also influences a patient's prognosis. A frequency of 0.98 implies that it has a significant role in the building of the neural network. There are no reported studies in the literature which show that race has an effect on ALL survival, but this model does. In ALL lymphocytes are the predominant cell types as prognosed in this model with a frequency of 0.93. Figure 5 shows model predictions vs. the clinical data.

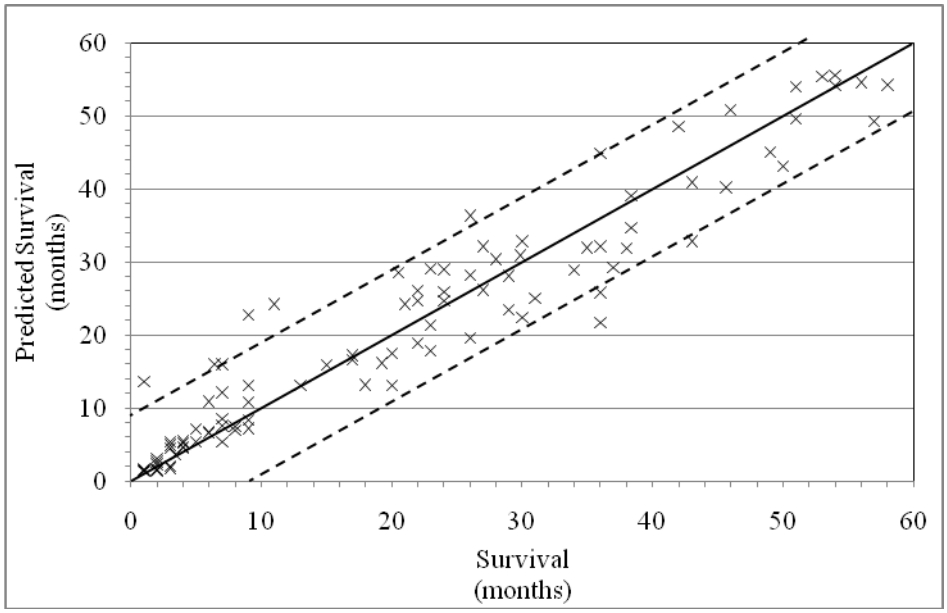

Fig. 5. Predicted 2-year survival for ALL

Case 2a - AML leukaemia type

The recommended model has architecture of 19-11-1, and a confidence interval of 7 months. The factors age, % lymphocytes and the CD34 count have had the most influence on the building of the neural network model. Cytogenetics is considered one of the key factors affecting prognosis but other factors like blast count and flow cytometry are used concurrently to determine the specific type of leukaemia. A predicted mean survival of 16.34 months compared to the actual mean survival of 16.86 months was obtained. Figure 6 shows model predictions vs. the clinical data.

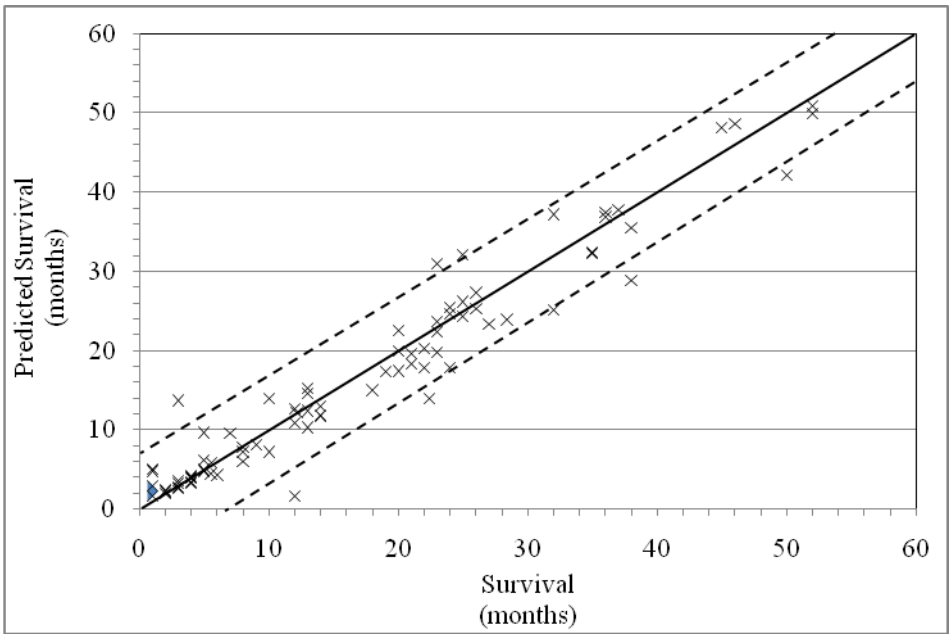

Fig. 6. Predicted 2-year survival for AML

Case 2a – CML-CLL leukaemia type

The model in figure 7 predicts the survival for CML and CLL patients with a confidence interval of 6 months. The mean survival rate is higher than both the AML and the ALL group. In chronic leukaemias the patients have the disease for long periods of time before symptoms are noticed. Even when diagnosed many live a normal life with minor symptoms. Those patients that have more severe symptoms usually lapse into an accelerated path to an acute leukaemia which eventually leads to death. This result is in keeping with a study done by Chase *et al* (2001) where a survival rate of 28 months was determined for various sub-groups of chronic leukaemias. Moore *et al* (2004) reports a median survival time of approximately 3 years.

Since this model is a combination of CML and CLL, prognostic factors are jointly predicted for both groups. The model has revealed that race (f = 92), platelet count (f = 0.99), CD3 (f=1) and CD34 expression (f = 0.92) are the most important variables in the prognosis of both CML and CLL, with age and monocytes also having a significant effect on the model. This subgroup consisted of only 50 patients, therefore this model would have to be updated with new CML-CLL patient data to confirm its reliability in predicting survival. Figure 7 shows model predictions vs. the clinical data.

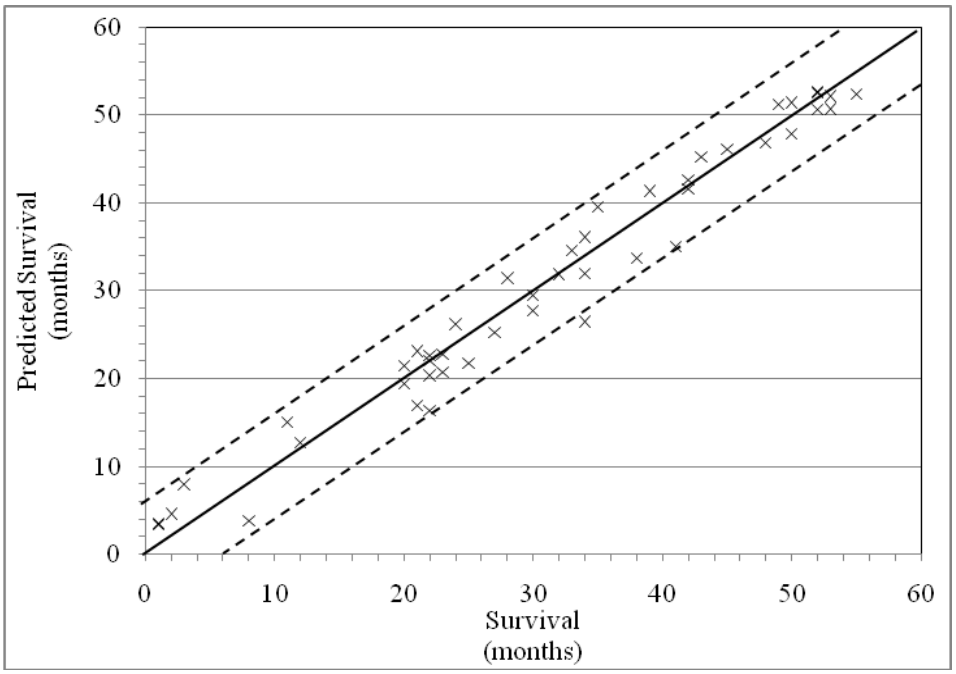

Fig. 7. Predicted 2-year survival for CML-CLL

Case 2b – ALL leukaemia type

The results in this model are similar to the 2-year model for ALL. The 95% confidence interval of 9 months is the same but the 3-year model has more outlying patients as can be seen in Figure 8, thus making the 2-year ALL model more reliable. The common prognostic factors between the 2- and 3-year models are age, race, mean haemoglobin concentration, neutrophils, lymphocytes, CD22, CD56 and chromosomes. Figure 8 shows model predictions vs. the clinical data.

Case 2b – AML leukaemia type

A model with 20-12-1 architecture is proposed. If a patient is deemed to be terminally ill with no response to a treatment regime then the treatment is stopped and palliative care is prescribed. This means that the clinicians ask the patients' families or care givers to make their final days as comfortable as possible while all treatment is terminated. A confidence interval of 4 months will give clinicians a clear indication whether to treat and how to treat the patient. Patients treated for AML should show a favourable response by the 4th month of treatment with some patients going into remission. Clinicians will be able to make important decisions for a shorter period of time. The following prognostic factors were derived for both models: age, haemoglobin, mean corpuscular haemoglobin, mean corpuscular haemoglobin concentration, mean platelet volume, neutrophils, lymphocytes, CD7, CD34 and chromosomes. The variable age, neutrophils, lymphocytes and chromosomes have also been found to be significant factors for predicting survival. Figure 9 shows model predictions vs. the clinical data.

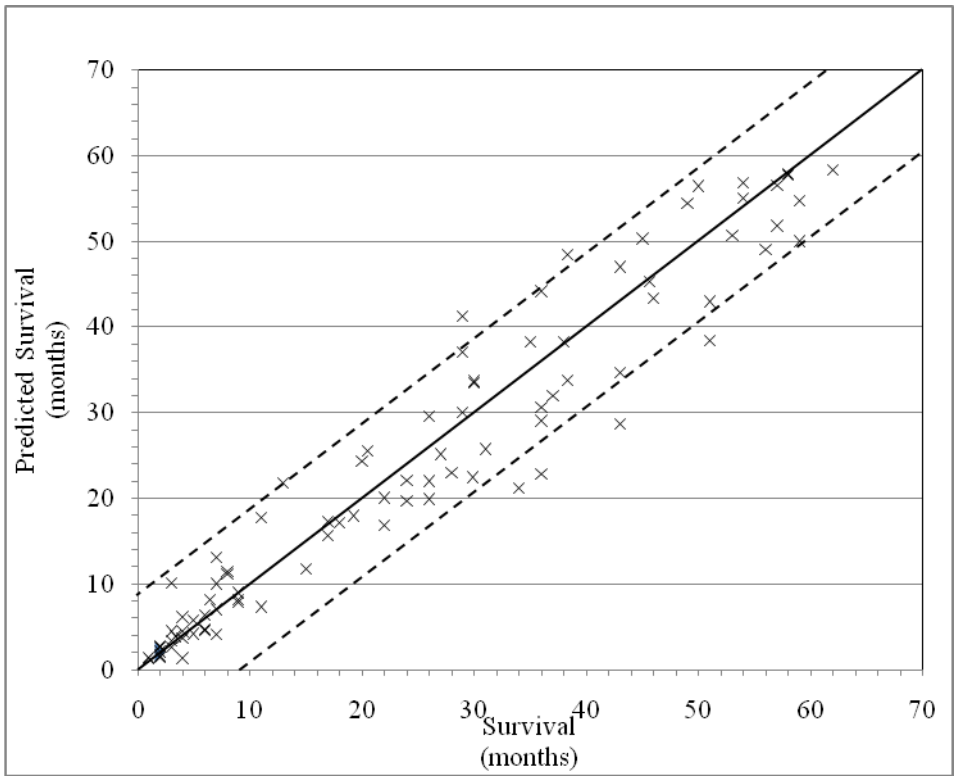

Fig. 8. Predicted 3-year survival for ALL

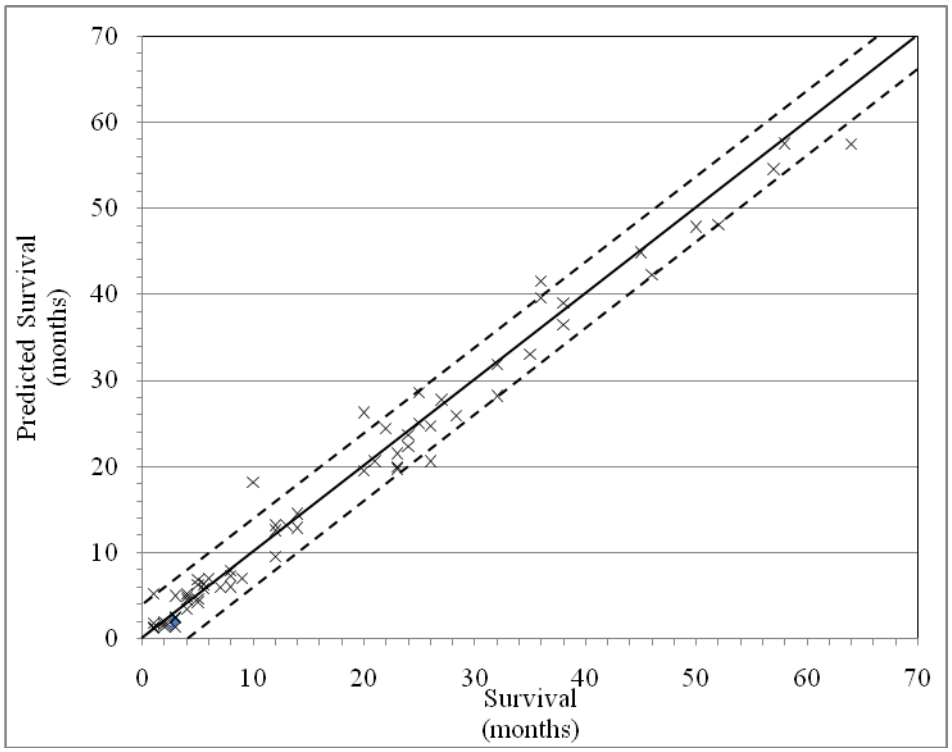

Fig. 9. Predicted survival for 3-year AML

Case 2b – CML-CLL leukaemia type

The model proposed has architecture 17-7-1. When compared to the 2-year model the confidence interval of 6 months is favoured when compared to the 8 months proposed by this model. This group was made up of 43 patients. The model can predict quite well as illustrated in Figure 10, with only 2 patients outside the confidence bands. However for validation of this model for use in future predictions, more data points from new uncensored patients need to be added and the model retrained. The common prognostic factors determined by both models are age, race, haematocrit, platelet count, CD3 and CD13. The predicted mean survival of 30.55 months compares well with the actual value of 30.76 months. The mean survival is quite high, but realistic since patients with chronic leukaemia live longer with the symptoms, sometimes without any adverse effects. Chronic means long term but there are cases that rapidly deteriorate and transform into acute leukaemias with a very poor prognosis for survival. Figure 10 shows model predictions vs. the clinical data.

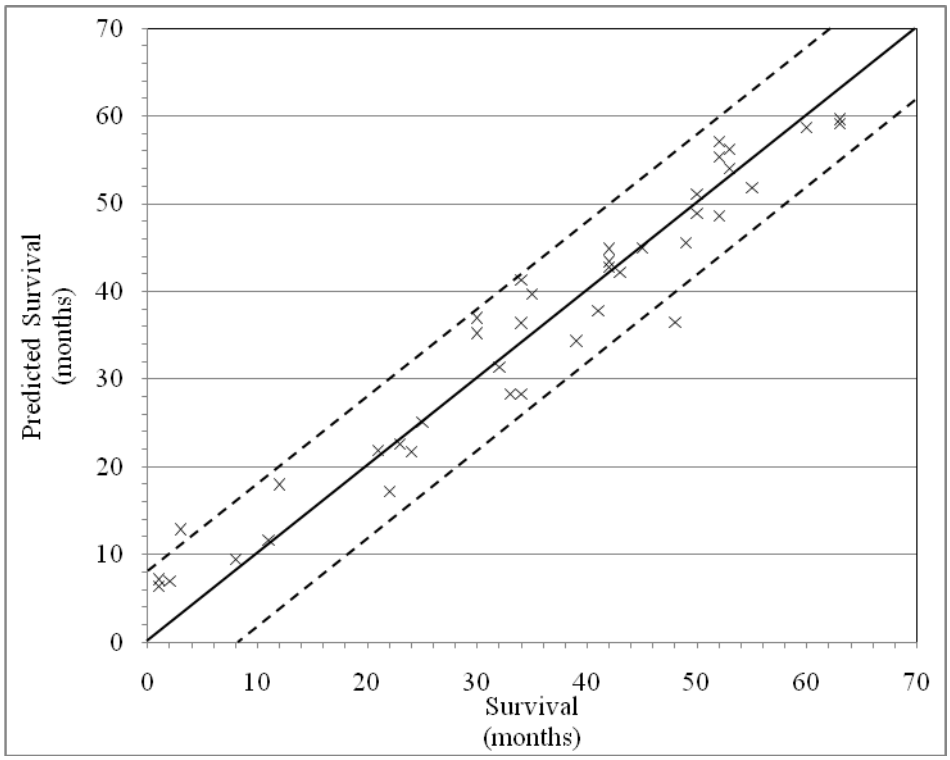

Fig. 10. Predicted survival for 3-year CML-CLL

Conclusions

A two-stage method based on neural network models has been developed in order to predict quality of a phenolic antioxidant characterised by the "Lovibond colour index" from GC analysis of the crude post-reaction product. In the 1st stage the neural network model trained for the whole range of data provided an approximate predictions of the colour index. Should the predicted value exceed value of 1, corrective measures are implemented immediately even before the crude product proceeds through the purification process. Otherwise its prediction is made more accurately in the 2nd stage, using the model developed for index valued in the range 0 – 1. Then the prediction is compared with the limiting value of the Lovibond colour index

(0.7) given by the product specifications and is accordingly either further processed or re-worked.

The neural network models were capable of "learning" the relationship between input variables (results of GC analysis of a crude product) and the final product colour index very well, even for the relatively limited number of data used in model building. The paper has shown that neural network modelling can be successfully applied to complicated processes with many variables and their unclear relation to the outputs.

An early knowledge of the final product quality enables corrective measures to be conducted timeously, either by crude product re-processing or discarding of recycled raw materials where the impurity build-up was impossible to identify by the direct analysis. In the leukaemia predictions the early survival prediction can be decisive for ~~the~~ future treatment. However, there exist some limitations, e g. the patient data recorded for this study was assumed to have all information correct, i.e. no incorrect diagnoses. Also, some patients' cytogenetic results were not confirmed as the sample was insufficient or the test was not successful, thus the normal male and female karyotype was used. Some patients do not stick to the treatment schedule, they leave the treatment program or default and some do not take their medication according to the prescription which can affect their survival. However, the models presented show the variables that are used to build the neural network, it does give any indications whether the individual factors affecting the patient's prognosis is favourable or not.

Nomenclature

$\boldsymbol{w}$	array of weights of neural network interconnections
$\boldsymbol{x} = (x_1,...,x_l)$	array of inputs to neural network
$\boldsymbol{y} = (y_1,...,y_m)$	array of hidden layer outputs
$\boldsymbol{z} = (z_1,,...,z_n)$	array of neural network outputs

References

Bulsari, A.B., 1995. *Neural network for Chemical Engineers*. Amsterdam, Elsevier.

Chase, A. Humtly, B.J. and Cross, N.C.P., 2001. Cytogenetics of chronic myeloid leukaemia. *Best Practice and Research Clinical Haemotology*. **14**(3):553:571.

Fahlmann, S.E., and Lebiere, C., 1988. *The cascade-correlation learning architecture. Advances in neural information processing systems*. Morgan Kaufmann.

Haykin, S., 1994. *Neural Networks: A comprehensive Foundation*. New Jersey. MacMillan College Publishing.

Moore, H. and Li, N.K., 2004. A mathematical model for chronic myelogenous leukaemia (CML) and T cell interaction. *Journal of Theoretical Biology*. **227**:513:523.

Morris, A.J., Montague, G.A., and Willis, M.J., 1994. Artificial Neural Networks: Studies in Process Modeling and Control. *Transaction of Institute of Chemical Engineering*, **72** (Part A): 3:19.

NeuralWorks Predict, 1995. Complete solution for neural data modelling. NeuralWare. Inc.: Pittsburgh.