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Neural Networks in Biochemical Analysis

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Abstract Artificial neural networks are more and more used to solve problems which are mathematically hard to describe. They are capable to solve non-linear problems often better than conventional methods. Thus, the application of neural networks in the area of biochemical analysis, e.g. in complex biochemical processes is very promising. In a laboratory or medical system the integration of the neural network system into the decision making process may be required. This can be done, first, by developing graphical visualisation methods and second, by generating rules out of the neural network in a form, which can be understood by humans and used in knowledge based systems.

Keywords: Neural network, biochemical analysis, genetic algorithm, decision making, visualisation, knowledge based systems

Neural Networks

Artificial neural networks are capable to approximate non linear relations in data. They deal with knowledge in a subsymbolic form. In addition, incomplete and imprecise data can be processed. Neural networks learn in a massively parallel and self-organising way. Unsupervised learning neural networks, like Kohonen's self organising feature maps, learn the structure of high-dimensional data by mapping it on low dimensional topologies, preserving the distribution and topology of the data. But large neural networks can only be interpreted with analysing tools. We developed a visualisation method, the so called U-Matrix methods, to detect the structure of large two-dimensional Kohonen maps. It generates a three-dimensional landscape on the map, whereby valleys indicate data which belongs together and walls separate subcategories.

In a laboratory or medical system the integration of the neural network system into the decision making process may be useful. The knowledge of neural networks, however, is in this form not communicable; i.e. it is necessary to transform the knowledge into a form, which, first, can be understood by humans and second, can be processed by knowledge based systems. Knowledge based systems have the advantage that they can give an explanation of a diagnosis. This is very important especially in the domain of medicine where the user wants to have the diagnosis proved. But a main difficulty when dealing with knowledge based systems is the acquisition of the domain knowledge. There are several problems with it. It is difficult to transform the explicit and implicit knowledge of the expert's domain, which also partly consists of own experience, in a form which is suitable for a knowledge base. The knowledge can also be inconsistent or incomplete. A second problem is that knowledge based systems are not able to learn from experience or to operate with cases not represented in the knowledge base. By integrating both paradigms, knowledge based systems and neural networks, the disadvantages of both approaches can be redressed.

We are developing a hybrid system REGINA which consists of several parts. An unsupervised learning neural network maps the (preprocessed) data space onto a two-dimensional grid of neurons, whereby it preserves the distribution and topology of the input space. But only together with a visualisation module, called U-Matrix methods, we are able to detect structure in the data and classify it. A three-dimensional coloured landscape will be generated in which walls separate distinct subclasses and subcategories are represented by valleys. A machine learning algorithm sig* extracts rules out of the learned neural network (6). In distinction to other machine learning algorithms like ID3 our algorithm considers the attributes by selecting those which are relevant for the classification. This corresponds to the proceeding of a medical expert. The rules can be used as a knowledge base for an expert system. Also fuzzy rules can be extracted out of the neural network.

Application

We have applied neural networks to biochemical analysis (6), e.g. in complex radioactive processes (1). The above named advantages of neural Networks can be used to make measurement methods easier, to analyse measured data more precise, to detect unknown structure in this data and to minimise the experimental overhead. Genetic algorithms have been used to optimise the topology of the underlying neural networks.

In order to test our hybrid system we applied it to two medical applications. First, we used it to diagnose acidosis diseases. The data set consists of 11 attributes originating from the blood analysis. Several classification methods according to (2) were used to explain these data. The Neural Network together with the U-Matrix method was able to classify the data into the subcategories healthy, lacacidemia, metabolical acidosis, respiratory acidosis and one patient with cerebral deficiency. With our rule generation module sig* we extracted rules out of the Neural Network, which were described by 4 or 5 attributes resembling more closely the decisions made by medical experts (7). Second, we used a data set with patients suffering from different types of the blood disease anaemia. Here no classifications were known a-priori. Deviations of blood values were indicators for a diagnosis of anaemia diseases. The extracted rules are quite similiar to the diagnosis rules in a medical text book (4). But additional rules were also found and could be verified by medical experts (5).

In near future results from CSF analysis (3) to diagnose different forms of meningitis will be presented. The problems of the course of disease (time series) and multi-diseases (multi-clustering, pattern segmentation) will be also considered in this application. Further applications of our system lie in the area of environment and in the area of industrial processes.

References

1. Beiersdorf, S., Esterlund, R.A., Heßberger, F.P., Ultsch, A. Nucl. Instruments and Methods A 1994
2. Deichsel, G,; Trampisch, Clusteranalyse und Diskriminanzanalyse, Fischer 1985
3. Kleine, T.O. J. Clin. Chem. Clin. Biochem. 27, 1989, 895-932
4. Müller, F.; Seifert, O. Taschenbuch zur medizinisch-klinischen Diagnostik, Springer 1989
5. Ultsch, A. Proc Europ. Conf. Artific. Intellig. Wien 1992, 208-210
6. Ultsch, A., Beiersdorf, S. in (Hilty et al.) Informatik für den Umweltschutz, Hamburg 1994, Bd. 1, 379-386
7. Ultsch, A., Li, H. Intl. Conf. Signal Proc. Peking 1993, Vol.2, 1201-1204