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LR-KFNN: Logistic Regression-Kernel Function Neural Networks and the GFR-NN Model for Renal Function Evaluation

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Abstract

This paper introduces a novel knowledge based neural network models that incorporate and adapt both existing logistic regression formulas and kernel functions in there structures to improve the learning and adaptation ability of a connectionist model when there is an existing knowledge on the problem in the form of a logistic regression. Different from standard feed-forward neural networks, the proposed model uses several non-linear function pairs as neurons in its hidden layer. Each of these pairs consists of one knowledge-based function and one distance based function. An existing global model – a logistic regression formula, is transformed into a set of sub-models each representing a cluster of the problem space. These sub-models constitute new, local knowledge functions. The Gaussian kernel functions are taken as the distance functions. After modifying each sub-model individually, all these sub-models are aggregated through incremental learning. The gradient descent method is applied for parameter optimization. The method is illustrated on a model called GFR-NN, for creating an accurate estimation of glomerular filtration rate (GFR) based on an existing formula MDRD and real data from the clinic. The performance of the GFR-NN is compared with the MDRD formula, MLP neural network, ANFIS and DENFIS fuzzy models on the same data. The results show that the GFR-NN is effective on this task and superior over the other models.

Keywords: *Logistic regression neural networks, kernel function neural networks, glomerular filtration rate; renal function evaluation.*

1. Introduction: Logistic Regression-Kernel Function Neural Networks (LR-KFNN)

The introduced here LR-KFNN can be represented as the following generic function and its structure is shown in Fig.1:

$$y(\boldsymbol{x}) = G_1(\boldsymbol{x})\, F_1(\boldsymbol{x}) + G_2(\boldsymbol{x}_i)\, F_2(\boldsymbol{x}) + \ldots + G_M(\boldsymbol{x})\, F_M(\boldsymbol{x}) \quad (1)$$

where, $\boldsymbol{x} = [x_1, x_2, \ldots, x_P]$ is the input vector; y is the output vector; G_l are kernel functions and F_l , are logistic regression functions, for $l = 1, 2, \ldots$ M.

Using different G_l and F_l, Eq.1 can represent different kinds of neural networks: if the G_l are *Gaussian* kernel functions and the F_l are constants it is a RBF neural network; if the G_l are sigmoid transform functions and the F_l are constants it is a generic MLP neural network; if the G_l are fuzzy rule based weighted functions and the F_l are linear functions it is a first-order TSK fuzzy inference model; and in the simplest case, if each G_l represents a single input variable and the F_l are constants it is a linear regression function.

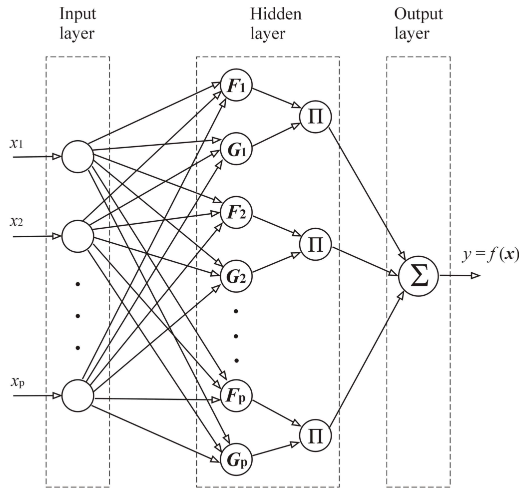

Fig.1 A generic structure of the LR-KFNN

The proposed LR-KFNN can also be represented by Eq.1. Different from standard feed-forward back-propagation (MLP) or radial basis function (RBF) neural networks, which usually use sigmoid transfer functions or Gaussian kernel functions as the neurons in their hidden layer(s), in the case of LR-KFNN, the F_l are non-linear functions that represent the knowledge in local areas, and the G_l are *Gaussian* kernel functions that control the contribution of each F_l to the system output.

In this paper we will develop as an illustration of the LR-KFNN a model that incorporate both existing formula (the MDRD [4]) and new clinical data for the evaluation of renal functions. The model is called GFR-NN.

The MDRD formula [4], which will be introduced in Section 3, is popular to use in the clinic and in research of nephrology for calculating the estimate value of glomerular filtration rate (GFR), and the modified MDRD formula is taken as F_l – the knowledge functions in the LR-KFNN.

The paper is organized as follows: Section 2 presents the LR-KFNN learning algorithm. Sections 3 illustrates the implementation of the LR-KFNN on the GFR data collected at hospitals in New Zealand and Australia and conclusions are drawn in Section 4.

2 LR-KFNN Learning Algorithm

The LR-KFNN learning procedure performs the following steps:

(1) Cluster the whole training data set into M clusters and each of these clusters includes a sub-dataset.
(2) In each cluster l, l = 1, 2, …, M, take an existing logistic formula (e.g. MDRD) as the initial function F_l and then, using gradient descent method to modified the function on the sub-dataset.
(3) Create a Gaussian kernel function as the distance function G_l: the cluster centre and radius are respectively taken as the initial values of the centre and width of G_l.
(4) Aggregate F_l and G_l and optimize the parameters in the LR-KFNN using the gradient descent method on the whole data set.

The parameter optimisation procedure is described below:

Consider the system having P inputs, one output, and M neuron pairs in the hidden layer, the output value of the system can be calculated on input vector $\boldsymbol{x}_i = [x_1, x_2, \ldots, x_P]$ by the re-wrote Eq. 1:

$$y(\boldsymbol{x}_i) = G_1(\boldsymbol{x}_i)\, F_1(\boldsymbol{x}_i) + G_2(\boldsymbol{x}_i)\, F_2(\boldsymbol{x}_i) + \ldots + G_M(\boldsymbol{x}_i)\, F_M(\boldsymbol{x}_i)$$

In the case of the GFRNN model an MDRD-type logistic regression formula is used:

$$F_l(\boldsymbol{x}_i) = b_{l0}\, x_1^{b_{l1}}\, x_2^{b_{l2}} \cdots x_p^{b_{lp}}, \qquad \text{(the MDRD-type logistic regression formula)} \quad (2)$$

and $$G_l(\boldsymbol{x}_i) = \alpha_l \prod_{j=1}^{P} \exp\left[-\frac{(x_{ij} - m_{lj})^2}{2\sigma_{lj}^2}\right] \quad \text{(Gaussian kernel function)} \qquad (3)$$

In the LR-KFNN learning algorithm, the following indexes are used:

- Training Data pairs: $i = 1, 2, \ldots, N$;
- Input Variables: $j = 1, 2, \ldots, P$;
- Neuron pairs in the hidden layer: $l = 1, 2, \ldots, M$;
- Learning Iterations: $k = 1, 2, \ldots$

Suppose the LR-KFNN is given the training input-output data pairs $[\boldsymbol{x}_i, t_i]$, the system minimizes the following objective function (an error function):

$$E = \frac{1}{2}\sum_{i=1}^{N} [y(\boldsymbol{x}_i) - t_i]^2 \qquad (4)$$

The gradient descent algorithm (back-propagation algorithm) is used to obtain the recursions for updating the parameters $\boldsymbol{b}$, $\boldsymbol{\alpha}$, $\boldsymbol{m}$ and $\boldsymbol{\sigma}$ such that E of Eq. 4 is minimized:

$$b_{l0}(k+1) = b_{l0}(k) - \frac{\eta_b}{b_{l0}(k)} \sum_{i=1}^{N} \left\{G_l(\boldsymbol{x}_i) F_l(\boldsymbol{x}_i)[y(\boldsymbol{x}_i) - t_i]\right\} \qquad (5)$$

$$b_{lj}(k+1) = b_{lj}(k) - \eta_b \sum_{i=1}^{N} \left\{\log(x_{ij}) G_l(\boldsymbol{x}_i) F_l(\boldsymbol{x}_i)[y(\boldsymbol{x}_i) - t_i]\right\} \qquad (6)$$

$$\alpha_l(k+1) = \alpha_l(k) - \frac{\eta_\alpha}{\alpha_l(k)} \sum_{i=1}^{N} \left\{G_l(\boldsymbol{x}_i) F_l(\boldsymbol{x}_i)[y(\boldsymbol{x}_i) - t_i]\right\} \qquad (7)$$

$$m_{lj}(k+1) = m_{lj}(k) - \eta_m \sum_{i=1}^{N} \left\{\frac{G_l(\boldsymbol{x}_i) F_l(\boldsymbol{x}_i)[y(\boldsymbol{x}_i) - t_i](x_{lj} - m_{lj})}{\sigma_{lj}^2}\right\} \qquad (8)$$

$$\sigma_{lj}(k+1) = \sigma_{lj}(k) - \eta_m \sum_{i=1}^{N} \left\{\frac{G_l(\boldsymbol{x}_i) F_l(\boldsymbol{x}_i)[y(\boldsymbol{x}_i) - t_i](x_{lj} - m_{lj})^2}{\sigma_{lj}^3}\right\} \qquad (9)$$

here, η_b, η_α, η_m, and η_σ are learning rates for updating the parameters $\boldsymbol{b}$, $\boldsymbol{\alpha}$, $\boldsymbol{m}$ and $\boldsymbol{\sigma}$ respectively.

3 KFNN for the GFR Estimation – the GFR-NN Model

Here, the LR-KFNN is applied for the creation of a knowledge based neural network model for the evaluation (identification) of renal functions of patients in a renal clinic – the GFR-NN model. Real data is collected in a clinical environment.

The accurate evaluation of renal function is fundamental to sound nephrology practice. The early detection of renal impairment will allow for the institution of appropriate diagnostic and therapeutic measures, and potentially maximize preservation of intact nephrons [4].

Glomerular filtration rate (GFR) is traditionally considered the best overall index to determine renal function in healthy and in diseased people. Most clinicians rely upon the clearance of creatinine (CrCl) as a convenient and inexpensive surrogate for GFR. CrCl can be determined by either timed urine collection, or from serum creatinine using equations developed from regression analyses such as that by Cockcroft-Gault formula, but the accuracy of CrCl is limited by methodological imprecision and the systematic bias [4].

Recently, the Modification of Diet in Renal Disease (MDRD) study group developed a new formula to more accurately evaluate the GFR [4]. The formula uses six input variables: age, gender, Screat, Race, Salb and Surea and is defined as follows:

$$GFR = 170 \times Screat^{-0.999} \times Age^{-0.176} \times 0.762(\text{if female}) \times 1.18(\text{if race is black}) \times Surea^{-0.17} \times Salb^{0.318} \qquad (10)$$

In Eq. (10) Screat (Serum creatinine) is a protein which is expected to be filtered in the kidneys and the residual of it - released into the blood. The creatinine level in the serum is determined by the rate it is being removed in the kidney and is also a measure of the kidney function. Surea (Serum urea) is a substance produced in the liver as a means of disposing of ammonia from protein metabolism. It is filtered by the kidney and can be reabsorbed to the bloodstream. Salb (Serum albumin) is the protein of the highest concentration in plasma. Decreased serum albumin may result from kidney disease, which allows albumin to escape into the urine. Decreased albumin may also be explained by malnutrition or liver disease.

However, prediction of GFR with the use of the existing formulas that constitute global and fixed models, can be misleading as to the presence and progression of renal disease [4]. Using proposed model on a GFR data set (447 samples) collected in hospitals in New Zealand and Australia, we have obtained more accurate results than with the use of the MDRD formula or the use of other connectionist models. For comparison, the results produced by the MDRD function [4], MLP and RBF neural networks [5], adaptive neural fuzzy inference system (ANFIS) [1] and dynamic evolving neural fuzzy inference system (DENFIS) [3] along with the results produced by proposed GFR-NN, are also listed in Table1. The results include the number of fuzzy rules (for ANFIS and DENFIS), or neurons in the hidden layer (for RBF and MLP), the testing RMSE (root mean square error), and the testing MAE (mean absolute error).

All experimental results reported here are based on 10 cross-validation experiments with the same model and parameter values, and the results are averaged. In each experiment, 70% of the whole data set is randomly selected as training data and another 30% as testing data.

The proposed model, GFR-NN, performs better than the other neural networks and fuzzy models. This is a result of the fine tuning of each local model in GFR-NN and the fine aggregating of these local models.

Table 1. Experimental results on GFR data

Model	Neurons or rules	RMSE	MAE
MDRD	–	7.74	5.88
MLP	12	8.44	5.75
ANFIS	36	7.49	5.48
DENFIS	27	7.29	5.29
RBF	32	7.22	5.41
GFR-NN	**11.3 (Average)**	**7.05**	**5.14**

4 Conclusions

This paper presents a knowledge based neural network – LR-KFNN for the integration of sub-models and new data related to the same problem resulting in incrementally adaptive model. The GFR-NN model is an application of LR-KFNN for the GFR Estimation. The GFR-NN performs local generalization and its learning is a procedure of knowledge-insertion, knowledge-modification and knowledge extraction. The new knowledge can be extracted from the GFR-NN:

(1) In each local area, there is a modified MDRD function (or sub-model) that can represent the knowledge best in this area.
(2) For a new input vector, the contribution, each local function gives to the output, can be known.

Further directions for research include: (1) in each local area, the best one will be selected as the knowledge function from several different formulas, e.g. MDRD, CG, Gates and Walser [4]; (2) the weighted data normalization [6] will be applied to the GFR-NN.

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