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Diagnosis of patients with chronic kidney disease by using two fuzzy classifiers

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ABSTRACT

The feasibility of two in-house fuzzy classifiers, fuzzy rule-building expert system (FuRES) and fuzzy optimal associative memory (FOAM), for diagnosis of patients with chronic kidney disease (CKD) was investigated. A linear classifier, partial least squares discriminant analysis (PLS-DA), was used for comparison. The CKD data used in this work were taken from the UCI Machine Learning Repository. Composite datasets were created by adding different levels of proportional noise to evaluate the robustness of the two fuzzy approaches. Firstly, 11 levels of proportional noises were added to each numeric attribute of the training and prediction sets one after another, and then these simulated training and prediction sets were combined in pairs. Thus, a grid with 121 groups of simulated data was generated, and classification rates for these 121 pairs were compared. Secondly, the performances of two fuzzy classifiers using the simulated datasets, in which 11 levels of noise were randomly distributed to each numeric attribute, were compared and the average prediction rates of FuRES and FOAM were 98.1 ± 0.5% and 97.2 ± 1.2%, respectively, with 200 bootstrap Latin partitions. The PLS-DA can give 94.3 ± 0.8% with the identical evaluation. Confluent datasets comprised of the original and modified datasets were also used to evaluate FuRES, FOAM, and PLS-DA classification models. The average prediction rates of FuRES and FOAM obtained from 200 bootstrapped evaluations were 99.2 ± 0.3% and 99.0 ± 0.3%. PLS-DA yields slightly worse accuracy with 95.9 ± 0.6%. The results demonstrate that both FuRES and FOAM perform well on the identification of CKD patients, while FuRES is more robust than FOAM. These two fuzzy classifiers are useful tools for the diagnosis of CKD patients with satisfactory robustness, and can also be used for other kinds of patients.

1. Introduction

Chronic kidney disease (CKD) is a global public health problem, affecting approximately 10% of the population worldwide and is increasing in prevalence [1,2]. CKD is often associated with an increased risk of hospital admission, morbidity, and death due to cardiovascular disease, and the progressive loss of kidney function. Patients with CKD have a high potential for developing atherosclerosis and other types of syndromes. These syndromes have significant effects on their quality of life and survival. Currently, measurement of estimated glomerular filtration rate (eGFR) and urinary albumin:creatinine ratio (UACR) based on the Chronic Kidney Disease Epidemiology Collaboration equation (CKD-EPI) are recommended for the diagnosis of CKD and its stages by the Kidney Disease Improving Global Outcomes (KDIGO) guideline 2012 [3] and subsequently the National Institute for Health and Care Excellence (NICE) Guideline 2014 [4]. The diagnosis of CKD patients still requires evidence of kidney damage, such as an eGFR below 60 mL/min/1.73 m^2 and/or a UACR above 30 mg/g [5]. Also, serum creatinine and potassium are vital parameters for monitoring CKD [6–8]. Many symptoms or risk factors, e.g., anemia [9,10], diabetes [11–15], and hypertension [16–18] are also associated with the development of CKD, so that these variables would be available sources for identifying and screening for CKD patients by chemometrics.

Chemometrics provides a multivariate tool for exploring the relationships between objects and variables. Multivariate classifiers based on chemometrics can be suitable for the diagnostic classifications of CKD, which can develop from many causes. Considering the progressive development of CKD, diagnostic models based on fuzzy logic and fuzzy mathematics would be helpful for better understanding the disease development and diagnosis of CKD patients. Fuzzy set theory was introduced by L.A. Zadeh in 1965 to accommodate inexact models of reality [19]. Fuzzy set theory lends itself to inexact reasoning and may be regarded as an infinite-values logic system. A crisp consist of objects that either belong or do not belong to the set. Fuzzy sets have elements that may partially belong. Therefore the set boundary is not so crisp that the set appears blurred. In short, fuzziness is a measure of uncertainty in representation and differs from probability which measures uncertainty in frequency of occurrence [20]. In previous studies, fuzzy approaches have been introduced into the areas of bioinformatics, system biology to solve various problems. C.T, Zhang et al. applied fuzzy

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clustering approach to predict protein structure classes from amino acid composition [21,22]. H.B. Shen et al. used supervise fuzzy clustering approach to predict protein structural classes [23] and fuzzy *K*-nearest neighbor to predict membrane protein types from pseudo amino acid composition [24]. Y.S. Ding et al. utilized fuzzy support vector machine network [25] and fuzzy *K*-nearest neighbor [26] for prediction of protein structure classes with pseudo amino acid composition. The fuzzy *K*-nearest neighbor approach was also adopted by X. Xiao et al. to solve various biological problems, e.g., identification of nuclear receptor subfamilies [27] and G-protein receptors [28], prediction of the interaction of channel-drug [29], the interaction between GPCRs and drug in cellular networking [30], and different types of antimicrobial peptides [31]. Except for the fuzzy approaches above, the fuzzy rule-building expert system (FuRES) and the fuzzy optimal associative memory (FOAM) were also developed to solve many classification problems, such as the diagnosis of endometrial carcinoma [32,33] and cervical carcinoma [34], identification of herbal medicine [35], and diagnosis of diabetes mellitus [36]. FOAM is a modeling method that utilizes similarities of features within a class so that it is useful for one-class classification. FuRES is a complementary classification method that discerns differences among features that characterize different classes, but all classes must be defined unlike FOAM [37]. Partial least squares-discriminant analysis (PLS-DA) is commonly applied as a linear multivariate classification technique based on the typical partial least squares regression method [38]. Actually, PLS-DA can be regarded as a particular case of PLS, in which response matrix *Y* contains a series of variables or labels describing the categories of samples corresponding to the predictor matrix *X* [39].

As demonstrated by a series of recent publications [40–44] in compliance with the 5-step rule [45], to establish a really useful classifier for a biomedical system, we should adhere to the following five guidelines: (a) construct or select a valid benchmark dataset to train and test the classifier; (b) formulate the samples concerned with an effective mathematical expression that can truly reflect their intrinsic correlation with the target to be investigated; (c) introduce or develop a powerful algorithm (or engine) to operate the classification; (d) properly perform cross-validation tests to objectively evaluate the anticipated accuracy of the classifier; (e) establish a user-friendly web-server for the classifier that is accessible to the public. Below, we are to describe how to deal with these steps one-by- one.

In this work, we followed the above rules, and used two fuzzy classifiers, i.e., FuRES and FOAM, for the diagnosis of 386 chronic kidney disease patients and the feasibility of the two fuzzy approaches were testified. The original data and composite data were used to compare the robustness of these two fuzzy classifiers. Average prediction rates with 95% confidence intervals were evaluated using bootstrapped Latin partitions.

2. Data description and computation methods

2.1. Data description

2.1.1. Original chronic kidney disease data

The chronic kidney disease (CKD) data used in this work is taken from the UCI Machine Learning Repository [46]. The data were collected during a nearly 2-month period and donated by Soundarapandian et al. on July 3, 2015. The dataset includes a total of 400 samples depicted by 14 numeric and 10 nominal attributes and a class descriptor. Out of 400 samples, 251 samples belonged to the chronic kidney disease group, and the other 149 samples belonged to the non-chronic kidney disease group. Table 1 lists the information about each attribute. However, some samples are provided with missing values in the original data. For those numeric attributes, each missing value was filled with the average of the corresponding attribute within the category (CKD or not CKD) to which it belongs. Two nominal attributes, i.e., red blood cells and pus cells, were removed from the dataset due to the unpredictability and less regularity within their class. All of the nominal variables were defined as numbers to facilitate the calculation. Positive responses, i.e., yes, good, and present, were defined as 1, whereas those negative responses, i.e., no, poor and not present, were defined as 0. Fourteen instances were deleted because too many missing values (more than 9 for each sample) were found within each deleted sample. All of these eliminated samples belonged to the CKD class. Besides, attribute age was not used as an inputted variable for model building. Eventually, 386 samples with 21 features were used as the original dataset for the evaluations.

Table 1
Information for each attribute of the CKD dataset.

	Attributes	Indication	Average for CKD patients	Average for not CKD patients	Missing value
1	Age (year)*	Numerical	54.57	46.56	Yes
2	Blood pressure (mm/Hg)	Numerical	79.79	71.29	Yes
3	Specific gravity	Numerical	1.01	1.02	Yes
4	Albumin	Numerical	1.78	0.00	Yes
5	Sugar	Numerical	0.80	0.00	Yes
6	Red blood cells*	Normal or abnormal	–	–	Yes
7	Pus cell*	Normal or abnormal	–	–	Yes
8	Pus cell clumps	Present or not present	–	–	Yes
9	Bacteria	Present or not present	–	–	Yes
10	Blood glucose random (mg/dl)	Numerical	175.81	107.50	Yes
11	Blood urea (mg/dl)	Numerical	72.60	32.96	Yes
12	Serum creatinine (mgs/dl)	Numerical	4.27	0.87	Yes
13	Sodium (mEq/L)	Numerical	133.94	141.79	Yes
14	Potassium (mEq/L)	Numerical	4.88	4.33	Yes
15	Hemoglobin (gm)	Numerical	10.65	15.19	Yes
16	Packed cell volume	Numerical	32.95	46.32	Yes
17	White blood cell count (cells/cumm)	Numerical	9064.79	7686.64	Yes
18	Red blood cell count (cells/cumm)	Numerical	3.97	5.39	Yes
19	Hypertension	Yes or no	–	–	Yes
20	Diabetes mellitus	Yes or no	–	–	Yes
21	Coronary artery disease	Yes or no	–	–	Yes
22	Appetite	Good or poor	–	–	Yes
23	Pedal edema	Yes or no	–	–	Yes
24	Anemia	Yes or no	–	–	Yes

* Age, red blood cells, and pus cell were not used as input attributes in this work.

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2.1.2. Simulated dataset

To investigate and validate the robustness of the two fuzzy classifiers, different levels of noise were added to the original CKD dataset, and then the effects of noise on the average prediction rates were assessed. In generating the composite dataset, two types of proportional error were randomly distributed among the numeric values of the dataset. The composite datum x_{new} is obtained by

$$x_{new} = x_{old} + l \cdot x_{old} \cdot d \quad (1)$$

in which x_{old} is the original data point, l is level of noise. During each evaluation, the sign indicator d varied randomly among −1, 0, and 1, which correspond to negative, non, and positive noises added, with probabilities of 45%, 10%, and 45%, respectively.

In this study, three types of composite data were generated. First, 11 levels (i.e., 0%, 1%, 2%… 10%) of noise were respectively added to form training and prediction sets so that the levels of noise in the prediction and training sets were various. In this way, 121 training and prediction set combinations were generated to represent all possible combinations. Second, the training and prediction sets were generated so as the 11 levels of noise were distributed randomly to each numeric attribute. Third, the composite data that was generated in the second process was fused with the original data so as to investigate the effect of data fusion.

In this work, each numeric attribute or variable was measured on different scales. The numeric data were scaled by their range so that for each attribute the range became [0, 1].

2.2. Computational methods

2.2.1. Fuzzy rule-building expert system (FuRES)

FuRES constructs a classification tree that comprises minimal neutral networks. Initially, FuRES projects data from a multidimensional space onto a normalized weight vector to yield scalar scores [20,37]. The fuzzy entropy of classification is calculated based on these scores. FuRES generates classification rules to find the weight vector with the lowest fuzzy entropy. This method continues to partition the data by fuzzy membership functions. The fuzzy logistic values are the results of each rule. Multivariate rules, which are modified neural network processing units, comprise the branches of the classification tree. The rules at each branch of the tree divide the data space into regions of objects that belong to only a single class. The classification tree allows the visualization of the inductive structure of the rules.

2.2.2. Fuzzy optimal associative memory (FOAM)

FOAM is an enhancement of an optimal associative memory (OAM) [34,47]. This approach encodes multivariate data as a two-way binary image instead of a one-way vector. FOAM requires encoding and decoding steps. A data objects are binary-encoded by mapping the object onto a uniformly sized grid. Grid elements containing signals or data points are assigned a value of unity and otherwise a value of zero. A fuzzy membership function is applied to blur the binary encoded image. An orthogonal basis is built that spans the spaces defined by the fuzzy images of the input data. Predictions are made by projection onto the orthogonal basis and the decoding the reconstructed fuzzy grid image. Classification can be achieved by constructing a basis for each class and assigning an object to the class with the minimum reconstruction error.

2.2.3. Partial least squares discriminant analysis (PLS-DA)

PLS-DA, a particular case of PLS algorithm, is a supervised method that models the relationship between the measured features and the target variables containing the class label [48]. PLS-DA is a commonly used linear classifier for solving classification problems based on its easy operation and excellent ability to classification. In this algorithm, latent variables need to be estimated. Through extracting the latent variable, the explanation for the variance of the measured variables as well as the correlation with the response matrix that encodes the class membership [49], data dimension can be reduced and the maximum separation among the classes can be achieved.

In this work, the optimal latent variable was determined by using a self-optimizing PLS-DA from the training datasets and such optimization performs within each bootstrap Latin partition. The number of latent variable with the lowest mean square error was chosen and then used to construct the PLS-DA classifier.

2.2.4. Performance metrics

This section describes performance metrics that are utilized to evaluate the performance of classifiers. In many statistical analyses, prediction accuracy is a common metric that indicates the ability of the model to predict correctly the class of new objects (i.e., objects that were unused during model construction). Moreover, sensitivity and specificity are also used as indicators of accuracy with respect to true positive and negative predictions in medicine science. These three figures of merit are calculated from the equations below.

$$\text{Accuracy} = \frac{TP + TN}{TP + TN + FP + FN} = 1 - \frac{N_-^+ + N_+^-}{N^+ + N^-} \quad (2)$$

$$\text{Sensitivity} = \frac{TP}{TP + FN} = 1 - \frac{N_-^+}{N^+} \quad (3)$$

$$\text{Specificity} = \frac{TN}{TN + FP} = 1 - \frac{N_+^-}{N^-} \quad (4)$$

for which *TP* is the number of correct CDK predictions of CKD objects, and *FN* is the number of CDK objects that are misclassified as not CKD. *TN* is the number of correct predictions as not CKD, and *FP* is the number of not CDK objects that are misclassified as CKD.

To make the three metrics more easy-to-understand for scientists in medicine and biology, the three metrics can also be displayed intuitively according to Refs. [42,50–52], as the right parts of Eqs. (2)–(4). N^+ presents the total number of the CKD patients, while N^- is the total number of not CKD patients. N_-^+ is the number of the CKD patients incorrectly predicted as not CKD, while N_+^- is the number of not CKD patients incorrectly classified as CKD. By the right parts of Eqs. (2)–(4), one can easily understand, when $N_-^+ = N_+^- = 0$ meaning that none of CKD and not CKD patients was incorrectly diagnosed as their opposite groups, therefore, the Accuracy = 1. Conversely, the Accuracy = 0 when $N_-^+ + N_+^- = N^+ + N^-$, which means that all CKD patients and all not CKD patients were predicted as their opposite groups. In addition, the Sensitivity = 1 when none of CKD patients was incorrectly diagnosed as not CKD ($N_-^+ = 0$). Whereas the Sensitivity = 0 when all CKD patients were predicted as not CKD ($N_-^+ = N^+$). Similarly, when $N_+^- = N^-$ meaning all of not CKD patients ware incorrectly classified as CKD, we have the Specificity = 0. Whereas $N_+^- = 0$ meaning none of the not CKD patients was incorrectly predicted as CKD, at this point, we can obtain Specificity = 1.

It should be pointed out that the above set of metrics is valid only for the single-label systems, in which an object investigated belongs to one, and only one class. For the multi-label systems whose existence has become more frequent in systems biology [53,54] and systems medicine [31], a completely different set of metrics as defined in Ref. [55] is needed.

2.2.4.1. Cross-validation. Reliable and robust models are important for applications. In this work, the performance of each fuzzy classifier and PLS-DA was evaluated using bootstrapped Latin partitions to cross-validate the data, which provides a systematic approach to classifier evaluation and measurement of precision [56].

The Latin partition randomly divides a dataset into training and prediction sets so that the distribution of objects with respect to class will

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Table 2
Comparisons of average prediction accuracy, sensitivity, specificity of FuRES and FOAM based on datasets with various deviations added and their corresponding 95% confident intervals from bootstraps Latin partitions (4 × 200).

	Accuracy/%	Sensitivity/%	Specificity/%
Original data			
FuRES	99.6 ± 0.2	99.3 ± 0.4	100.0 ± 0.0
FOAM	98.0 ± 0.7	99.9 ± 0.2	95.0 ± 1.8
PLS-DA	95.5 ± 0.6	100.0 ± 0.0	89.5 ± 1.3
Composite datasets with random noise levels added			
FuRES	98.1 ± 0.5	97.2 ± 0.7	99.4 ± 0.7
FOAM	97.2 ± 1.2	99.3 ± 0.4	93.7 ± 3.1
PLS-DA	94.3 ± 0.8	100.0 ± 0	87.2 ± 1.6
Fused datasets of original and composite data			
FuRES	99.2 ± 0.3	99.0 ± 0.4	99.7 ± 0.3
FOAM	99.0 ± 0.3	99.2 ± 0.3	98.7 ± 0.7
PLS-DA	95.9 ± 0.6	99.9 ± 0.1	90.4 ± 1.2

be the same for the two datasets. Furthermore, samples are partitioned so that replicates from the same sample will never be split between the training and prediction set. Because the objects are only used once for prediction per bootstrap, the results from each partition may be pooled to generate comprehensive statistics for the dataset. The results then may be averaged across the bootstraps to provide statistical figures of merit for the prediction accuracy. Therefore, the bootstrap Latin partition validation makes efficient use of the data, eliminates the bias of using only a subset of well-behaved prediction objects, and yields statistical measures of prediction performance.

3. Results and discussion

3.1. Original dataset

In the simplest case, performances of FuRES and FOAM classifiers based on the original dataset (i.e., the dataset without any perturbation) were compared based on accuracy, sensitivity, and specificity. FuRES and FOAM classifiers were constructed and evaluated with 4 Latin partitions and 200 bootstraps. For each bootstrap, a dataset was randomly divided into four parts (i.e., 96 or 97 samples comprised each partition) and each subset was utilized once for prediction and combined three times with the other sets to form 3 training sets. All evaluations were conducted in parallel so that the compositions of the training and prediction sets were identical for these two fuzzy classifiers and PLS-DA classifer, and the statistical power would be high. Table 2 reports the results acquired from the original data. FuRES and FOAM both performed well with similar accuracies. The average prediction rates exceeded 98%. FuRES gave slightly better results on the overall accuracy and specificity, while FOAM had greater sensitivity. Compared with these two fuzzy classifiers, the PLS-DA classifier gives the lowest accuracy and specificity with 95.5 ± 0.6% and 89.5 ± 1.3%, respectively, but achieves the best sensitivity with 100%.

3.2. Robustness of fuzzy classifiers

To verify the robustness of the two fuzzy classifiers, composite datasets with various levels of noise as described in the previous section were used for model building and validation. In this work, 11 levels of deviations (i.e., 0%, 1%, 2%… 10%) were used to generate 11 datasets each for the training and prediction sets. From the 22 sets of data, 121 pair-wise combinations of the training and prediction were used to evaluate the classification performance.

Fig. 1 gives three-dimensional shaded surface plots of the average accuracy, sensitivity, and specificity. The FuRES classifier has a wider plateau in Fig. 1 than FOAM, which indicates that the FuRES prediction rates are less affected by noise. Particularly, for cases where the training and prediction sets contained large amounts of noise, the prediction accuracy was maintained. However, the prediction accuracy became worse when the training set was perturbed and the prediction set contained low amounts of noise. See Fig. 1 (A). The sensitivity becomes slightly worse when the noise level increases for both training and prediction sets. The specificity is maintained when the training set contains some level of noise, even when the level of noise in the prediction set

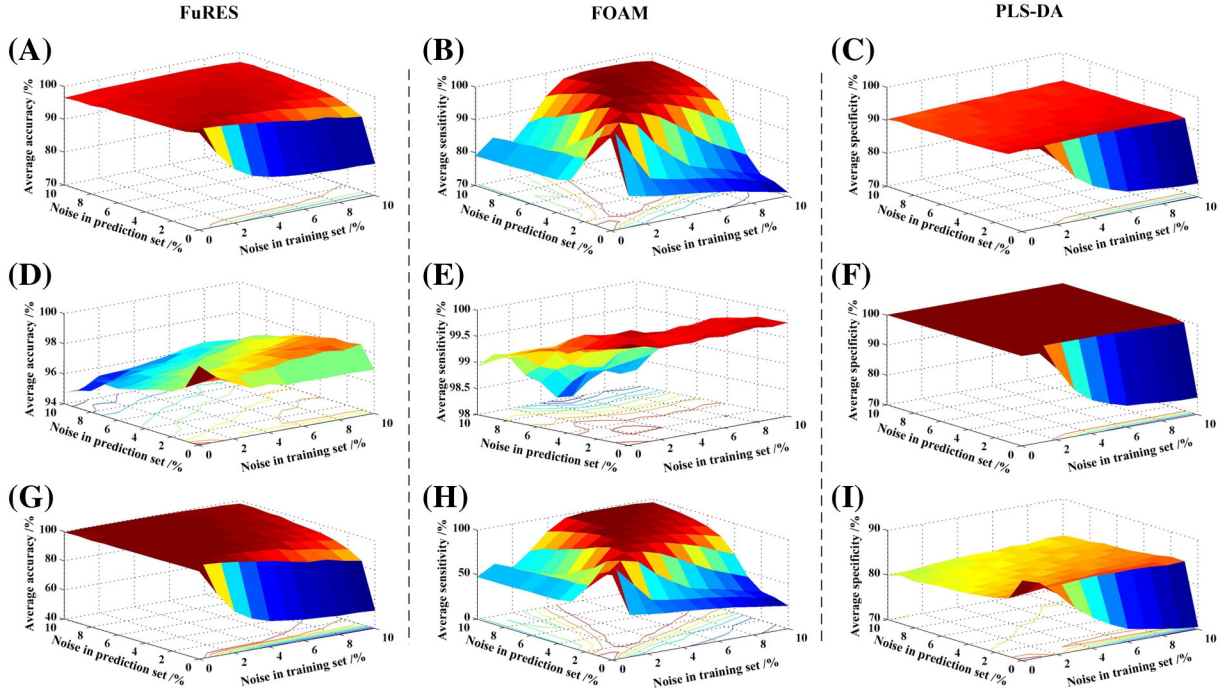

Fig. 1. Comparison of robustness for two fuzzy classifiers and PLS-DA based on the evaluation of composite data with different noise levels added. Left column: three-dimensional shaded surface plots of FuRES classifier with respect to (A) accuracy, (D) sensitivity, and (G) specificity. Middle column: three-dimensional shaded surface plots of FOAM classifier for (B) accuracy, (E) sensitivity, and (H) specificity. Right column: three-dimensional shaded surface plots of PLS-DA classifier for (C) accuracy, (F) sensitivity, and (I) specificity. The results are for prediction sets and obtained from 100 bootstraps of 4 Latin partitions for each pair.

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was 10%. The above results imply that when the training set contains some noise, the robustness of the model is improved.

In comparison to FuRES, FOAM predicts well only when the noise levels were similar for the training and prediction sets, as indicated by the plateaus along with the diagonals in Fig. 1 (B) and (F). Nevertheless, the FOAM classifier had a better ability to recognize CKD patients with greater and more stable sensitivities in Fig. 1 (D).

Compared with FuRES and FOAM, PLS-DA can perform similarly with FuRES in that wide plateaus were displayed in Fig. 1 (C), (F), and (I), which mean that the noise contained in prediction and training sets has slight influence on the performance of PLS-DA. Even though the accuracies and specificities within the plateau area of Fig. 1 (C) and (I) cannot achieve so high as FuRES and FOAM does, but the sensitivities within the platform in Fig. 1 (F) can reach near 100%.

In practical applications, every measurement may be affected by environmental and instrumental variations. Therefore, the noise levels may be randomly distributed. The second study built composite data for which the noise levels varied randomly within 0%–10%. New composite data were created within each bootstrap by modifying the original dataset. For this case, two fuzzy classifiers and PLS-DA classifier are evaluated by 200 bootstraps with 4 Latin partitions so that 200 different composite training and prediction sets were created. Table 2 gives the results of this study. The average accuracies of FuRES and FOAM were 98.1 $\pm$ 0.5% and 97.2 $\pm$ 1.2%, respectively. The FOAM classifier yielded a greater sensitivity than FuRES, which is also consistent with the initial study. PLS-DA performs slightly worse in accuracy and specificity although it has the best ability to recognize the CKD instances with a sensitivity of 100%.

The third study investigated the effect of data fusion of the original data with the composite data. Again, the noise levels varied from 1% to 10% for the composite data. With the same approach as described above, the fused dataset was evaluated by using 200 bootstraps with 4 Latin partitions. New composite data was generated within each bootstrap and then fused to the original data by concatenation. The average classification rates for the fuzzy classifiers (FuRES and FOAM) and PLS-DA are given at the bottom of Table 2. The prediction rates were 99% for both FuRES and FOAM, while PLS-DA achieved an average accuracy of 95.9% at this point. The results using the fused dataset are better than those for the composite data as would be expected. The use of the fused data improved the prediction accuracy for FOAM that resulted from a smaller loss in sensitivity coupled with a larger gain in specificity. Fusing data with added noise together with the unmodified data has the potential to increase prediction rates and improve the robustness of the models. These robust models are more suitable for the diagnosis of CKD patients and can be used for other diagnostic applications.

4. Conclusion

In the present work, two fuzzy classifiers, FuRES and FOAM, are applied for the classification of chronic kidney disease (CKD) patients. Based on the CKD data cited from the UCI Machine Learning website, their feasibility and robustness were investigated. In principle, fuzzy logic-based classifiers have advantages over conventional multivariate classifiers, like PLS-DA, with regards to robustness. As a comparison, PLS-DA was used in this work. For the original dataset from the UCI, FuRES and FOAM both performed well for classifying CKD patients with overall accuracies of more than 98%, which are higher than the accuracy of 95.5% given by PLS-DA. Furthermore, new composite data, for which different noise levels were added to the training and prediction sets, was generated and used to validate the robustness of the two fuzzy classifiers and PLS-DA classifier. FuRES and FOAM both demonstrated good robustness and yielded high prediction rates when the training set contained some added proportional noise, while FuRES had better robustness than FOAM especially when the training and prediction sets each contained similar levels of noise. The results indicate that the FOAM classifier was more affected by noise added to the training and prediction sets. In this comparison, PLS-DA has a similar performance with FuRES classifier in tolerance of noise while it cannot yield such high prediction rates as FuRES does. The prediction rates were greater than 97% for these fuzzy classifiers when different levels of noise were randomly added to construct the composite data, while an accuracy of 94.3% was yielded by PLS-DA at this case. Lastly, a fused dataset of original data and composite data with random levels of noise was used for model building and validation. Two fuzzy classifiers achieved prediction rates greater than 99%, which is better than the result given by PLS-DA. The prediction rate for the FOAM was greater than the rate obtained from the original data. The results presented in this paper indicate that FuRES and FOAM both performed satisfactorily for the recognition of CKD patients, and the FuRES classifier was more robust than FOAM with a better tolerance to deviations in measured data. The use of fused data from original and composite datasets for building classification models would be a promising approach for the diagnoses of other diseases as well as CKD diagnostic classifications.

In addition, as demonstrated in a series of recent publications (see, e.g., [42,43,50,57–64]) in developing new classification or prediction methods, user-friendly and publicly accessible web-servers will significantly enhance their impacts [65,66]. This work proved that the two fuzzy approaches, FuRES and FOAM, are feasible for the classification of biomedical data. To promote the application of fuzzy approaches in the biomedical field, we shall make efforts in our future work to provide a web-server for the classification method presented in this paper.

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