Disease Prediction from Electronic Health Records Using Generative Adversarial Networks

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Abstract

Electronic health records (EHRs) have contributed to the computerization of patient records so that it can be used not only for efficient and systematic medical services, but also for research on data science. In this paper, we compared disease prediction performance of generative adversarial networks (GANs) and conventional learning algorithms in combination with missing value prediction methods. As a result, the highest accuracy of 98.05% was obtained using stacked autoencoder as the missing value prediction method and auxiliary classifier GANs (AC-GANs) as the disease predicting method. Results show that the combination of stacked autoencoder and AC-GANs performs significantly greater than existing algorithms at the problem of disease prediction in which missing values and class imbalance exist.

1 Introduction

As the medical system being computerized, electronic health records (EHRs) have greatly contributed to making efficient and systematic medical services possible compared to previous written medical records systems. One of the important benefits of electronic health records is that big data produced from electronic health records can be used for various data science studies, including statistical analysis of disease and personalized disease prediction.

The problems that can occur in data analysis using electronic health records are as follows. First, there are a lot of missing data in the dataset to be analyzed. When the patients’ health status is recorded for a long time, checking on a new feature often begins at a specific point in time due to the development of medicine or changes in the system. For this reason, the missing values of electronic health records tend to be biased toward specific new features that were introduced during data collection [2]. Figure 1 is a graphical representation of the characteristic sparsity inherent in electronic health records data.

Second, there is a class imbalance problem because the number of electronic health records of normal people is generally more than that of people suffering from a specific disease. When using these data for learning, we can add class weights to the loss function considering the number of samples of each class. This also can be mitigated to some extent by oversampling techniques such as SMOTE (Synthetic Minority Over-sampling Technique) [3] or ADASYN (Adaptive Synthetic Sampling Approach for Imbalanced Learning) [4]. However, there are some limitations such as overfitting or increasing the memory and time required for learning. These drawbacks are summarized in Elrahman et al [5]. Therefore, it is necessary to develop the learning method which is more robust against the class imbalance problem without using the oversampling techniques.

Generative adversarial networks (GANs) [6] are a class of generative models that learn through a competitive process composed of two networks: The discriminator (D) that learns to discriminate between real and fake data, and the generator (G) that learns to generate fake data that can fool the discriminator. Although there were studies on generating electronic health records with statistical characteristics and classification performance similar to actual data using generative neural networks...
But, to the best of our knowledge, there have been no studies to date on using generative adversarial networks directly for disease prediction from electronic health records.

In this paper, we suggest a method for disease prediction using Generative adversarial networks. We compare the predictive performance of Auxiliary Classifier GANs (AC-GANs) with existing models such as support vector machine (SVM) and adaptive boosting (AdaBoost) which are widely used in studies using medical data such as disease prediction. In the proposed method, stacked autoencoder, one of the unsupervised learning algorithm, is used to impute missing data in electronic health records. We also compare the predictive performance of methods for imputation of missing values.

2 Methods

This section describes methods used for predicting missing values and disease prediction, datasets, and experimental detail.

2.1 Missing Value Prediction

Two imputation methods were used to fill in missing values. The first is simply to replace missing values with mean values of each feature. When inputting dataset into a disease prediction algorithm as it is, errors occur if the training dataset contains missing values. When all missing values are replaced by zero, these zeros have a large influence in a decision boundary. Therefore, the method is to impute missing values with mean in order to minimize the influence.

The second is a method using autoencoder (AE) [9], which is one of the unsupervised learning algorithms. Autoencoder learns the model parameters to give output values to be equal to the inputs. In the experiment, Samples with few missing values (which means missing value ratio of that samples are under the threshold value) are drawn and divided into training and validation set. Patterns are stored in the model parameters of autoencoder by encoding and decoding the training data. The validation set is used to find the epoch where validation error was minimized. Then, missing values are imputed with the most appropriate values among the stored patterns by the learned autoencoder. In the proposed method, we adopted the stacked autoencoder with three hidden layers to cope with missing values. Binary cross entropy was used as loss function and Adam Optimizer [10] was used for optimization. We implemented autoencoder in Keras [11]. Since Keras supports early stopping, training is stopped automatically before convergence to avoid the overfitting. The learning curve of autoencoder is shown in Figure 2.

2.2 Disease Prediction (Classification)

Several methods are used for comparative experiments of disease prediction. Support vector machine (SVM) is one of the most widely used machine learning methods. It finds a hyperplane that maximizes the margin between two classes in feature space. A kernel function can make the SVM to separate the data in the nonlinear feature space. In the experiment, we used the Gaussian Radial Basis Function as the kernel function.
Ensemble methods used extensively in competitions such as Kaggle’s because they improve the generalization power by training multiple weak estimators. In those methods, RandomForest, Adaboost and GradientBoosting with 10 estimators are used for comparison. In addition, as the basic neural network architecture, a multilayer perceptron (MLP) was used. To guarantee the fairness of the comparison, we used the same architecture as the AC-GAN discriminator.

Recently, many different variants of generative adversarial networks have been proposed. In this study, we used Auxiliary classifier GANs (AC-GANs). A generative model $G$ of AC-GANs receives the same value as the class label ($c$) of the real data ($X_{real}$) as condition in addition to the noise $z$, and generates fake data ($X_{fake}$). A discriminative model $D$ receives the real data and the data generated by $G$ as inputs and estimates not only the probability that a sample is real or fake ($S$) but also the class label distribution ($C$). All layers except the output layer are shared by $D$. The loss functions for AC-GANs can be expressed as the following equations [12]:

$$
L_s = \mathbb{E}[\log P(S = real \mid X_{real})] + \mathbb{E}[\log P(S = fake \mid X_{fake})] 
$$

and

$$
L_c = \mathbb{E}[\log P(C = c \mid X_{real})] + \mathbb{E}[\log P(S = c \mid X_{fake})],
$$

where $D$ is learned to maximize $L_C + L_S$ and $G$ is learned to maximize $L_C - L_S$. In this way, $G$ is trained to generate data similar to the real data of each class, and $D$ is trained to better classify the data in each class as the fake data from $G$ fool $D$.

In the original paper, AC-GANs was designed as a model that focuses on the learning of generator that generate images of various classes well without causing mode collapse. But in this paper, we focused on improving the classification performance of discriminator by generator of AC-GANs generating both benign and malignant data. This makes robust disease prediction possible.
Table 1: Performance evaluation based on missing value prediction and disease prediction methods.

| Method    | ACC 1  | SE 2    | SP 3    | ACC 1  | SE 2    | SP 3    |
|-----------|--------|---------|---------|--------|---------|---------|
| SVM_rbf   | 0.9367 | 0.8396  | 0.9944  | 0.9385 | 0.8491  | 0.9916  |
| RF        | 0.9420 | 0.9104  | 0.9608  | 0.9508 | 0.9057  | 0.9776  |
| AB        | 0.9455 | 0.9292  | 0.9552  | 0.9473 | 0.9104  | 0.9692  |
| GB        | 0.9455 | 0.9292  | 0.9552  | 0.9543 | 0.9292  | 0.9692  |
| MLP       | 0.9596 | 0.9292  | 0.9776  | 0.9631 | 0.9245  | 0.9860  |
| AC-GAN    | 0.9664 | 0.9453  | 0.9860  | 0.9805 | 0.9528  | 0.9947  |

TP: $\sum$ true positive, TN: $\sum$ true negative, FP: $\sum$ false positive, FN: $\sum$ false negative

1 $\text{ACC (accuracy)} = (\text{TP}+\text{TN}) / (\text{TP}+\text{TN}+\text{FP}+\text{FN})$
2 $\text{SE (sensitivity)} = \text{TP} / (\text{TP}+\text{FN})$
3 $\text{SP (specificity)} = \text{TN} / (\text{TN}+\text{FP})$

2.3 Dataset and Experiments Detail

We used Breast Cancer Wisconsin (Diagnostic) Data Set [13]. The dataset consists of total 569 records, with 357 benign and 212 malignant for breast cancer. The dataset has some class imbalance problems. In the original data set, there are only about 0.46% of the missing data filled with zeros. However, in order to realize the characteristic missing value problem of the electronic health records data mentioned in the introduction, fifteen features, half of the total 30 features, are removed from half of the examples in each class.

All results were obtained using a 5-fold cross-validation procedure, in which all data were divided into five, one of which was used as a test set and the rest were used for training. Disease prediction algorithms are implemented in Scikit-learn [14] and Tensorflow [15].

Figure 3 is a schematic diagram of the disease prediction process proposed in this paper. A brief description of the overall process is that missing values of the electronic health records data are filled with optimal values by stacked autoencoder. The filled data are entered into AC-GAN to learn to classify benign and malignant, and the learned AC-GAN is used for specific disease prediction.

3 Results and Discussion

Table 1 shows the performance measurements for the combination of missing value prediction methods and disease prediction (classification) methods. Comparing the missing value prediction methods, the method using the autoencoder showed higher accuracy than the method of filling missing values with mean value of each feature in every model. It can be understood that filling the missing value with the pattern associated with the remaining features, as compared with the case where missing values are filled with the mean value so as to have less effect on the classifier, provides more information to the classifier. Thereby, this enhances the classifier’s performance.

Comparing disease prediction methods, at 96.64% imputing missing values with mean and 98.05% with autoencoder, the accuracy of AC-GANs was higher than that of other models. In every model, results showed a tendency of higher specificity than sensitivity. It is expected that this tendency is due to the high frequency of negative (benign) predictions because there exist class imbalance problem that the number of benign samples is more than the number of malignant samples in the dataset. Results of support vector machine showed that there is the largest gap between sensitivity and specificity. This means that support vector machine is not robust against class imbalance problem without the help of other methods such as oversampling techniques and adding class weights. On the other hand, AC-GAN showed much less difference between sensitivity and specificity, and showed stable and the highest accuracy. Compared to multilayer perceptron which has the same architecture with discriminator of AC-GAN, AC-GAN showed that the adversarial training further boosted the performance in the disease prediction.

The best combination of missing value prediction methods and disease prediction methods is to predict missing values with stacked autoencoder and then to predict the disease with AC-GANs,
which showed accuracy of 98.05%, sensitivity of 95.28% and specificity of 99.47%. The results mean that proposed method is more robust against the class imbalance and missing values than previously used methods.

4 Conclusion and Future Work

In this paper, we analyzed the performance of algorithms for predicting diseases in electronic health records with missing values and class imbalance problem. As a result, the accuracy of filling missing values with stacked autoencoder is higher than that of simply filling missing values with mean value. Without using oversampling methods which consume additional memory, generative adversarial networks are more robust against class imbalance problem and have better disease prediction performance than existing methods widely used in electronic health records data.

Several follow-up studies can be considered in order to make generative adversarial networks more robust against missing values and class imbalance problems, which are two main problems in electronic health records. In this work, stacked autoencoder is used for missing value prediction by learning separately. However, by using generative adversarial networks as a generation model, it can be possible to use the generator itself to fill missing data or to use the model constrained for the generator to fill missing values. We plan to implement this idea as a future work.

Class imbalance problem can also be solved by generated data from the generative adversarial network. As an idea of developing the algorithm of AC-GAN, it is possible to modify class conditions that are given to a generator to be opposite to a class ratio of mini-batch of real data so that classes of mini-batch entering discriminator can be balanced. In this way, while the generator is learning the distribution of the entire data, it performs oversampling for each mini-batch, so it enables oversampling with little additional memory consumption. However, since the balance between real and fake data for each class is broken, GAN training may become unstable. So a sophisticated learning procedure modification may be necessary.

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