Early Prediction of Sepsis via SMOTE Upsampling and Mutual Information based Downsampling

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Abstract

Sepsis is a life-threatening response to infection that can lead to tissue damage, organ failure and death. Effective early prediction of sepsis would improve patients’ diagnosis process and reduce the cost associated with late-stage sepsis infection by applying appropriate early intervention. However, effective early prediction is challenging, because sepsis biomarkers are not obvious nor definitive, and sepsis datasets is heavily imbalanced against positive diagnoses of sepsis. In this paper, we suggest a two-step method which consists of a mutual information based downsampling algorithm and Synthetic Minority Over-sampling Technique (SMOTE), in order to effectively perform early prediction of sepsis. Our best results indicate that by using the proposed two-step method, the LSTM based neural network can obtain an F1 score of 0.356 for 12-hour early prediction.

1. Introduction

Sepsis is a life-threatening disease, claiming over 75 thousand lives every year in the United States [1], and is a leading cause of mortality amongst intensive-care unit (ICU) patients. Septic shock occurs when chemicals in the body are imbalanced and unable to deal with a serious infection, potentially causing mortality [2]. Early identification of sepsis amongst ICU patients is thus essential to prevent organ failure and death. However, effective early prediction of sepsis has proven to be difficult as sepsis biomarkers are not definitive, and often, patients at risk of sepsis have various disease complications [3]. As few patients are diagnosed with sepsis, a dataset of sepsis patients is often imbalanced. Within the PhysioNet Challenge 2019 dataset [4], only 7.98% of patients develop sepsis at one point or another. A classified trained on an imbalanced dataset will bias in favour of the majority class, causing misclassification of minority class samples [5].

In this paper, we propose a two-step method to address the imbalance in data, consisting of a mutual information-based downsampling algorithm to reduce the majority class, and the Synthetic Minority Over-sampling Technique (SMOTE) to increase the minority class. These changes on the data make the early prediction of sepsis more effective. Using this method along with a long short-term memory (LSTM) based neural network, we can obtain an F1 score of 0.356 for 12-hour early prediction.

2. Downsampling and Upsampling

Downsampling and upsampling are two common strategies employed to deal with imbalanced dataset. When data from the majority class is downsampled, a relatively smaller number of representative instances are selected. Downsampling is beneficial as it mitigates the overfitting effects, but excessive downsampling will cause a loss in useful information, and degrade the performance of the classifier [6]. Upsampling refers to the generation of synthetic samples from the minority class, to boost the number of samples so that the number of samples in minority class (after generation) is equal to the sample size of majority class. However, generating synthetic samples is difficult, and may cause overfitting as well if the generated samples are too similar to the original ones [7]. Ideally, both downsampling and upsampling methods should be used in tandem. In this section, we introduce a two-step method that maintains the balance between downsampling and upsampling methods.

2.1. Mutual Information Based Downsampling Algorithm

Mutual information (MI), a concept formed from information theory, can reliably quantify the dependency between random variables [8]. MI is a scalar quantity between two random variable, measuring the uncertainty of a random variable, given knowledge of another. Our MI-based downsampling algorithm is used to select representative patients. Firstly, we assign a score to each patient, according to the following scoring function:
Figure 1. Illustration of Mutual Information based Downsampling Algorithm

\[
J(P_i) = \sum_{P_j \in D, P_j \neq P_i} I(P_i, P_j), \quad (1)
\]

where \(P_i, P_j \in \text{dataset } D\) represent for \(i^{th}\) and \(j^{th}\) patient, respectively. The data length of patients may differ due to length of stay. Therefore, we estimate the MI via nearest-neighbor based MI estimators [9]. After scoring each patient, we divide all patients into \(L = 10\) groups (of approximately equal size) based on the descending order of all scores. Therefore, patients with similar scores will be grouped together and patients within the same group will tend to be highly dependent on each other (see Figure 1). Random sampling from each group will select representative patients of each group. Random proportional sampling from all groups gives selective patients of the whole dataset.

2.2. SMOTE

SMOTE [10] is considered as an effective upsampling algorithm to generate synthetic samples. SMOTE firstly identifies the feature vector, its nearest neighbour and take the difference between two. Then it generates a new point on the line segment by adding the random number to feature vector (see Figure 2). Unlike making copies of existing samples, SMOTE learns the topological properties of the neighbourhood of points in the minority class. Therefore, the classifier trained on the synthetic data generated by SMOTE is less likely to overfit.

3. Performance Evaluation

3.1. Data Information and Preprocessing

The PhysioNet Computing in Cardiology Challenge 2019 dataset [4] contains the demographic, vital sign information and lab test results of 27148 patients, at regular 1-hour intervals. A large number of features have missing values, so we impute these corresponding features with the latest historical values. We shift the target class ahead by 6 hours, so that we can predict sepsis 12 hours early. Finally, we perform normalization on the dataset, so that the range of feature values is between 0 and 1.

3.2. Benchmark Models

Four benchmark models from statistics, deep learning are shortlisted and described as follow.

- The decision tree (DT) [11] is a tree-based algorithm for classification. Training data is repeated split according to splitting criteria (eg. entropy) with respect to an outcome variable, such that child nodes are more homogenous. Decision tree handles imbalance data classification problems well, and are benchmark models in many problems.
- The Random Forest (RF) [12] is an ensemble of decision trees. Bootstrapped samples of the training data are trained, and majority voting is performed for the final classification process. RF is cost-sensitive as it can incorporate class weights in the training process, penalising misclassification of minority class instances.
- The Gradient Boosting algorithm (GB) [13] minimizes loss in decision trees, by training instances in a sequential manner. The additional boosting step occurs to successively train on incorrectly classified examples, thus significantly improving the performance with respect to imbalanced data classifications [14, 15].
- The long short-term memory (LSTM) unit [16] is capable of learning information over a long sequence of temporal inputs. The unit utilises input, output and forget gates to store information over long time intervals, regulating the flow of information in and out of the cell. By overcoming the problem of vanishing or exploding gradients through memory blocks, the LSTM is designed for time-series data predictions.
### Table 1. Performance of Decision Tree with and without down/up sampling method

<table>
<thead>
<tr>
<th></th>
<th>No D-sample</th>
<th>D-sample to 75%</th>
<th>D-sample to 50%</th>
<th>D-sample to 25%</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>F1</td>
<td>AUC-ROC</td>
<td>F1</td>
<td>AUC-ROC</td>
</tr>
<tr>
<td>Have U-sample</td>
<td>0.245</td>
<td>0.522</td>
<td>0.284</td>
<td>0.519</td>
</tr>
<tr>
<td>No U-sample</td>
<td>0.236</td>
<td>0.529</td>
<td>0.265</td>
<td>0.514</td>
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</tbody>
</table>

### Table 2. Performance of Random Forest with and without down/up sampling method

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<th>D-sample to 75%</th>
<th>D-sample to 50%</th>
<th>D-sample to 25%</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>F1</td>
<td>AUC-ROC</td>
<td>F1</td>
<td>AUC-ROC</td>
</tr>
<tr>
<td>Have U-sample</td>
<td>0.186</td>
<td>0.513</td>
<td>0.235</td>
<td>0.541</td>
</tr>
<tr>
<td>No U-sample</td>
<td>0.153</td>
<td>0.531</td>
<td>0.101</td>
<td>0.516</td>
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### Table 3. Performance of Gradient Boosting with and without down/up sampling method

<table>
<thead>
<tr>
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<th>D-sample to 75%</th>
<th>D-sample to 50%</th>
<th>D-sample to 25%</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>F1</td>
<td>AUC-ROC</td>
<td>F1</td>
<td>AUC-ROC</td>
</tr>
<tr>
<td>Have U-sample</td>
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<td>0.522</td>
<td>0.322</td>
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<tr>
<td>No U-sample</td>
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<td>0.533</td>
<td>0.146</td>
<td>0.522</td>
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</table>

### Table 4. Performance of LSTM with and without down/up sampling method

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<th>D-sample to 75%</th>
<th>D-sample to 50%</th>
<th>D-sample to 25%</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>F1</td>
<td>AUC-ROC</td>
<td>F1</td>
<td>AUC-ROC</td>
</tr>
<tr>
<td>Have U-sample</td>
<td>0.285</td>
<td>0.505</td>
<td>0.303</td>
<td>0.504</td>
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<tr>
<td>No U-sample</td>
<td>0.112</td>
<td>0.519</td>
<td>0.267</td>
<td>0.504</td>
</tr>
</tbody>
</table>

### 3.3. Experiment Setup

The whole dataset $D \in \mathbb{R}^{N \times M}$ ($N$: number of samples; $M$: number of features) is randomly split into two subsets: training dataset and test dataset at patient level. Namely that 80% of patients are used to train the classifier and the rest 20% of patients are used for evaluation. Then we perform MI based sampling algorithm on the majority class of training data to sample 75%, 50% and 25% of training dataset, respectively. After downsampling, we apply SMOTE to do upsampling on the downsampled training dataset to make sure that the number of samples in minority class and majority class are equal.

For decision tree (splitting criterion = entropy), gradient boosting (number of estimator = 100) and random forest (number of estimator = 45), we train them to perform 12-hour early prediction. During testing, the missing values of test data are imputed with the corresponding mean values obtained from training data and only the latest time step of test data is used for evaluation. For the LSTM based neural network, it consists of 6 hidden layers while first two layers are LSTM with 5 and 10 units, respectively. The rest four layers are dense layer with size = \{256,128,64,32\}. As LSTM requires three dimensional input to capture the temporal relationship, we reshape the training dataset into a three dimensional array $\in \mathbb{R}^{K \times 3 \times M}$ via a sliding observation window of size equal to three (i.e., time step = 3). Moreover, the LSTM based neural network is trained for 300 epochs using Adam [17] with a learning rate of 0.001, batches of 128 and sigmoid activation function. During testing, the missing values of test data are imputed with the corresponding mean values obtained from training data and all past observations of each patient are used to perform classification task. Finally, AUC-ROC and F1 score [18] are used to evaluate the performance and both of them are averaged over 10 runs.

### 3.4. Performance Comparison

The performance for various classifiers with and without down/up sampling are shown in Table 1 to Table 4. The best performance for each classifier is highlighted in red and bolded. In Table 1 to Table 4, the D-sample and U-sample represents MI based downsampling and SMOTE upsampling respectively. Using the SMOTE upsampling method improves the performance (compare row 1 to row 2 in Table 1 - Table 4), while applying MI based down-sampling algorithm further boosts the performance. The best performance is observed using LSTM based neural network (25% downsampling rate & SMOTE upsampling), with an F1-score of 0.356 for 12-hour early prediction of sepsis.
To examine the performance of different prediction horizons (e.g., 9-hour early prediction), we also evaluate the proposed two-step method via LSTM based neural network (25% downsampling rate & SMOTE upsampling) and the results are shown in Table 5. We observe that the performance roughly increases while we reduce the prediction horizon. We believe it is mainly because that the relationship between past features and future label are stronger as we reduce the prediction horizon, leading to better performance.

### 4. Conclusion

In this paper, we suggest a two-step method which consists of a mutual information based downsampling algorithm, and SMOTE upsampling method, to address the imbalanced issue of PhysioNet Challenge 2019 dataset. By using the proposed method, the LSTM based neural network can obtain a F1 score of 0.356 for 12-hour early prediction and this performance roughly increases while we reduce the prediction horizon.

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### References


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