

Event-Based Pathology Data Prioritisation: A Study Using Multi-Variate Time Series Classification

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Abstract: A particular challenge for any hospital is the large amount of pathology data that doctors are routinely presented with. Pathology result analysis is routine in hospital environments. Some form of machine learning for pathology result prioritisation is therefore desirable. Patients typically have a history of pathology results, and each pathology result may have several dimensions, hence time series analysis for prioritisation suggests itself. However, because of the resource required, labelled prioritisation training data is typically not readily available. Hence traditional supervised learning and/or ranking is not a realistic solution and some alternative solution is required. The idea presented in this paper is to use the outcome event, what happened to a patient, as a proxy for a ground truth prioritisation data set. This idea is explored using two approaches: k NN time series classification and Long Short-Term Memory deep learning.

1 INTRODUCTION

The challenge of prioritising pathology time series data using the tools and techniques of machine learning is that, in most cases, we do not have sufficient amounts of training data, because of the clinical resource required to create such data, to support effective supervised learning. This means that some alternative mechanism needs to be adopted. The fundamental idea presented in this paper is to use some form of proxy for the training data set using meta-knowledge about patients. More specifically using meta-knowledge concerning the “final destination” of patients, the *outcome event* for each patient, and use this to build a outcome event classification system. Three outcome events were considered: Emergency Patient (EP), an In-Patient (IP) or an Out Patient (OP). Then, given a new pathology result and the patient’s pathology history, it would be possible to predict the outcome event and then use this to prioritise the new pathology result. For example if we predict the outcome event for a patient to be EP, then the new pathology result should be assigned *high* priority; however, if we predict that the outcome event will be IP the new pathology result should be assigned *medium* priority, and otherwise *low*.

The hypothesis that this paper seeks to establish is that there are patterns in patients’ historical lab test results, which are markers as to where the pa-

tient “ended up” and which can hence be used for prioritisation. To act as focus, the work presented is directed at pathology lab test results related to renal function, namely Urea and Electrolytes (U&E) tests. This test provides an extra challenge in that it features five components (tasks) each with an associated test result value. In addition each task within a U&E test has three values associated with it. Thus there are five historical multi-variate time series per patient.

There are a number of multi-variate time series classification algorithms that could be adopted to classify time series. Two are considered in this paper: (i) k Nearest Neighbour (k NN) (Xing and Bei, 2019) and (ii) Long short-term memory (LSTM). The first was selected because it was the most frequently used algorithm with respect to time series classification. A value of $k = 1$ was adopted, as suggested in (Bagnall et al., 2017). Dynamic Time Warping (DTW) was used as the similarity measure.

The remainder of the paper is organised as follows. Section 2 presents previous work relating to the work in this paper. An overview of the U&E application domain is then given in Section 3, followed by a formalism in Section 4. The two proposed approaches to event-based prioritisation, using k NN and LSTM, are presented in Section 5. The evaluation of the proposed approaches is then presented in Section 6. Finally, in Section 7, some conclusions and directions for future work are considered.

2 PREVIOUS WORK

The prioritisation mechanism proposed in this paper is founded on time series classification. Many time series classification approaches have been proposed. One of the most popular, and that used with respect to the work presented in this paper, is k Nearest Neighbour (k NN) classification. The fundamental idea of k NN classification is to compare a previously unseen time series, which we wish to label, with a “bank” of time series whose labels are known, identify the k most similar and use the labels from the k most similar to label the previously unseen time series. Usually $k = 1$ is adopted because it avoids the need for any conflict resolution.

Time series classification using k NN entails two challenges: (i) the data format for the input time series, and (ii) the nature of the similarity (distance) measure to be used to establish similarity (Wang et al., 2013). There are two popular time series formats: (i) instance-based and (ii) feature-based. Using the instance-based format the original time series format is maintained. Using the feature-based representation, properties of the time series are used (Wang et al., 2008). For the work presented in this paper the instance based format was used. There are a number of similarity measure options including Euclidean, Manhattan and Minkowski distance measurement, but Dynamic Time Warping (DTW) is considered to be the most effective with respect to the instance-based format, and offers the additional advantage that the time series considered do not have to be of the same length (Wang et al., 2013). For the work presented in this paper DTW was adopted.

The recent success of deep learning offers a more substantive way of processing time series than in the case of traditional models. Among many deep learning techniques, Recurrent Neural Networks (RNNs) are considered as an effective way of classifying time series, because they allow for the processing of variable length inputs and outputs by maintaining state information across time steps. There are many examples in the literature where RNNs have been used with respect to time series classification; see for example (Choi et al., 2016; Esteban et al., 2015). Long Short-Term Memory (LSTM) networks are a popular form of RNNs. The advantage of RNNs in general, and LSTMs in particular, is that they have shown to be more accurate, with respect to time series classification, than k NN. However, k NN does not require significant training or large amounts of training data as in the case of RNNs (LSTMs). There are many variations of LSTMs (Greff et al., 2016). In this paper, the standard “vanilla” LSTM setup was used.

3 APPLICATION DOMAIN

The work presented in this paper is focused on the Urea and Electrolytes (U&E) test; a commonly used test to detect abnormalities of blood chemistry, primarily kidney (renal) function and dehydration. A U&E test is usually performed to confirm normal kidney function or to exclude a serious imbalance of biochemical salts in the bloodstream. The U&E test data considered in this paper comprised, for each test, measurement of levels of: (i) Sodium (So), (ii) Potassium (Po), (iii) Urea (Ur), (vi) Creatinine (Cr), and (v) Bicarbonate (Bi). The measurement of each is referred to as a “task”, thus we have five tasks per test. In other words each U&E test results in five pathology values. It is suggested that U&E pathology results can be prioritised more precisely if the trend of the historical records is taken into consideration, therefore providing more efficient treatment for patients with a potential risk of renal function conditions. Given a new set of pathology values for a U&E test we wish to determine the priority to be associated with this set of values.

4 FORMALISM

In the context of the foregoing, the assumption is that the training data comprises a set of pathology results, $\mathbf{D} = \{P_1, P_2, \dots\}$, where the class (event) label c for each pathology record $P_j \in \mathbf{D}$ is known. As the focus of the work is U&E test data, which comprises five tasks (components), each record $P_j \in \mathbf{D}$ is of the form:

$$P_j = \langle Id, Date, Gender, T_{So}, T_{Po}, T_{Ur}, T_{Cr}, T_{Bi}, c \rangle \quad (1)$$

Where T_{so} to T_{bi} are five multi-variate time series representing, in sequence, pathology results for the five tasks typically found in a U&E test: Sodium (So), Potassium (Po), Urea (Ur), Creatinine (Cr) and Bicarbonate (Bi); and c is the class label taken from a set of classes C . Each time series T_i has three dimensions: (i) pathology result, (ii) normal low and (iii) normal high. The normal low and high dimensions indicate a “band” in which pathology results are expected to fall. These values are less volatile than the pathology result values themselves, but do change for each patient over time. Thus each time series T_i comprises a sequence of tuples, of the form $\langle v, nl, nh \rangle$ (pathology result, normal low and normal high respectively).

To derive the class label for each record $P_j \in \mathbf{D}$ reference was made to the outcome event(s) associated with each patient. For the evaluation presented later in this paper, three outcome events were considered: (i) Emergency Patient (EP), an In-Patient (IP)

or an Out Patient (OP) which were correlated with the priority descriptors “high”, “medium” and “low” respectively. Hence $C = \{high, medium, low\}$.

Given a new pathology result for a patient j , comprised of five tuples, one per task, $\{V_{So_{n+1}}, V_{Bu_{n+1}}, V_{Ur_{n+1}}, V_{Cr_{n+1}}, V_{Bi_{n+1}}\}$, these will be incorporated into the patient record P_j for the patient in question by appending each new pathology tuple to the appropriate time series T_i to give $\{V_{i_1}, V_{i_2} \dots V_{i_n}, V_{i_{n+1}}\}$. The patient record P_j thus becomes the “query record”, the record we wish to label.

5 MULTI-TIME SERIES EVENT-BASED PATHOLOGY DATA PRIORITISATION

The fundamental idea promoted in this paper is that pathology results can be prioritised in terms of the trend of a given patients’ pathology. In order to validate this idea, two approaches were adopted, the k NN-DTW approach and the LSTM-RNN approach. Each is discussed in more detail below.

5.1 Event-based data prioritisation using k NN

The k NN classification model uses a parameter k , the number of best matches we are looking for. As already noted, $k = 1$ was used with respect to the evaluation reported later in this paper because this avoids the need for a conflict resolution mechanism where $k > 1$. As also noted earlier, Dynamic Time Warping (DTW) was used for similarity measurement because of its ability to operate with time series of different length (Wang et al., 2013). The disadvantage of DTW is its high computational complexity, which is $O(x \times y)$ where x and y are the lengths of the two time series under consideration. There are many techniques available for reducing this time complexity in the context of k NN classification. For the work presented here “early-abandonment” (Rakthanmanon et al., 2012) and LB-Keogh lower bounding (Vikram et al., 2013) were used.

The traditional manner in which k NN is applied in the context of time series analysis is to compare a query time series with the time series in the k NN bank. In the case of the U&E test data prioritisation scenario considered here the process involved five comparisons, once for each time series in the query record P_j , $T_{q_{so}}$, $T_{q_{po}}$, $T_{q_{ur}}$, $T_{q_{cr}}$ and $T_{q_{bi}}$. In addition, although traditional k NN is applied to univariate time series; in this case three-dimensional, multi-variate,

time series were used.

For each comparison five distance measures were obtained. With respect to the proposed k NN the five tasks were considered independently and the final prioritisation decided using a “High priority first and voting second” mechanism. Given the foregoing, the application of k NN to label P_j was as follows:

1. Calculate the LB-keogh overlap for the five component time series separately and prune all records in D where the overlap for any one time series was greater than a threshold ϵ , to leave D' .
2. Apply DTW, with early-abandonment to each pair $\langle T_{q_i}, T_j \in D' \rangle$ where i indicates the U&E task.
3. Assign the class label c associated with the most similar time series $T_i \in D'$ to the time series T_{q_i} of a patient record P_j .
4. Use the “High priority first and voting second” mechanism to decide the final priority level for P_j . The intuitions underpinning the mechanism were: (i) if any of the five time series T_{q_i} is assigned as *high* prioritisation label, the final label for a patient record P_j should be *high*, (ii) else the final label is the one that receives more than half of the votes (given a “tiebreak” the higher level of the two labels is assigned to the patient).

The choice of value for the lower bounding threshold ϵ was of great importance as it affected the efficiency and the accuracy of the similarity search. According to (Li et al., 2017), there is a threshold value for ϵ whereby the time complexity for the lower bounding is greater than simply using DTW distance without lower bounding. The experiments presented in (Li et al., 2017) demonstrated that this threshold occurred when the value for ϵ prunes 90% of the time series in D . For the evaluation presented in this paper $\epsilon = 0.159$ was used because, on average, this resulted in 10% of the time series in D being retained.

5.2 EVENT-BASED DATA PRIORITISATION USING LSTM-RNN

The event-based data prioritisation process founded on LSTM commenced with the training of five LSTM models one per task: $LSTM_{so}$, $LSTM_{po}$, $LSTM_{ur}$, $LSTM_{cr}$ and $DLSTM_{bi}$. Once we have the LSTMs they can be used.

The overall architecture comprised three “layers”: (i) the input layer, (ii) the model layer and (iii) the decision layer. In the input layer the component time series $T_{q_{so}}$, $D_{q_{po}}$, $D_{q_{ur}}$, $D_{q_{cr}}$ and $D_{q_{bi}}$ are extracted from the query record P_q . Thus for each task we

have a multi-variate time series $T_i = \{V_1, V_2, \dots, V_m\}$, where $V - J$ is a tuple of the form presented earlier, and $m \in [l_{min}, l_{max}]$. Where necessary each time series T_i is padded to the maximum length, l_{max} using the mean values for the pathology test values, normal low and normal high values in T_i . Each time series T_i is then passed to the appropriate LSTM in the model layer. Each LSTM comprised: (i) an input layer, (ii) an LSTM layer with two layers of LSTM cells and (iii) an output layer. The output layer included the logits and softmax components.

The last layer is the architecture is the decision layer where the final label is derived. After obtaining all of the five outputs and predicted labels from the five LSTM models, a decision logic module was used to decide the final prioritisation level of the patient. The Softmax function for normalising was as follows:

$$y_i = \frac{e^{a_i}}{\sum_{k=1}^{|C|} e^{a_k}} \quad \forall i \in 1 \dots C \quad (2)$$

Where: (i) $|C|$ is the number of classes (three in this case) and (ii) a_i is the output of the LSTM layer. Finally the following ‘‘High priority first and voting second’’ rule was applied to produce the end classification: *if any one of the five LSTMS produces a prediction of ‘‘High’’ the final prediction is ‘‘high’’, otherwise average the five outputs produced by Softmax function and then choose the class with the maximum probability.*

The adopted individual LSTM architectures comprises 2 hidden layers and Logits plus Softmax function in the output layer, because multi-classes classification is being undertaken. For the LSTM to operate five parameters needed to be tuned during the training process. The parameters belong to two categories: (i) optimization parameters and (ii) model parameters. The optimization parameters were: Learning rate, batch size and number of epochs. The model parameters were the number of hidden layers and the number of hidden units. For the optimization, Adam optimization was chosen due to its efficiency and the nature of adaptive learning rate. For finding the optimal parameters, cross-entropy was used as the loss function and the parameters tuned by observing the loss and accuracy plots of the training and validation data.

6 EVALUATION

This section presents the evaluation of the proposed multi-time series event-based pathology data prioritising approach using k NN and LSTM as described above. The metrics used were accuracy, precision and

recall. In all cases the evaluation was conducted using a desktop machine with a 3.2 GHz Quad-Core Intel Core i5 processor and 24 GB of RAM. For the LSTM a GPU laptop was used fitted with a NVIDIA GeForce RTX 2060 unit. Five-fold cross validation was used through-out. For the evaluation U&E pathology data provided by the Wirral Teaching Hospital in Merseyside in the UK was used. This was used to create three data sets: (i) D_{female} , (ii) D_{male} and (iii) D_{all} (where $D_{all} = D_{female} \cup D_{male}$). An overview of the U&E evaluation data sets is given in Sub-section 6.1. The objectives of the evaluation were:

1. To identify the optimum parameter settings in the context of LSTM approach.
2. To compare the operation of the k NN and LSTM approaches in terms of effectiveness.
3. To compare the operation of the k NN and LSTM approaches in terms of efficiency (runtime).

The results with respect to each of the above are discussed in sub-sections 6.2 and 6.3 respectively.

6.1 Evaluation Dataset

The Wirral Teaching Hospital U&E pathology test data comprised four data tables. The first three were event data tables: (i) Emergency Patient (EP), (ii) Inpatient (IP) and Outpatient (OP); comprised of 180,865, 226,634 and 955,318 records respectively and corresponding to High, Medium and Low priority. The fourth was a Laboratory (Lab) data table, comprised of 532,801 records, holding the pathology results; this included results for patients in the event data tables and patients that had never visited the hospital, but were treated at their local surgery. The data sets contain patient records over a two year span. The LAB dataset was the primary dataset used for the evaluation reported here. The event data sets were used for generating outcome event labels (classes) for the time series held in the LAB dataset.

Some statistics concerning the data set are given in Table 1. From the table it can be observed that there is a significant imbalance between the number of records associated with each class, this is not an issue when using k NN with $k = 1$, but it is an issue when using LSTMs, as highly imbalanced data may pose bias towards the majority class. An oversampling technique was adopted to address this issue with respect to the RNN training.

Each record in the LAB table, R_i , representing a pathology result for a single task in a U&E test, was of the form:

Event (Priority)	Num. Patients
Emergency Patient (High)	255
In Patient (Medium)	123
Out Patient (Low)	3,356
Total	3,734

Table 1: U&E Data set statistics

$$R_i = \langle ID, Task, Date, Value, Unit, Max, Min, Gender \rangle \quad (3)$$

Where: (i) ID is the unique code for the patient, (ii) $Task$ is the name of the task (Sodium, Potassium, Urea, Creatinine and Bicarbonate). (iii) $Date$ is the date the test was conducted, (iv) $Value$ is the pathology value for the task, (v) $Unit$ is the units for the $Value$, and (vi) Max and Min are the bounds for the anticipated normal range for the $Value$ (for the patient and task in question, not the same for all patients). Some data cleaning was first undertaken, removing patients with missing or non-numeric task values and feature scaling to benefit the faster convergence of the LSTM.

The time series data set $D = \{P_1, P_2, \dots\}$, where each P_j patient record was of the form $\langle ID, TestDate, Gender, T_{So}, T_{Po}, T_{Ur}, T_{Cr}, T_{Bi}, c \rangle$ (see Section 4), required five time series equating to the five tasks included in the U&E test data (Sodium, Potassium, Urea, Creatinine and Bicarbonate). The time series were constructed by processing the data for each patient up until an outcome event. The values, up to and including the event value, were then used to construct the relevant time series. If a patient appeared in more than one event data set, for example a patient was an “out patient” and then became an “in patient” and finally became an “emergency patient”, then the time series prior to the “emergency event” was used, because the pattern of the “emergency patient” indicates the highest priority. Also there were a small number of patients (less than 1% of the total data set) who did not appear in any of the event data sets, in other words the patients remained with their general practitioners. This group of patient records was removed from the training data. Time series comprised of less than three time stamps were also removed. Each P_j patient record was then labelled according to the priority indicated by the event value time stamp.

The final data set, D_{all} , comprised 3,734 time series; 255 high priority, 123 medium priority and 3,356 low priority, covering all five tasks. Thus there were 747 records (3,734/5) in each fold of the cross validation. The records in each fold were stratified so that there was an equal distribution of classes in each fold. The D_{female} data set was comprised of 1,960 time series; 136 high priority, 55 medium priority and

1,769 low priority. The D_{male} , comprised of 1,774 time series; 119 high priority, 68 medium priority and 1,587 low priority. All three data sets were used for the evaluation. The reason for exploring the distinction between genders was because it had been suggested that there maybe gender differences for the prioritisations being investigated (Halbesma et al., 2008; Tomlinson and Clase, 2019).

Para.	Task				
	Bo	Cr	Po	So	Ur
Learning Rate	0.01	0.01	0.01	0.01	0.01
Batch Size	512	128	256	512	512
Epochs	1000	1000	1000	1000	1000
Hidden Layer	2	2	2	2	2
Hidden Units	32	32	16	32	32

Table 2: LSTM Parameter Settings for the five LSTMs (one per task)

6.2 Parameter Settings for LSTM

The general way for finding the best parameters for deep neural network models is to analyse the learning curve and accuracy plot of the training and validation data. The most popular learning curve used for this purpose is loss over time. Loss measures the model error, in other words, “how bad the performance of the model is”. Thus, the lower the loss is, the better the model performance. Figure 1 shows the average loss and accuracy plots for each of the three data sets considered. For each graph in Figure 1 the x-axis gives the number of times the weights in the network were updated, and the y-axis the loss value. From the figures, we can observe that oscillations appear in all of the loss and accuracy plots and that convergence is not obvious. Possible reasons for this include: (i) the oversampling solution for dealing with the class imbalanced problem meant that there were insufficient sequences for the LSTM to learn from; and (ii) that the event-based mechanism used as the proxy ground truth of the data set may not be entirely representative. The final best settings for the parameters are given in Table 2.

6.3 COMPARISON OF APPROACHES

The average accuracy, precision and recall results for each fold of the five-cross validation, for the k NN and LSTM approaches, are given in Tables 3 and 4. Note

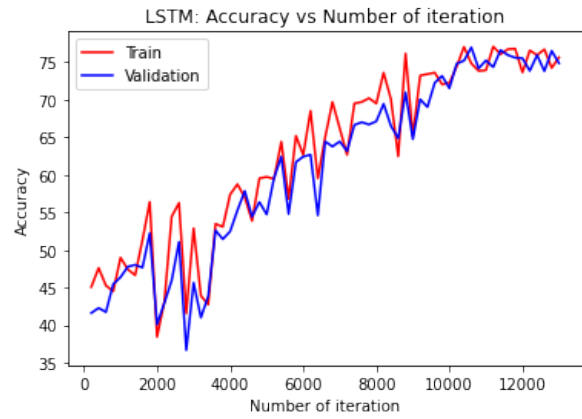
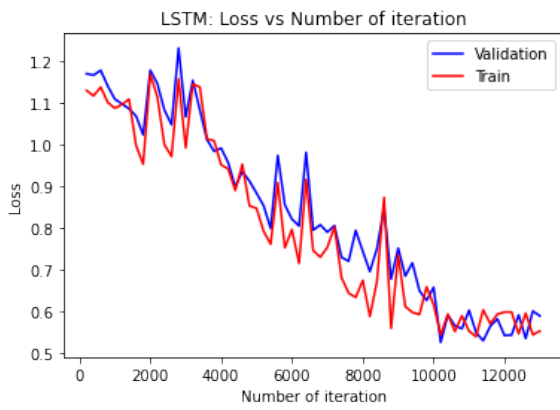
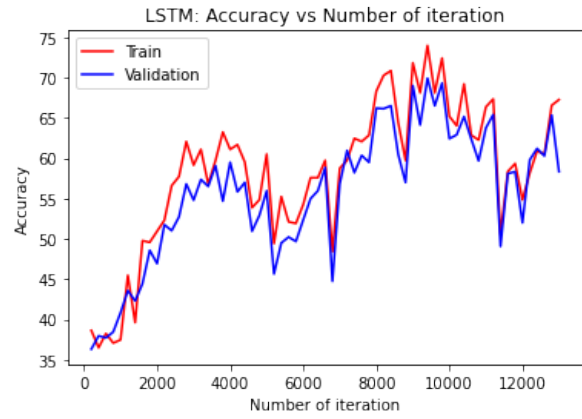
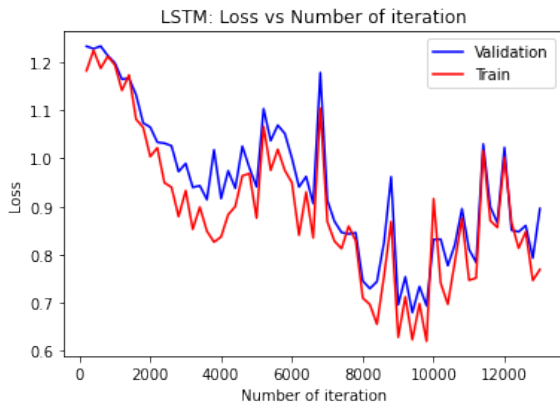
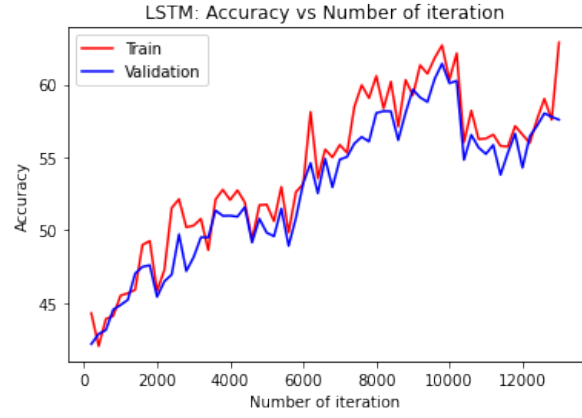
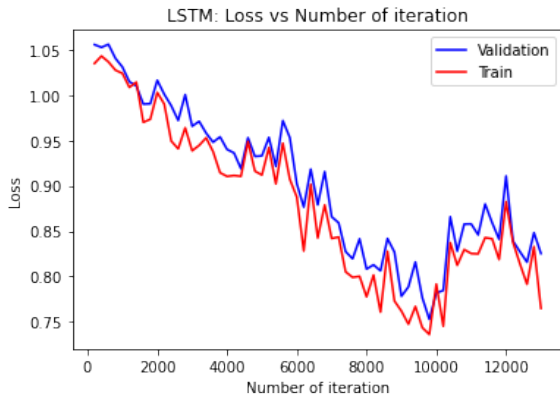


Figure 1: Loss and Accuracy curves for the LSTM generation process

Fold Num.	Acc.	Pre. High	Pre. Medium	Pre. Low	Rec. High	Rec. Medium	Rec. Low
1	0.585	0.414	0.400	0.545	0.637	0.577	0.666
2	0.632	0.534	0.688	0.578	0.678	0.467	0.714
3	0.576	0.412	0.541	0.674	0.588	0.535	0.647
4	0.523	0.598	0.541	0.634	0.712	0.4688	0.505
5	0.566	0.444	0.384	0.598	0.541	0.487	0.785
Ave	0.576	0.480	0.510	0.605	0.631	0.507	0.663
SD	0.039	0.082	0.124	0.050	0.068	0.047	0.103

Table 3: Average Precision and Recall (Three data set) of k NN

Fold Num.	Acc.	Pre. High	Pre. Medium	Pre. Low	Rec. High	Rec. Medium	Rec. Low
1	0.671	0.578	0.374	0.711	0.811	0.641	0.412
2	0.642	0.475	0.552	0.735	0.758	0.468	0.577
3	0.622	0.553	0.577	0.708	0.669	0.547	0.703
4	0.608	0.615	0.714	0.699	0.712	0.563	0.697
5	0.645	0.466	0.766	0.596	0.699	0.476	0.778
Ave	0.638	0.538	0.597	0.690	0.730	0.539	0.633
SD	0.024	0.065	0.120	0.054	0.056	0.071	0.143

Table 4: Average Precision and Recall (Three data set) of RNN

Models	Acc.	Pre. High	Pre. Medium	Pre. Low	Rec. High	Rec. Medium	Rec. Low
LSTM-RNN-G	0.612	0.575	0.551	0.689	0.788	0.587	0.633
LSTM-RNN-F	0.645	0.541	0.415	0.711	0.678	0.615	0.612
LSTM-RNN-M	0.657	0.648	0.825	0.670	0.724	0.415	0.654
KNN-G	0.597	0.421	0.512	0.852	0.695	0.546	0.745
KNN-F	0.565	0.387	0.673	0.678	0.645	0.498	0.698
KNN-M	0.566	0.632	0.345	0.285	0.553	0.477	0.546
Ave	0.607	0.534	0.554	0.648	0.681	0.523	0.648

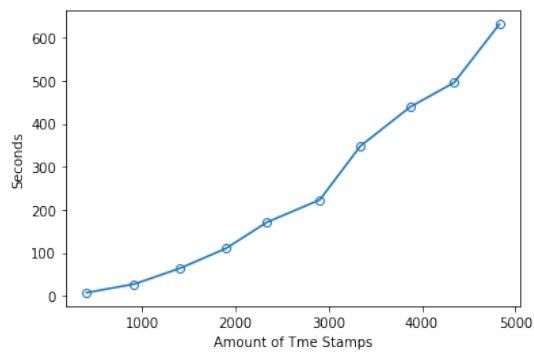
Table 5: Average Cross-Validation Precision and Recall of All Models

that the results are the average results of the three evaluation data sets. The results of the precision and recall for the class *high* are highlighted. The overall average (Ave) and standard deviation (SD) are given in the last two rows. Note that the SD values are low, indicating that there is little variation across the folds. From the table it can be seen that the RNN approach consistently out performed the k NN approach. A general observation is that the precision and recall values might be argued to be on the low side, possibly indicating either: (i) that the hypothesised event-based prioritisation approach, is not as good a predictor of priority, as anticipated, (ii) the irregular nature (distribution of time stamps) of the time series, which was not considered, may have an adverse effect. For the LSTM-RNN models, the way that the class imbalanced problem was dealt with may also have adversely affected performance.

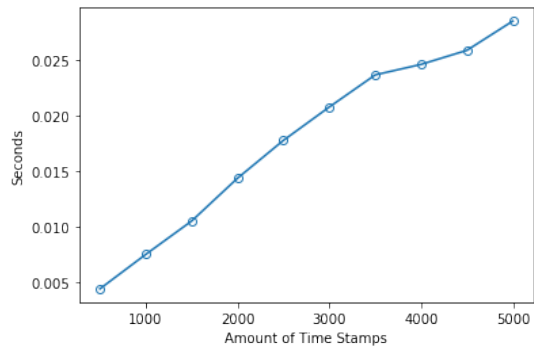
Table 5 gives the overall average performance results when the three data sets are considered in isolation. From the table it is interesting to see that for the gender LSTM-RNN models, the accuracy is slightly better than the general LSTM-RNN model, whilst this

does not feature with respect to k NN models applied to the different data sets. Thus there is still no obvious evidence to demonstrate whether the prioritisation pattern from the data is related to gender, more investigation is needed here.

Figure 2, presents the runtimes for the k NN and LSTM models with respect different sizes of input data from 500 to 5,000 increasing in steps of 500 and using one fold of the five-cross validation. From the figure it can be seen that when using k NN with DTW is considerably less efficient than when using the LSTM model. An improvement can be made by changing the representation approach of the time series to optimise the data structure, so as to enable a more efficient implementation of k NN and DTW. For the training time of a single task LSTM in a single epoch we can see from the figure that the time efficiency is considerably higher than in case of the k NN model. We can also observe that the run time line is not linear in the case of the LSTM, as the run time is also influenced by other parameters from the hidden layers.



(a) Run time of kNN



(b) Run time of single task LSTM-RNN

Figure 2: Run time with different data size, (a) k NN model, (b) LSTM-RNN model

7 Conclusion

In this paper, a mechanism for event-based pathology data prioritisation has been proposed for multivariate time series pathology result data. The motivation was the large amount of pathology data received by hospital departments which necessitates some form of prioritisation. The challenge was that there is no ground-truth prioritisation data available, because of the resource required to create this. Two approaches were explored, one using the k NN with DTW as a distance measurement, and one using an LSTM mechanism. The fundamental idea underpinning the event-based prioritisation is to classify newly generated pathology data in terms of the anticipated outcome event and then to use this outcome event as a prioritisation marker. The proposed mechanism was evaluated using U&E laboratory test data. The results demonstrated that the LSTM mechanism produced the best recall and precision of 0.788 and 0.648 respectively. A criticism of the proposed RNN approach is that the process of running five LSTMs separately is time consuming and complicated, methods using a stacked deep learning network ensemble might be more preferable. Another criticism is that the classification was conducted using crisp bound-

aries which may not be the most appropriate.

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