Impact of Medical Data Imprecision on Learning Results

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ABSTRACT
Test data measured by medical instruments often carry imprecise ranges that include the true values. The latter are not obtainable in virtually all cases. Most learning algorithms, however, carry out arithmetical calculations that are subject to uncertain influence in both the learning process to obtain models and applications of the learned models in, e.g., prediction. In this paper, we initiate a study on the impact of imprecision on prediction results in a healthcare application where a pre-trained model is used to predict future state of hyperthyroidism for patients. We formulate a model for data imprecisions. Using parameters to control the degree of imprecision, imprecise samples for comparison experiments can be generated using this model. Further, a group of measures are defined to evaluate the different impacts quantitatively. More specifically, the statistics to measure the inconsistent prediction for individual patients are defined. We perform experimental evaluations to compare prediction results based on the data from the original dataset and the corresponding ones generated from the proposed precision model using the long-short-term memories (LSTM) network. The results against a real world hyperthyroidism dataset provide insights into how small imprecisions can cause large ranges of predicted results, which could cause mis-labeling and inappropriate actions (treatments or no treatments) for individual patients.

CCS CONCEPTS
• Computing methodologies → Neural networks; • Applied computing → Health informatics.

KEYWORDS
Prediction, neural networks, imprecise data, healthcare

1 INTRODUCTION
Clinical lab tests play an increasingly important role in today’s healthcare. From early detection of diseases to diagnosis to personalized treatment programs, lab tests guide more than 70% of medical decisions and personalized medication [1]. The availability of medical and healthcare datasets makes healthcare one of the focused areas of applying machine learning techniques in order to improve healthcare [3, 6]. However, due to limitations of equipment, instruments, materials, test methods, etc., data inaccuracy always occurs, leading to uncertainty in measured results. It becomes an interesting problem to understand the impact of accuracy of clinical laboratory test results on effectiveness of machine learning. This paper initiates a study to quantify the impact of medical data imprecision on LSTM [4] prediction results.

Imprecision of clinical lab test results is often due to systematic and random factors. Systematic factors are mostly reproducible and tend to skew results consistently in the same direction. For example, the attenuation of the light source of the instrument will cause test results to shift to one side. Random factors are unpredictable during operations, examples include expired reagents, expired controls or calibrators, or failure in sampling system. Since random factors cannot be easily attributed to certain reasons, it is difficult to eliminate them. Usually large imprecision margins are unallowable for lab tests. Therefore, each lab follows some specified quality control and process control protocols to ensure that the test results are within respective tolerable ranges (or imprecision ranges, values in this range are acceptable, though imprecise). Such ranges for common biochemical tests are provided in [2].

Earlier studies focused on how the noise (erroneous values, missing or incomplete values) in datasets would impact the model learning and the way to deal with them [7–9]. However, it is not clear what effect imprecision ranges have in prediction results when a pre-trained model is used to make prediction for new sample. Based on a dataset in the study of hyperthyroidism progress prediction, we study in this paper the impact of imprecision on prediction results. We first formulate a model to represent data imprecision with a parameter to control the degree of imprecision. Imprecise samples for comparison experiments can be generated using this model. A group of measures are then defined to evaluate the different impact in a quantitative way. More specifically, the statistics to measure the inconsistent prediction for individual patients is defined. We carried out a set of experiments to compare the prediction results based on the data from the medical database and its corresponding ones generated from the proposed imprecision model. The experiments are conducted against a real world dataset. The experimental results provide fresh insights into the reasons that the small imprecise could cause the inconsistent prediction results for individual patients, and lead to unreliable results.

The paper is organized as follows. Section 2 motivates the study with a real application example. Section 3 introduces an imprecision model and measurements. Section 4 presents experimental results. Section 5 concludes the paper.

2 MOTIVATIONS
Test data measured by medical instruments often carry imprecise ranges that include the true values that are not obtainable in almost all cases. Most learning algorithms, however, carry out arithmetical calculations in both the learning process to obtain models and applications of the learned models in, e.g., prediction. In this section, we present an application example and illustrate how the imprecision could cause prediction results to be wrong.

The application occurs in a collaboration between researchers in Donghua University (Shanghai, China) and physicians in Ruijing Hospital (Shanghai, China). The aim is to develop a personalized prediction service to identify hyperthyroidism progress for patients.
Patients with hyperthyroidism (a chronic disease) always experience stages of occurrence, remission, cure or recurrence. Hyperthyroidism occurs when the thyroid gland produces too much thyroxine (hormone). Lab tests are an integral part of the diagnosis process to assess the progressing stage of hyperthyroidism. Typical thyroid tests include blood tests for thyroid-stimulating hormone (TSH), free thyroxine and TSH receptor antibodies (TRAb). Low TSH levels may be a sign of an overactive thyroid (hyperthyroidism).

For a patient with a period of treatment, TSH may become normal. After stopping treatment for a while, if the TSH level becomes low again, it could mean a recurrence of hyperthyroidism. If such recurrence is predicted in advance for a patient with a high probability, additional treatments can be carried out early, such as the special medication strategy, unconventional inspection, or ablative therapies including radioactive iodine treatment (RAI) or the surgical removal of the thyroid tissue. In the collaboration, a prediction model was developed [5] to predict the progress of hyperthyroidism two years in advance based on the feature data in the first six months. The feature data includes the patient’s basic information such as gender, age as well as the value of the key tests FT3, FT4, TSH, and TRAb.

Accuracy of clinical lab test results is fundamental. Under ideal circumstances, none of systematic and random factors occur, but this is not achievable in daily practice. Thus the test results are given allowable imprecision ranges. For example, the desirable and optimum levels of allowable imprecision specifications for TSH are 9.65% and 4.825% resp. [10] On the other hand, even test results fall in small ranges, the imprecise values may cause large range of predicted results, which may further cause mis-labeling and wrong actions (treatments or no treatments). This is best explained with a representative clinical case presented below.

Consider a patient from the dataset studied in the collaboration mentioned in the above. Patient X (female, 34 years old) first visited the hospital with a low TSH level. The trained prediction model is used to learn whether she has a high risk of recurrence. The top left table in Fig. 1 shows the 5 lab test results in the first 6 months. Based on these original lab test data the prediction result is shown in the second line of the bottom table in Fig. 1: the predicted TSH level was at 0.352764 and within the normal range.

To understand the impact of imprecision margin on behavior of the prediction model, for the obtained value \( x \), we define \( x' \) that has a small difference with \( x \) as follows:

\[
x' = x \pm \Delta x \ast x
\]

(1)

where \( \Delta x = \frac{x - \text{normal range}}{x} \) is used to control the variation of \( x \).

Let \( f \) be a prediction function. Then the predicted value \( y' = f(x') \) is calculated from \( x' \). Typically, imprecision in the input variables will propagate through the calculation to an imprecision in the output \( y' \). To numerically measure the degree of \( \Delta_x \) affecting \( y \), we define:

\[
f(x') = f(x) \pm \Delta y \ast f(x)
\]

(2)

where \( \Delta y = \frac{f(x') - f(x)}{f(x)} \) measures the change of \( y \) due to \( \Delta_x \).

In general measuring changes of \( \Delta y \) as \( \Delta x \) varies provides a fairly informative indication of imprecision propagation. For the dataset and prediction in our study, we would also like to measure the mis-labelings due to the imprecise prediction results. After predicting \( f(x) \), the label \( f(x) \) can be obtained by comparing the value of \( f(x) \) with the reference range. For example, we know the normal range of the blood test measurement TSH is [0.34, 5.6] (mIU/L). A predicted value of 5.8458 indicates abnormal high label. Assume a group of \( n \) tested patients forms the test dataset \( D_{\text{Test}} =...
(x_1, x_2, \ldots, x_n). Since \( l(f(x)) \) is a classification label, accuracy is used to measure the prediction performance. Given one label \( l \), let \( TP \) model the positive samples in the test set and the predictions are correct. \( TN \) represents the negative samples and the predictions are correct. Accuracy is then defined as follows:

\[
\text{Accuracy} = \frac{|TP| + |TN|}{|D_{\text{Test}}|}
\]

Similarly, for each \( x_i \), we generate the corresponding \( x'_i \) according to Eq. (1). The \( x'_i \)'s samples form \( D'_{\text{Test}} \). For prediction model \( f \) and test dataset \( D'_{\text{Test}} \), we can calculate \( TP' \) and \( TN' \), then we have:

\[
\text{Accuracy}' = \frac{|TP'| + |TN'|}{|D'_{\text{Test}}|}
\]

We further define:

\[
\Delta_{\text{Accuracy}} = \frac{\text{Accuracy}' - \text{Accuracy}}{|TP'| + |TN'| - (|TP| + |TN|)}
\]

We also define the following two patient sets:

\[
N - P = (TP' \cup TN') - (TP \cup TN)
\]
\[
P - N = (TP \cup TN) - (TP' \cup TN')
\]

Finally, we obtain:

\[
\text{Count\_gain} = |(N - P)| - |(P - N)|
\]
\[
\text{Count\_inconsistent} = |(N - P)| + |(P - N)|
\]

Here \( N - P \) denotes the patients whose predicted label on \( x \) are wrong, while the predicted label on \( x' \) are correct. \( P - N \) denotes the patients whose predicted label on \( x \) are correct, while the predicted labels on \( x' \) are wrong. \( \text{Count\_gain} \) denotes the positive gain. Since \( TP \cap TN = \emptyset \) and \( TP' \cap TN' = \emptyset \), we have \( \Delta_{\text{Accuracy}} = \text{count\_gain}/n \). We can see \( \Delta_{\text{Accuracy}} \) only counts the difference between \( N - P \) and \( P - N \). While in real application, we need to pay attention to every patient whose predicted result changes. Thus we define \( \text{Count\_inconsistent} \) which denotes number of the inconsistent label prediction. This provides new insight into a disagreement between predictions for individual patients.

4 EXPERIMENTAL EVALUATIONS

To measure how imprecision margins effect prediction results, we run experiments against a large real-world clinic hyperthyroidism dataset. We exploit LSTM [4] to predict two measurements closely related with hyperthyroidism in future two years based on the test data in the first six months. TSH and TRAb are used as predicted targets.

4.1 Dataset

Our hyperthyroidism dataset is generated from Ruijin hospital, a reputable hospital in Shanghai, China, including nearly 10 years of patient records. The patients who satisfy the following two conditions are selected to the dataset. The first condition is that the first three diagnoses are about the hyperthyroidism and at least one of the of TRAb levels in the first three test results is abnormally high. This condition is used to filter out the pseudo-hyperthyroidism. The second condition is that the time periods of records are more than 2 years because our method is designed for a future prediction. There are 2,460 patients in the final dataset used in our experiments.

In the dataset patients have different numbers of measurement records. According to the statistics of the records, we found that almost half of the patients have about 7 records in the first six months. So we fix the number of the examination results at the first 6 month to be 7. For the patients whose records were less than 7 times, we filled missing ones with the test results closest in time.

After preprocessing the dataset, we divided the whole dataset into a training set and a test set. The training set consists of 1960 patients and the remaining 500 patients are in the test set.

In the LSTM network training, we use Truncated Normal Distribution to initialize the weights of the input and output layers. The hidden layer is expanded to 2 layers, each layer containing 128 LSTM cell units. We employ dropout method to reduce over-fitting and apply the Adam-Optimizer in training. Each experiment runs for 10 times and each data given in the experimental results is the average of the 10 runs.

4.2 Results

In experiments, we study the change trend of \( \Delta_y \), \( \Delta_{\text{Accuracy}} \), and \( \text{Count\_inconsistent} \) with \( \Delta_x \). The prediction model is trained based on the original training data.

Fig. 2 illustrates the ratio \( \Delta_y/\Delta_x \) when \( \Delta_x \) increases. From the figure, we can see that generally the ratio is larger than 1, and that \( \Delta_y \) grows faster than \( \Delta_x \). When \( \Delta_x = 0.04 \), the \( \Delta_y \) for TRAb expands more than 8 times. It clearly show that a slight change in \( x \) may cause a large change in \( y \). When \( \Delta_x \) is large, it seems that the ratio shows a slight downward trend. However, when \( \Delta_x \) is large, \( \Delta_y \) will be even larger.

Fig. 3 illustrates the change trend of accuracy when \( \Delta_x \) increases. It can be observed that when \( \Delta_x \) is small, there is little change in accuracy. Fig. 3 indicates that when \( \Delta_x \) is greater than 0.1, the accuracy begins to decline obviously. Also we could see that the decline is not stable. We observed the results and found that since the normal ranges of TSH and the abnormal lower range of TRAb is much smaller compared with their other ranges. The prediction label could easily change from correct to wrong or from wrong to correct for these ranges by introducing the imprecision to the data, leading to the unstable decline.

On the other hand, although accuracy did not decrease significantly when \( \Delta_x \) is small, we could not ignore the impact of the small \( \Delta_x \) on the prediction results. The prediction results might be unreliable for individual patient. It is demonstrated in Fig. 4. We provide the value of \(|N - P|, |P - N|, \text{Count\_gain}, \text{Count\_inconsistent}\) when \( \Delta_x \) takes different values in Fig. 4. From the figure, we can see that when \( \Delta_x = 0.05 \), \( \text{Count\_inconsistent} = 13 \), which means that 13 patients’ prediction results have changed. \( \text{Count\_inconsistent} \) provides a new way to evaluate the performance of the prediction model.

Finally, we also tried out an idea of using a training set with imprecision, hoping to learn a model that is less sensitive to imprecision. Specifically, for each \( x \) we generate sample \( x'_i = x + \Delta^i_x \cdot x \); \( x'_i = x - \Delta^i_x \cdot x \). Then we randomly choose \( x'_i \) or \( x'_i \) as \( x' \). Gather all of the \( x' \)s to form the supplementary data set. We combine the original data set with the supplemental data set to form the new dataset, then retrain the model based on the new dataset, and finally obtain the new prediction model \( h(x) \). At first, We count the
number of two patient sets $N - P$ and $P - N$ according to the prediction results of $h(x)$ and $f(x)$, and then obtain $\text{Count\_gain}(f, h)$, which is illustrated in Fig. 5. From the figure, we can infer that by comparing the accuracy, $h(x)$ definitely outperforms baseline prediction model, since $\text{Count\_gain}(f, h)$ is significantly greater than 1 especially when $\Delta x$ is small.

Also we use $h(x)$ to predict the samples in imprecision ranges and then calculate $\text{Count\_inconsistent}$ based on the original test set and the imprecise one. Fig. 5 shows that the $\text{Count\_inconsistent}$ of $h(x)$ is also very large. When $\Delta x = 0.05$, $\text{Count\_inconsistent} = 19$, which is even larger than that of $f(x)$. In $h(x)$ learning process, more data are involved in training process, it can be inferred that more delicate curve that fits the data were learned. Correspondingly, the global accuracy is improved. However, the model structure of $h(x)$ is same as $f(x)$, which did not deal with the imprecise problem, so the $\text{Count\_inconsistent}$ of $h(x)$ has not decreased.

5 CONCLUSION

Medical data imprecision is a common issue that could be easily ignored. This paper carried out a set of experiments to understand the impact of imprecision on prediction results in the applications of hyperthyroidism progress prediction. The study has direct guidance on practical healthcare applications. In addition, it motivates to build robust models that can take imprecisions into account with better generalization. Much work remains, including to understand and quantify the impact of imprecision in more general settings on learning models including specifically medical datasets. The general principles that guide the impact are also interesting to explore and develop; Based on such principles, more effective methods to deal with data imprecision are to be investigated.

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