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Artificial Neural Network Model for Hepatitis C Stage Detection

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Abstract: Hepatitis C is a liver disease caused by the hepatitis C virus (HCV). In 2015, WHO reports that 71 million people were living with HCV, and 1.34 million died. In 2017, 13.1 million infected people knew their diagnosis and around 5 million patients were treated. HCV can cause acute and chronic hepatitis, where 20% of chronic hepatitis progresses to final-stage chronic liver cancer. Currently, no vaccine of HCV exists, and no effective treatments are available for demolishing the progression of hepatitis C. So spotting the stages of the disease is essential for diagnostic and therapeutic management of infected patients. This paper attempts to detect stages of hepatitis C virus so that further diagnosis and medication of hepatitis patients can be prescribed. It uses a supervised artificial neural network to make a prediction. Evaluation of results is done by cross-validation using the holdout method. Hepatitis C Egyptian-patients' dataset from UCI Machine Learning Repository is used for feeding the algorithms. The research succeeds to detect the hepatitis C stages and achieves an accuracy of 97%.

1. INTRODUCTION

World Health Organization (WHO) Global hepatitis report 2017 [1] estimated that hepatitis C virus (HCV) affects more than 170 million people worldwide which is 1% of the global population. The report exposed that viral hepatitis caused 1.34 million deaths in 2015 where significant deaths were due to chronic liver disease (720,000 deaths due to cirrhosis) and primary liver cancer (470,000 deaths due to hepatocellular carcinoma). The disease also turns as the primary cause for liver transplantation worldwide. About 75 to 85% of HCV infected people may progress to chronic HCV infection and poses a high risk of developing extrahepatic, redressed and decompensated cirrhosis, and hepatocellular carcinoma (HCC). The risk of cirrhosis development is highly variable and is affected by several factors including alcohol consumption, age of initial HCV infection, degree of liver biopsy inflammation and fibrosis, HIV and HBV co-infection, and related conditions. An estimated 10 to 15 % of people diagnosed with HCV will switch in the initial 20 years to cirrhosis. Cirrhosis patients are at high risk of developing HCC [2]. Current antiviral drugs can help to cure hepatitis C if diagnosed at the early-acute stage. However, for most patients, acute hepatitis C will likely develop into a chronic condition that requires treatment.

Since HCV often doesn't show symptoms until after more significant liver damage occurs, it is urgent to detect its stages for medication and therapeutic management of patients. Depending on their stages of further treatment, such as the number of chemotherapy, radiotherapy, and hormone therapy, can be provided to the patient along with the proper dosage of medication. If the stages are not determined properly, a random dosage of medications will be given in sort of experimentation to different types of patients. It is evident that medication for a lower stage patient will have no or low effect in a lower stage patient, and will have a severe effect if vice-versa. Here emergent the importance of stage detection of hepatitis C Virus. Hussein et al. [3] used data mining techniques to diagnose hepatitis

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which helps to incorporate, build, and assess effective processes for promoting clinical decision making; where a correct diagnosis is the most dominant factor. Wai et al. [4] proposed a diagnostic method of chronic hepatitis C, using patient serum index data to predict the stage of fibrosis and chronic hepatitis C which aids to overcomes baselines relating to the fibrosis stage diagnosis and chronic hepatitis C inflammatory activity grade. Yarraguntla et al. [5] implemented a biosensor device capable of predicting hepatitis viruses (HAV, HBV, HCV) by immobilizing specific antibodies on the sensor component, which rapidly identify the types of virus. However, these researches do not detect hepatitis C stages in a clear-specific manner with maximum accuracy.

This research aims to estimate the different stages of hepatitis C disease in a vast number of patients using Artificial Neural Networks (ANNs). Neural networks are used in an unambiguous process of back propagation and error correction during the test section for a variety of unique concepts and ideas. By reducing the error accordingly, these profound systems will one day be able to learn and conceptualize ideas on their own, without human correction. The dataset from a platform named UCI Machine Learning Repository [6] has been used. The dataset holds information of 1385 Egyptian patients affected by Hepatitis C Virus and received dosages for treatment. The rationale behind choosing the dataset is that Egypt faces a significant public health and economic issue as 13 to 15 % population are HCV infected [7]. A pre-processing stage of refinements was then added based on feedback from the experts. The data that is then classified and marked as No Fibrosis (Stage0), Portal Fibrosis (Stage1), Few Septa (Stage2), Many Septa (Stage3), Cirrhosis (Stage4). Alshamrani et al. [8] proposed a framework for analyzing different hepatitis ailments using consolidated Strong Box-Cox Change and Neural System strategies. Analysis and result assessment are done based on grouping exactness, and an improved accuracy rate of 98.07 per cent is obtained in predicting hepatitis disease. Nahato et al. [9] developed a hybrid medical decision support system for diagnosing hepatitis disease using a rough set (RS) and an extreme learning machine (ELM). Redundant features were removed using the RS approach, and classification processes were applied using ELM technique. The classification accuracy achieved was 96.49 % by this model. Sartakhti et al. [10] proposed a system for diagnosing hepatitis using support vector machine and simulated annealing and aimed to solve complex problems with optimization. This model introduced 10-fold cross-validations obtained 96.25 % accuracy. Kumar et al. [11] suggested a hepatitis disease diagnosis program using three separate algorithms, such as decision trees C4.5, ID3, and CART. The program initially sorts out hepatitis diseases and compares the disease's effectiveness among them. The CART model gave the best precision of 83.2 % among them. Table 1 shows that most of the existing systems are suffering from over fitting or under fitting problems due to traditional machine learning agents.

Table 1. Taxonomy of related works for hepatitis disease prediction

Specification	Method	Limitation	Ref.
Focuses on detecting fatal hepatitis disorder using a primary classifier and information gain. The information gain technique is applied to condense the number of features for reducing computation time and classification complexity.	Adaptive neuro-fuzzy inference system.	Traditional classifiers, like the adaptive neuro-fuzzy inference system, have minimal impact on the reduction of computation time and classification complexity.	[12]
Emphasizes on predicting and staging fibrosis in children with chronic hepatitis C (CHC). Machine learning is used for data cleansing to build an intelligent model aimed at obtaining a new cut-off value for APRI (aspartate aminotransferase-to-platelet ratio) and FIB-4 (fibrosis score).	Random forest.	While training a model with Random forest, it quickly reaches a point where inputting more samples will not improve the accuracy. In contrast, a deep neural network not only requires large samples to deliver a similar level of accuracy but also improves accuracy by adding increasing samples.	[13]
Compares several machine learning algorithms to predict hepatitis C NS3 protease cleavage sites.	Sequence extraction methods	No single pseudo-model performed significantly better than others. Evaluation of performance measures also shows that the correct choice of model-scoring-system is essential for unbiased model assessment.	[14]
Proposes developing and comparing two machine learning algorithms to predict cirrhosis development in a sizeable CHC-infected cohort using longitudinal data (like the national Veterans Health Administration (VHA) data from 2000 to 2016).	Cross-sectional (CS) models, and longitudinal models.	It uses primitive machine learning algorithms where the use of state-of-art algorithms' like ANN or CNN can achieve more accuracy than primitive algorithms.	[15]
Focuses on only the classification of patients from Asia and Europe using ultra-deep genome sequencing of the hepatitis B virus (HBV).	Random forest.	Classifications of patients are done using demographic attributes. But patients' clinical data should take into consideration as it has a direct impact on disease prediction.	[16]
Proposes an accurate method for diagnosing hepatitis disease by taking advantage of ensemble learning.	Neuro-fuzzy inference system.	The results are compared with simple classifiers like neural networks, ANFIS, k-NN, and SVM.	[17]
Emphasizes on the prediction of the prognosis in chronic hepatitis patients using a novel hybrid artificial intelligence-based classifier.	Lagrangian support vector machine, multilayer perceptron.	It considers 19 features and achieves an accuracy of 100%, which is not realistic and reveals an overfitting issue.	[18]
Aims to develop an optimal model to predict HBsAg seroclearance from patients' data of South China Hepatitis Monitoring and Administration (SCHEMA) cohort.	Random Forest, Decision Tree, and Logistic Regression.	Basic classifiers like RF, DT, and LR suffer from model fitting.	[19]
Focuses on identifying prospectus populations tested for the hepatitis B surface antigen.	Oversampling Technique (SMOTE), and Logistic Regression.	The confusion matrix shows that the sensitivity is 70.8%, and specificity is 70.1% which is pretty low for clinical decision support systems.	[20]

Machine learning algorithms like Community Detection Algorithm [21], Convolutional Neural Network [22], K-nearest

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Neighbour [23], and artificial neural network [24]are widely used in decision support system [25]. Besides, rule-based expert systems [26] are famous for clinical decision support systems [27][28]. In this paper, a state of art algorithm to detect hepatitis C stages has been proposed.

2. METHODOLOGY

The prediction system incorporates two-tier architecture. The top tier is designed to process the dataset obtained from the information source. The bottom tier, post data pre-processing tier, is performed to deduce accuracy through train/test split iteration where cross-validation is done through the holdout method. Figure 1 shows the flow chart of the proposed model. This dataset contains multivariate characteristics, integer attribute, 1385 number of Instances, and 29 numbers of attributes. We used comprehensive search methods to identify and collect data from valid and unpublished accounts of patients with the hepatitis-C virus.

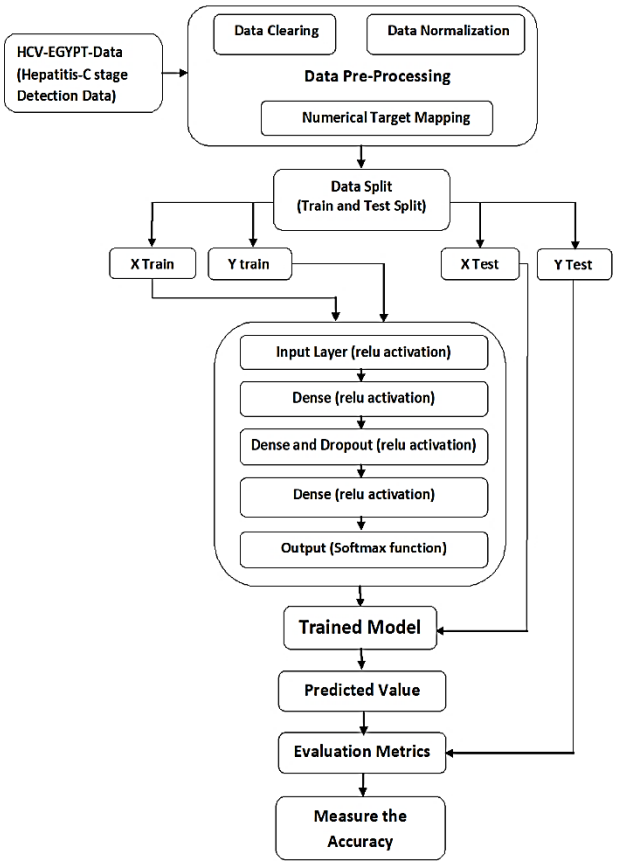

Figure 1. Flow chart of the proposed model

This dataset contains multivariate characteristics, integer attribute, 1385 number of Instances, and 29 numbers of attributes. We used comprehensive search methods to identify and collect data from valid and unpublished accounts of patients with the hepatitis-C virus. We obtained a processed dataset, shown in Table 2, where a row is considered as an instance of a patient data, while columns represent features. The right-most column represents stages of the disease, which is the main target of the classification algorithms. Afterword, we separate the dataset into a training set and testing set. This is accomplished by splitting the dataset at some point, 80% of our data instances for training and rest for the testing set. Then our predicted targets during the testing phase are compared to the bottom truth (actual) targets of the testing set. In practical terms, this can compare a brand new vector as y_pred to the present y_test vector. Our proposed model consists of an Artificial Neural Network (ANN), which can be closely related to the human nervous system. ANN is a combination of highly connected neurons in single or multiple layers; which has some processing capabilities on the input fed into it.

Table 2. Data set from UCI repository

Age	Gender	BMI	Fever	Nausea|Vomting	Headache	Diarrhoea	Fatigue & generalized bone ache	Jaundice	Epigastric pain	LT-36	ALT 48	ALT after 24w	RNA Base	RNA 4	RNA 12	RNA EOT	RNA EF	Baseline histological Grading	Baselinehistological staging
56	1	35	2	1	1	1	2	2	2	5	5	5	655330	634536	288194	5	5	13	2
46	1	29	1	2	2	1	2	2	1	57	123	44	40620	538635	637056	336804	31085	4	2
57	1	33	2	2	2	2	1	1	1	5	5	5	571148	661346	5	735945	558829	4	4
49	2	33	1	2	1	2	1	2	1	48	77	33	1041941	449939	585688	744463	582301	10	3
59	1	32	1	1	2	1	2	2	2	94	90	30	660410	738756	3731527	338946	242861	11	1

Figure 2 represents the neural network model used in this study, which is obtained using 'Tensor flow' in a neural net and has two layers, such as 'dense' and 'dropout'. ANN is breaking the barriers of classification problems and currently being used in a variety of areas to predict the unknown relations between inputs and corresponding outputs.

In ANN, the nodes of the input layer are fed with an array of number, which is the input x. These input signals then start to propagate through adjacent neurons of different layers, and the signals can even be amplified or contained through some weights w. The next layer nodes act as the summation point for the input of the previous layer. In equation (1), the input fed into the nodes is transformed into the signal using a threshold or activation function $f(x)$.

$$f(x) = \frac{1}{1+e^{x}} \qquad (1)$$

The value of $f(x)$ between 0 and 1, this value is used in equation (2) to generate the output Q_j where,

$$Q_j = \frac{1}{1+e^{-\sum x_i w_i}} \qquad (2)$$

Where j is the neuron number of the corresponding layer and i is the sample number of the input data fed into the neuron.

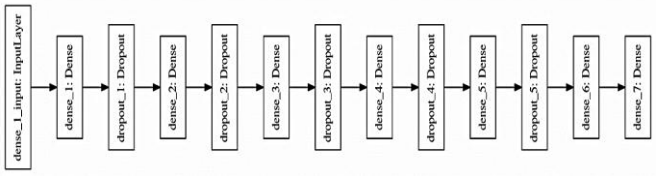

Figure 2. Neural network model layers

In the 'dense layer,' we accommodate 80% of the value and the rest 20% is used in the 'dropout layer'. The neural functions used in Figure 3 have the following description:

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'**Relu**' - rectified linear unit, this is the default activation when designing Perception multilayer and neural convolution networks.

```
def nural_net():
    model = Sequential()
    model.add(Dense(512, activation='relu', kernel_initializer='random_normal', input_dim=n_col))
    model.add(Dropout(.2))
    model.add(Dense(512,activation='relu'))
    model.add(Dropout(.2))
    model.add(Dense(512,activation='relu'))
    model.add(Dropout(.2))
    model.add(Dense(512,activation='relu'))
    model.add(Dropout(.2))
    model.add(Dense(512,activation='relu'))
    model.add(Dropout(.2))
    model.add(Dense(512,activation='relu'))
    model.add(Dense(4,activation='softmax'))
    model.compile(optimizer='adam',loss='sparse_categorical_crossentropy',metrics=['accuracy'])
    return model
```

Figure 3. Neural network model python code

'**Softmax**' - it is a sigmoid function, and it will tell us about the probability of our prediction.

'**Adam**' - this is an optimizer, which sends the wrong decision by backpropagation. Hence, the amount of loss becomes less.

'**Sparse_categorical_crossentropy**' - this is used for the reason of having few values, or else we would have used the word 'categorical' only.

At the final stage, we measured the prediction via a metric like an accuracy. This shows us how effective our model is, and provides us with a baseline to which we will compare future classification models. We used supervised learning through neural networks that tend to use gradient descent to scale back the number of losses.

3. RESULTS AND ANALYSIS

We plotted the 'heat map' shown in Figure 4 using our data set (Table 2). The graph shows a white lining which means that the same attributes of the x-axis and y-axis collide with their same values at a particular point and become '0'. Figure 4 also shows that the RNA virus (*Flaviviridae* family) virus has more impact on hepatitis C. We used the x-axis and y-axis for 'Baseline histological Staging'. The x-axis is used for 'feature matrices' and y-axis for 'target'. Each 'x' and 'y' axis is associated with a 'train' and 'test' value by which we perform both training and testing to our dataset using 'train_test_split' function. We take 80% as our training value and 20% as our test value or the test size.

In this Figure, we have normalized the value of x_train and x_test values. Thus, bringing the dataset values to a decent form by taking small values from the dataset, rather than the huge values, that does not collapse the other value anymore. Thus we plotted y_test plot bar in

Figure 5 (a) and y_train plot bar in Figure 5 (b). Figure 6 is the program code that categorizes hepatitis-C patients as Stage1, Stage2, Stage3, and Stage4. As we have to assign the 'Baseline histological staging' as Stage zero, we reassigned the stages as Stage1 = Stage zero, Stage 2 =Stage one, Stage 3 =Stage two, and Stage4 = Stage three. After detecting the stages of hepatitis C patients from our dataset, we plotted 'Bar Graph' and 'Pie Chart' shown in Figure 7 (a) and (b) respectively. The colour 'blue' defines Stage1, 'orange' defines Stage2, 'green' defines Stage3, and 'Red' defines Stage4.

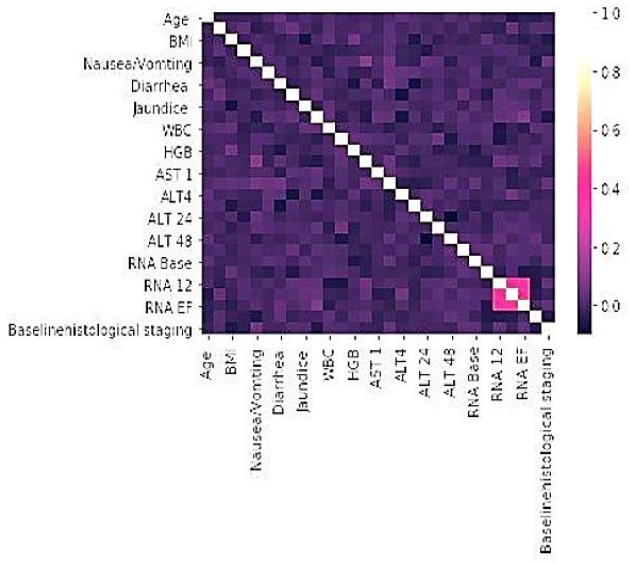
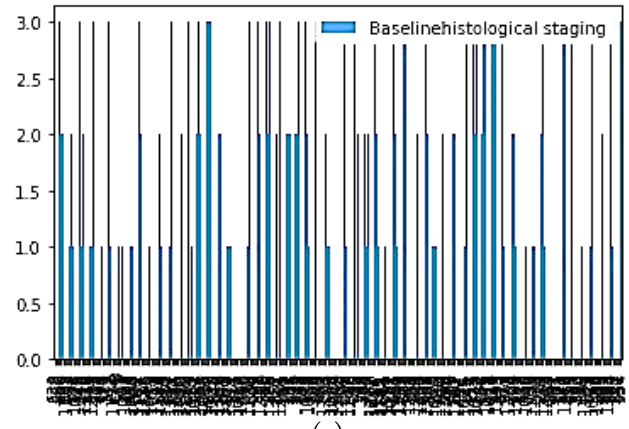
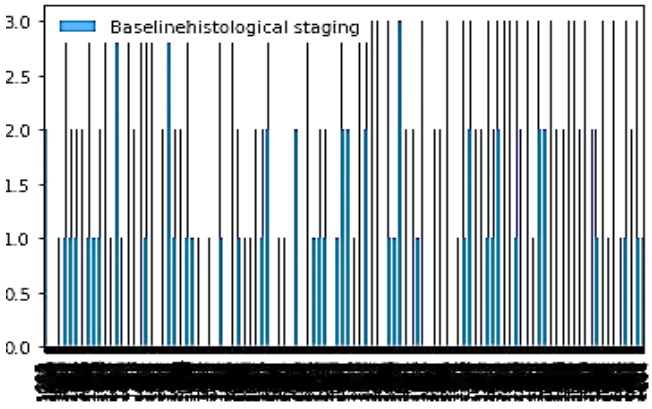


Figure 4. Data heat mapping for attributes



(a)



(b)

Figure 5. (a) Dataset y-test plot bar (b) Dataset y-train plot bar

The Figure 8 is plotted by using x-train and y-train of the dataset. The graph shows steeping downwards as the rate of loss is more than the rate accuracy for the first few cycles of our test-

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train-split process. Figure 8 (b) shows an increment in accuracy as the number of test cycles increases. We achieved the highest accuracy of 97% when the rate of loss decreases significantly to a low level.

```
zero=[]
one=[]
two=[]
three=[]
for item in y_test['Baselinehistological staging']:
    if item==3:
        three.append(item)
    if item==0:
        zero.append(item)
    if item==1:
        one.append(item)
    if item==2:
        two.append(item)
```

Figure 6. Python code for baseline histological staging

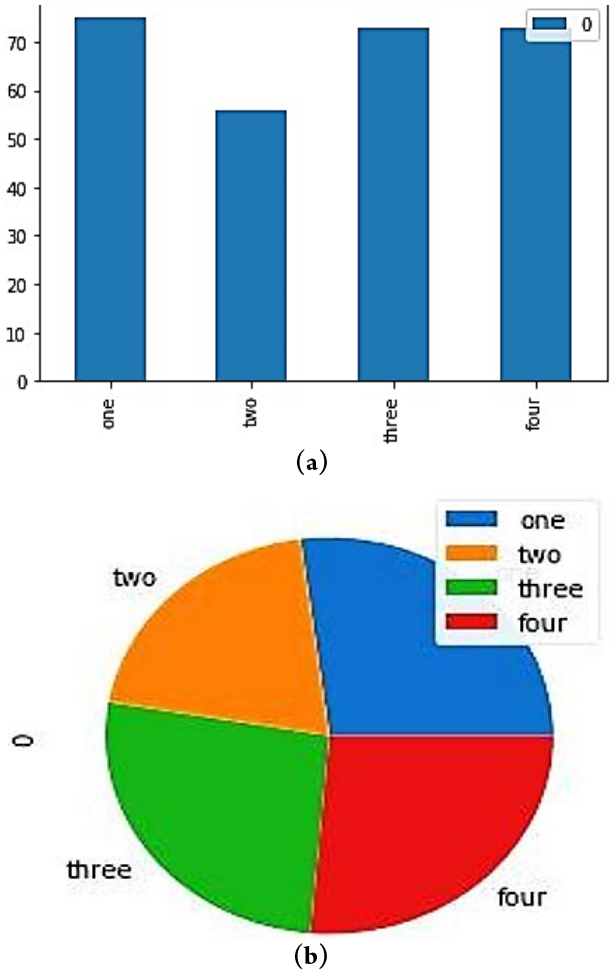

Figure 7. (a) Staging plot bar for Hepatitis C Stage (b) Staging pie chart Hepatitis C Stage

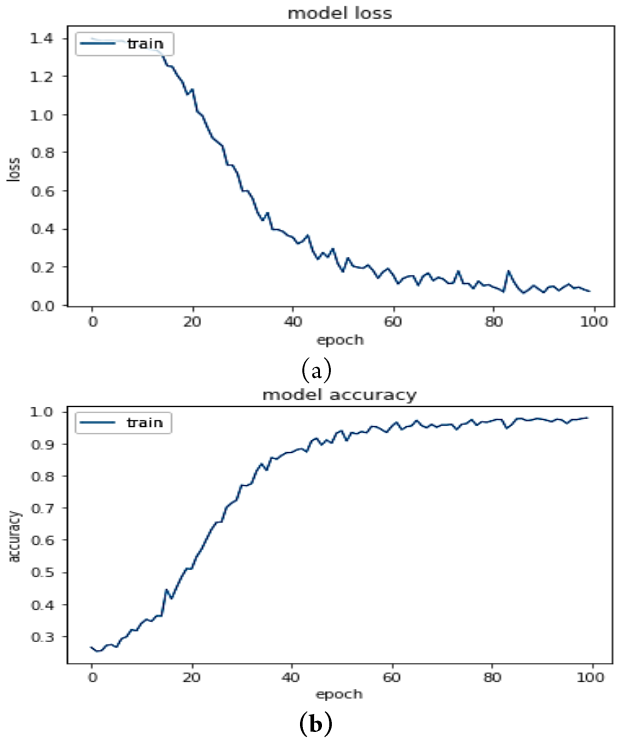

Figure 8. (a) Decreasing (b) Increasing accuracy Hepatitis C Stage detection

4. CONCLUSION

This paper successfully detects four stages of hepatitis C disease and thus enables the patients to have proper medications and treatments. An artificial neural network applied to our proposed model to detect the stages successfully as well as to achieve an accuracy of 97%. Data acquisition, pre-processing, and validation are done accordingly to achieve our goal. In our further studies, we would like to figure out the precious medications and aftercare for patients with different stages of the hepatitis C virus. This guideline will benefit them to follow up on their treatments independently.

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