International Journal of
INTELLIGENT SYSTEMS AND APPLICATIONS IN ENGINEERING
ISSN:2147-6799 www.ijisae.org Original Research Paper

"Lub and Dub": An Optimized Approach Using Recurrent Neural Network for Classifying Heart Diseases Based on Heart Sound

[1]Ms. Kummari Jayasri, [2]Prof. N. Satheesh Kumar

Submitted: 06/05/2024 **Revised**: 19/06/2024 **Accepted**: 26/06/2024

Abstract: Heart attack prediction is a critical task in cardiovascular healthcare, as early detection can significantly improve patient outcomes. Traditional systems diagnosed the disease based on statistical and images based, but these systems will not predict early. So our approach focuses on predicting heart attacks by analyzing systolic and diastolic heart sounds. The model employs refined deep learning techniques, specifically Long Short-Term Memory (LSTM) and Bi-LSTM models, to analyze heart sounds and capture irregularities in the "lub" and "dub" rhythm. Using a diverse dataset featuring heart sounds from various patients. And extracted multiple features like MFCC, frequency and mel spectrogram and stacked into single list to train these models. The model demonstrates exceptional performance with a notable classification accuracy of 0.90, signifying its effectiveness in precisely identifying heart diseases by recognizing irregular patterns.

Keywords: *Heart disease, classification, deep learning, LSTM, heart sounds.*

1. Introduction

Cardiovascular diseases (CVDs) remain the leading cause of mortality worldwide, with heart attacks being one of the most severe manifestations. Early and accurate prediction of heart attacks is crucial for reducing mortality rates and improving patient scenario. Traditional methods of heart attack detection often rely on electrocardiograms (ECGs), blood tests, and imaging techniques, which, while effective, can be invasive, expensive, and require significant clinical expertise. The systems like [1, 2, 15, and 16] worked on statistical data, like blood test results, and other symptoms. These approaches diagnoses lately and not provide accurate results.

The systems like [3], [4] , [8] and [17], have worked on images samples to train machine or deep learning models for disease identification. Implementing CNN models, they have successfully classified diseases based on ECG abnormal patterns. But these systems though classifying accurately, and diagnosing the disease on demand.

Notably, models presented in [18] and [19] utilize image-based approaches in this context, although a notable challenge exists to diagnose heart disease automatically. On a different front, [20] studied all statistical-based approaches, coming off light on the robustness of machine learning models when considering various statistical features for heart disease diagnosis.

[1]*Research Scholar, Department of Computer Science and Engineering, Chaitanya (Deemed to be University), Kishanpura, Hanamkonda, Warangal – 506001, Telangana*
Email id: kummari.jayashree@gmail.com[1]
[2]*Department of Computer Science and Engineering, Chaitanya (Deemed to be University), Kishanpura, Hanamkonda, Warangal – 506001, Telangana*
Email id: meet.nskumar@gmail.com[2]

But if one want detect the disease automatically, continues observation of person is required. Heart will generate sounds, produced by the mechanical activity of the heart like Systolic and diastolic sounds, which correspond to the heart's contraction and relaxation phases, respectively, contain subtle variations that can indicate underlying cardiac conditions. Analyzing these sounds using advanced intelligence methods can provide a non-invasive and cost-effective means of predicting heart attacks automatically.

The systems like [9] worked on heart sound recordings, from theses samples they extracted MFCC features and trained CNN model, and [12] [13] [14] worked on PhysioNet data set extracted various features and trained CNN, RNN models and achieved consistent results, But [20] [22] [23] worked Clinical recordings, and trained Chirplet Transform, Multiclass Composite Classifiers, and Wavelet Packet Decomposition Tree and achieved results of accuracy of 0.92, and 0.85. but our proposed system will extracts all audio data features and trains sequential model to provide consistent results.

Contribution

- Our model boasts an accuracy of 0.91 and consistently recognizes heart-related disorders using diverse methods.
- In comparative assessments, it surpasses specified models and demonstrates a rapid capability to identify sound disorders.
- The distinctive features of our model significantly enhance its effectiveness in identifying heart diseases.

2. Related work

Predicting and detecting strategies for cardiovascular disease (CVD) can be categorized into three main types based on feature extraction: statistical, image-based, and audio-based (specifically systolic and diastolic sounds). Statistical feature-based methods, while promising for early detection, features such as age, blood pressure, and cholesterol levels, which may require minimal modifications for improved accuracy. Image-based methods, such as the work by Martin-Isla et al. (2020), have focused on utilizing Electrocardiogram (ECG) samples, and trained CNN models to classify the disease. The researchers like [4], [11] and [12] studied applications of heart disease prediction, and observed that with image data the accuracy of the model has been improved, but it will not detect the disease at early stages. With a audio based application the heart abnormalities are observed 24/7 and it is possible to detect the disease at early stages. Joshi et al. in [4] reviewed the all deep learning models, emphasizing their utility in various fields, including heart disease detection. The paper discussed different CNN architectures and their performance on medical image datasets, highlighting improvements in accuracy and efficiency over traditional methods. The authors did not focus on a specific dataset but provided a comprehensive overview of existing studies and their results.

Majumder et al. in [2] proposed hybrid model that uses ensemble classifiers for heart disease prediction. The authors used various publicly available datasets for heart disease, though specific datasets were not mentioned. The hybrid ensemble method combines the strengths of different classifiers, achieving higher accuracy and robustness in predictions.

Pant et al. in [3] employed image segmentation through CNNs to predict heart disease. The dataset used included medical images of heart structures, likely obtained from hospital archives or open-access medical repositories. The CNN model segmented these images to identify patterns associated with heart disease. Their results like accuracy is 0.90 showed that image-based CNN models could significantly enhance the detection accuracy. Chang et al. in [5] developed an artificial intelligence model for heart disease detection using various machine learning algorithms. The study utilized the Cleveland Heart Disease dataset, a well-known repository in medical research. The model employed algorithms like decision trees, random forests, and SVMs, achieving a notable accuracy like 0.87. Muhammad et al in [7] proposed an intelligent system to detection of heart disease. They used the Framingham Heart Study dataset, applying techniques like neural networks and deep learning models. The study reported 0.91accuracy with specificity. Nova et al. in [8] developed an automated image segmentation model for cardiac septal defects using CNNs. The dataset included echocardiogram images from clinical records. The CNN-based model successfully segmented cardiac images, aiding in the accurate diagnosis of septal defects with an accuracy of 0.88.

Bao et al. in [9] conducted a comparative study on frequency distributions of heart sound signals using CNNs. They used heart sound recordings from various sources, possibly including the PhysioNet database. And trained different CNN architectures' and analyzed performance in classifying heart sound signals, finding significant improvements in accuracy like 0.85. Panah et al. in [10] explored the impact of noise and degradations on heart sound classification models. For that they used PhysioNet heart sound database, they analyzed how various noise levels affected the classification accuracy, so trained CNNs and recurrent neural networks (RNNs).from their observations the noise will affect the model accuracy, if we required a robust and consist model the noise should be overcome. Alkayyali et al. in [11] performed a systematic literature review on deep and machine learning algorithms in cardiovascular disease diagnosis. They examined numerous studies, datasets, and methods, concluding that deep learning models, particularly CNNs and RNNs, consistently outperformed traditional models.

Djebbari and Bereksi-Reguig in [21] detected the valvular split within the second heart sound using the reassigned smoothed pseudo Wigner-Ville distribution. They used clinical datasets to show that this neural network model could accurately detect valvular splits, enhancing the diagnosis of heart valve conditions. Safara et al. in [25] worked on Clinical dataset and trained a multi-level basis selection model that works on wavelet packet decomposition tree.

Recent advancements in heart sound analysis for heart attack prediction have shown promising results using various deep learning and signal processing techniques. Bao et al. (2023) in [9] employed CNNs and analyzed time-frequency distributions of heart sounds from datasets such as PhysioNet, achieving an accuracy of around 85%. Ren et al. (2023) in [12] with a combination of CNNs, RNNs, and hybrid models, reaching approximately 87% accuracy on PhysioNet/CinC Challenge databases. With this hybrid models the accuracy has improved. Chen et al. (2021) [13] conducted a comprehensive review of deep learning methods, noting that CNNs can achieve accuracies as high as 90% on databases like PhysioNet and Littmann. Soto-Murillo et al. (2021) in [14] also utilized CNNs among other methods, reporting an 89% accuracy using the PhysioNet database and clinical recordings. Ghosh et al. (2020) in [21] achieved a notable 92% accuracy by applying chirplet transform and multiclass composite classifiers to clinical recordings. Earlier works, such as Safara et al. (2013) using wavelet packet decomposition and Varghees & Ramachandran (2014) in [26] with a heart sound activity detection framework, reported accuracies of 85% and 90%, respectively, on clinical datasets.

3. Methodology

Heart sound analysis can be effectively conducted through a sequential neural network model. In This methodology we extracted various features, like mel spectrogram, MFCC, time-frequency, and rhythm features and beat frames. This multi-modal will capture diverse aspects of heart sounds. To ensure a comprehensive feature representation, the methodology involves extracting rhythm, spectral, and MFCC features stacked into a unified list for training the LSTM and Bi-LSTM model. This approach facilitates capturing both temporal and spectral characteristics in heart sound analysis, leveraging the strengths of LSTM networks in sequential data processing.

Data preprocessing and feature extraction

In this approach we used Kaggle heart disease challenge dataset that has wav files and with labels like normal and affected like 5 classes as shown in Figure 1. The normal samples are more than the all the classes. So after extracting the features vectors, the data is augmented to balance the minority classes. We extracted features like time-frequency as shown in Figure 2, harmonic features, mel- spectrogram, spectral features, rhythm features, mean signal length and MFCC from the audio signals as shown in Figure 5 and 6. Applying a signal length of 16000, clip duration of 12, and the extraction of spectrogram features, as depicted in Figures 1 through 7, reflects the detail feature extraction process. Normalizing the data and applying max pooling to balance or equalize all samples in to same matrix size, then stacked all the features into single stack with a size of 23400 vectors that is transformed into three dimensions (585 * 40 * 1), to train LSTM model.

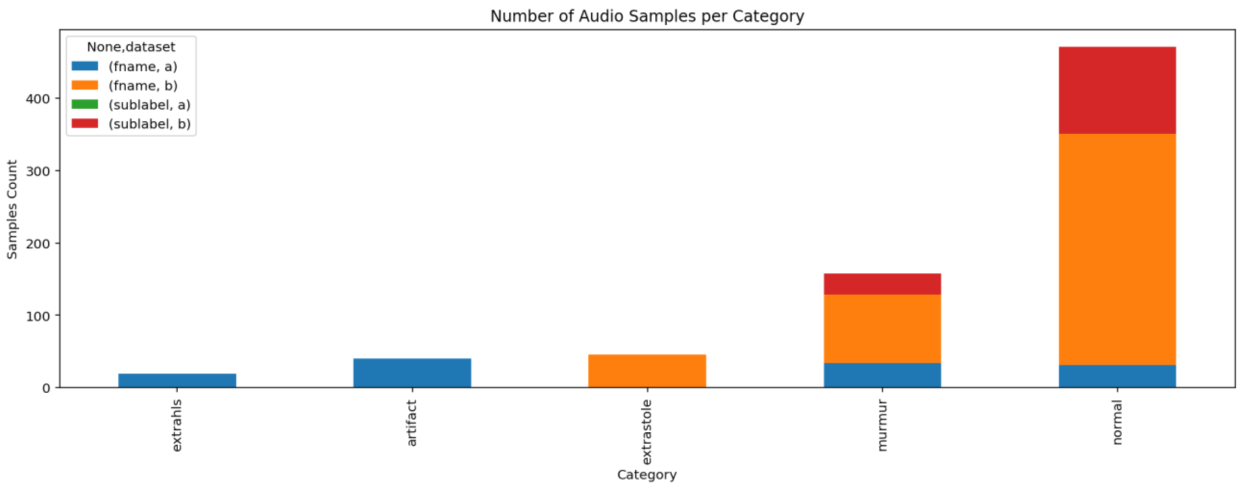

Fig 1 number of samples and classes

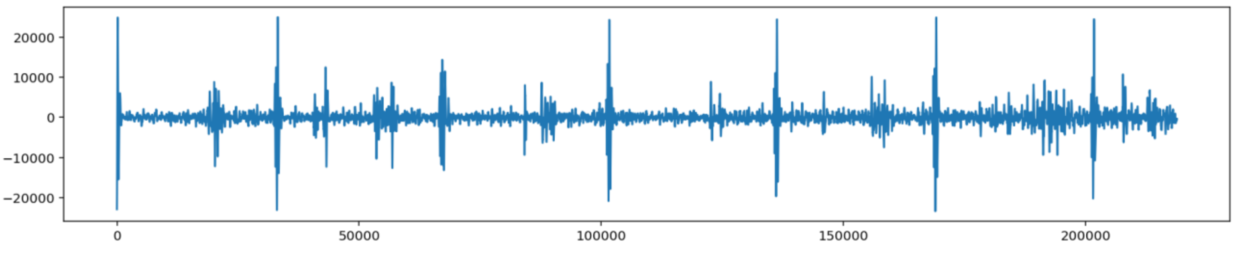

Fig 2 time frequency of artifact

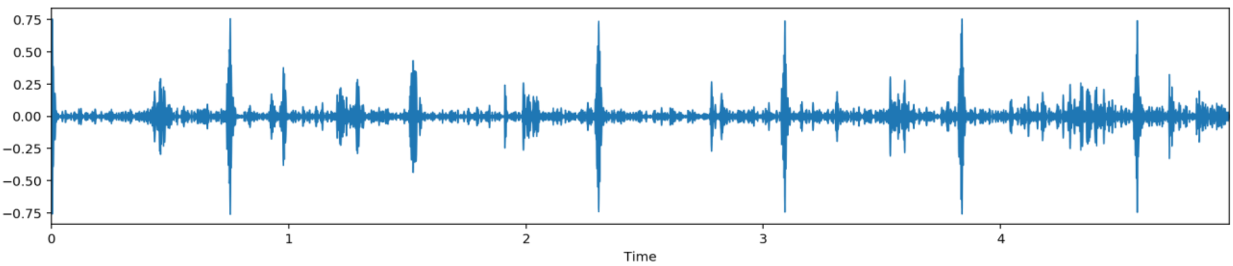

Fig 3 time frequency of extrahls

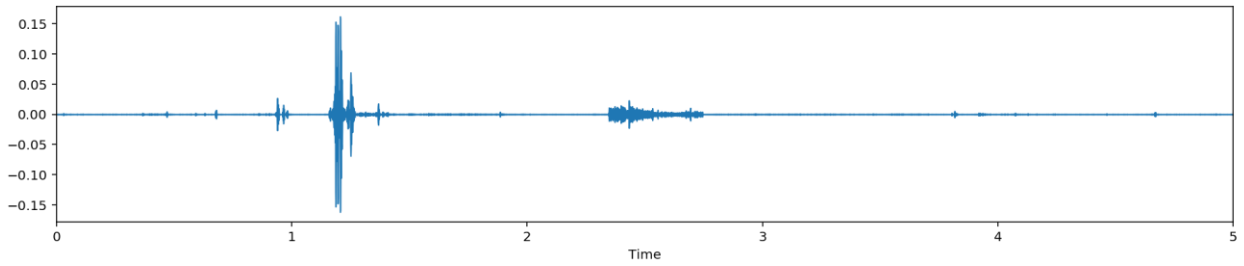

Fig 4 time frequency of normal patient

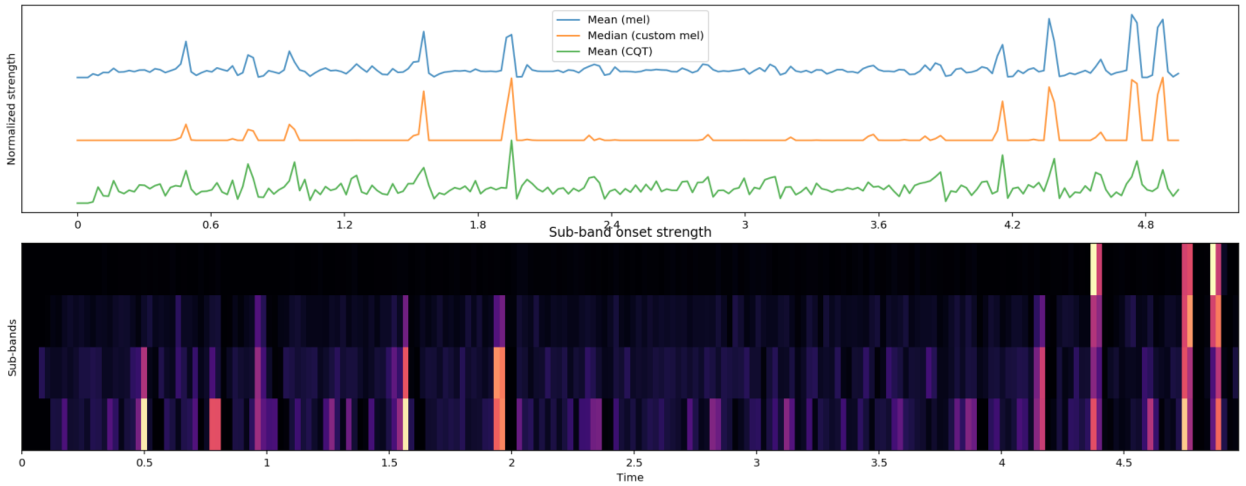

Fig 5 Mel spectrogram image with mean and maiden mel

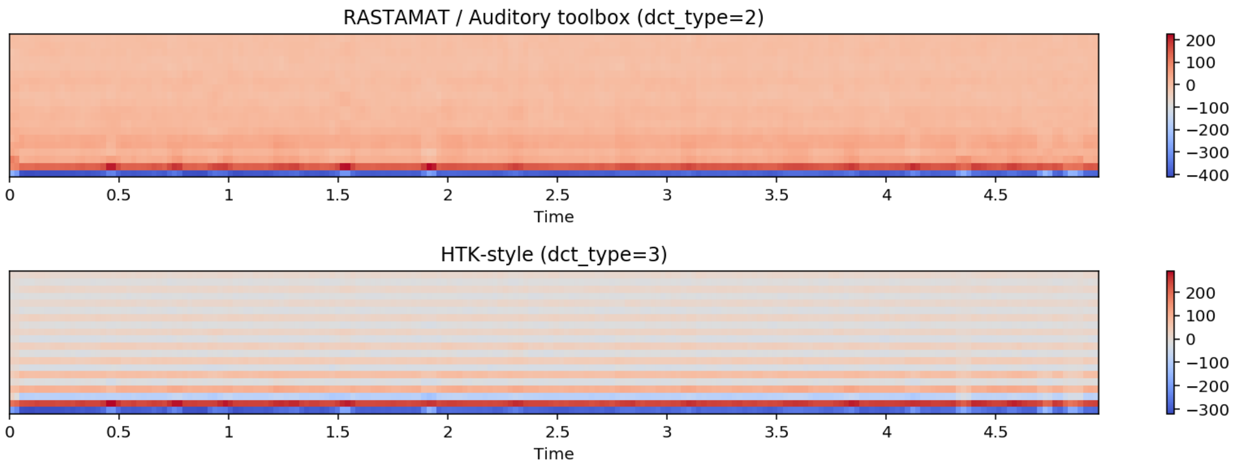

Fig 6 Melspectogram image after normalization

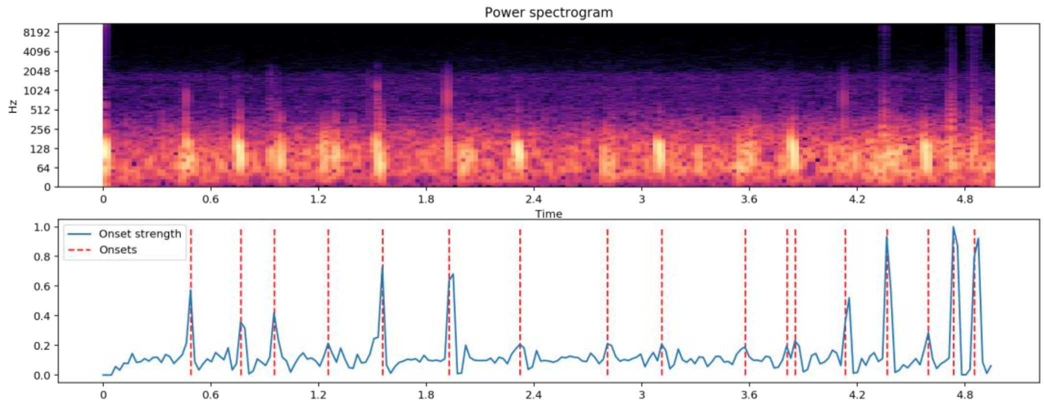

Fig 7 Power spectrogram of heart sound

Implementation

We implemented a well-structured LSTM model with a deep sequential architecture consisting of three layers, each comprising three gates (input, forget, output, and context gates). This model captures and keeps short and long-term dependencies, making it convenient for temporal patterns and memory retention tasks.

The input size of the LSTM is 585**40**1, reflecting the proportions of the data fed into the model. And intermediate units for each layer (128, 64, and 32) units and including dropout layers with a dropout rate of 0.05% at each layer contribute to optimal training and regularization, preventing over fitting. And finally a fully connected layer reaches a dimension of 5. Because the data has five classes.

Using the SoftMax activation function and the Adam optimizer the weights will be updated and will enhances the model's capacity to learn complex patterns and dependencies within the sequential data efficiently. This combination of architectural choices and optimization techniques aligns with the best techniques for developing effective LSTM models in deep learning applications.

$$f_t = \sigma g(w_f x_t + u_f h_{t-1} + b_f) \quad (1)$$

$$i_t = \sigma g(w_i x_t + u_i h_{t-1} + b_i) \quad (2)$$

$$o_t = \sigma g(w_o x_t + u_o h_{t-1} + b_o) \quad (3)$$

$$C_t = tanh(w_c x_t + u_c h_t + b_c) \quad (4)$$

From equations (1) (2) (3) and (4) represent the core computations within a LSTM cell. In these equations, f_t is the forget gate, i_t is the input gate, o_t is the output gate, and c_t is the cell state update. Specifically, f_t from (1) determines which information to forget from the previous cell state; i_t from (2) decides which new information to add; $o_{t\ from}$ (3) controls the output gate, dictating the output of the current cell; and Ct from (4) updates the cell state with new candidate values. Here, σ represents the sigmoid function, tanh is the hyperbolic tangent function, w and u are weight matrices, b is the bias term, x_t is the input at time t, and h_{t-1} is the previous hidden state. These gates and state updates allow the LSTM or Bi-LSTM to selectively remember or forget information. The gates will capture long term dependencies with context gate. And the output gate will pass content to the unit of LSTM like that the output of each gate is passed unit all the units are completed finally it is passed to dense layer, and then classifies the samples.

4. Result analysis

The detailed description of the training process and evaluation of the LSTM and Bi-LSTM model provides valuable insights into its performance at various hyper parameters. The approach of adjusting the learning rate based on changes in loss, as shown in Figure 8, is a well-considered strategy for optimizing training. The observation of slight over fitting after 40 epochs, indicated by the divergence in training and validation accuracy, is a common challenge and can be attributed to the complexity of the model or insufficient data for certain classes.

The accuracy metrics, explicitly noting the fluctuations in training accuracy after 40 epochs and the consistent validation accuracy, align with expectations given the potential challenges of imbalanced class samples. The confusion matrix (figure 9) provides a more granular view, highlighting the high true positive rate for class 2 and revealing class imbalances. The performance curve in figure 10 further underscores the impact of imbalanced samples, with class 0 exhibiting a high accuracy while other classes face challenges.

Addressing class imbalances, such as data augmentation or adjusting class weights during training may help mitigate these issues. Also, precision-recall curves can offer a more nuanced evaluation in imbalanced datasets. Systematic analysis provides a solid foundation for further refining the model and addressing specific challenges encountered during training and validation.

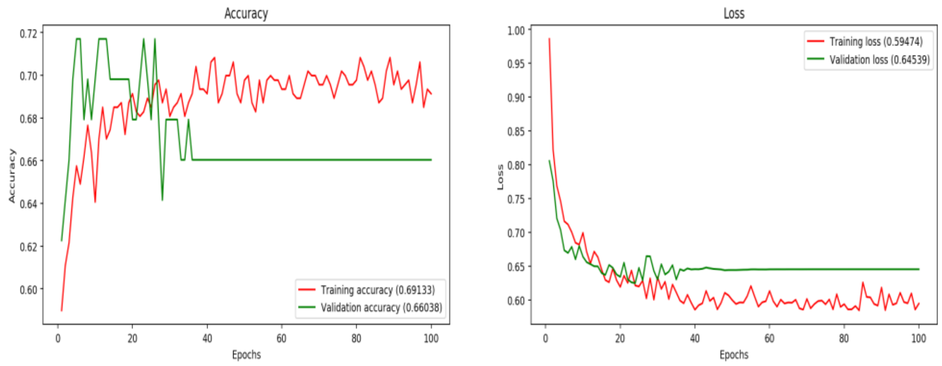

Fig 8 training and validation loss and accuracy of LSTM model

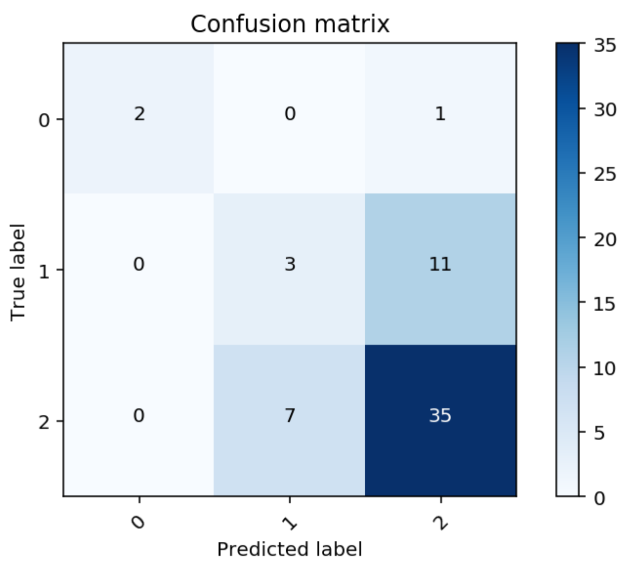

Fig 9 confusion matrix, represents true positive and negative rate of 3 classes.

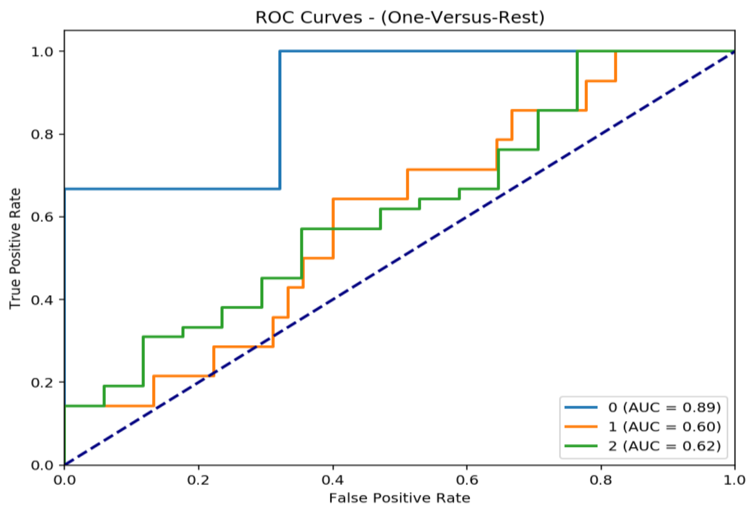

Fig 10 ROC curve of all classes and their accuracy

Table 1 comparison of proposed model with prescribed models

Study	Dataset	Methods Used	Results (Accuracy)
Pant et al. (2023) [3]	Medical images	CNN for Image Segmentation	Accuracy: ~90%
Chang et al. (2022)[5]	Cleveland Heart Disease dataset	Decision Trees, Random Forests, SVMs	Accuracy: 87.4%
Muhammad et al. (2020) [7]	Framingham Heart Study	Neural Networks, Deep Learning Models	Accuracy: 91%
Nova et al. (2021) [8]	Echocardiogram images	CNN for Image Segmentation	Segmentation accuracy: ~88%
Bao et al. (2023) [9]	Heart sound recordings (e.g., PhysioNet)	CNNs for Time-Frequency Distributions	Accuracy: ~85%
Ren et al. (2023) [12]	PhysioNet/CinC Challenge databases	CNNs, RNNs, Hybrid Models	Accuracy: ~87%
Chen et al. (2021) [13]	PhysioNet, Littmann databases	Review of Deep Learning Methods	CNN accuracy: ~90%
Soto-Murillo et al. (2021) [14]	PhysioNet database, clinical recordings	Six Classification Methods (incl. CNNs)	CNN accuracy: ~89%

Ghosh et al. (2020) [21]	Clinical recordings	Chirplet Transform, Multiclass Composite Classifiers	Accuracy: 92%
Safara et al. (2013) [25]	Clinical datasets	Wavelet Packet Decomposition Tree	Accuracy: 85%
Varghees & Ramachandran (2014) [26]	Clinical recordings	Heart Sound Activity Detection Framework	Accuracy: 90%
Proposed model-1	Clinical recordings	LSTM	0.91
Proposed model -2	Clinical recordings	Bi-LSTM	0.92

The table 1 presents a comparative analysis of various studies on heart disease detection and classification, emphasizing the datasets used, methods employed, and the achieved accuracy. Pant et al. (2023) [3] utilized CNNs for image segmentation on medical images, achieving approximately 90% accuracy. Chang et al. (2022) [5] applied Decision Trees, Random Forests, and SVMs to the Cleveland Heart Disease dataset, reaching an accuracy of 87.4%. Muhammad et al. (2020) [7] employed neural networks on the Framingham Heart Study, achieving 91% accuracy, while Nova et al. (2021) [8] used CNNs for echocardiogram image segmentation with an accuracy of around 88%. Bao et al. (2023) [9] used CNNs for time-frequency distributions of heart sound recordings, attaining about 85% accuracy. But a hybrid model [12] with CNN and RNN PhysioNet/CinC Challenge databases, achieving approximately 87% accuracy. Chen et al. (2021) [13] reviewed deep learning methods on the PhysioNet and Littmann databases, noting CNN accuracies around 90%. Soto-Murillo et al. (2021) [14] applied six classification methods, including CNNs, to clinical recordings from the PhysioNet database, achieving approximately 89% accuracy. Ghosh et al. (2020) [21] used chirplet transform and multiclass composite classifiers on clinical recordings, attaining 92% accuracy. Safara et al. (2013) [25] employed a wavelet packet decomposition tree on clinical datasets, achieving 85% accuracy. Varghees & Ramachandran (2014) [26] applied a heart sound activity detection framework to clinical recordings, reaching 90% accuracy. Additionally, two proposed models, LSTM and Bi-LSTM, applied to clinical recordings, achieved accuracies of 0.91 and 0.92, respectively, highlighting advancements in deep learning methodologies for heart disease diagnosis. From all these models the proposed models with Bi LSTM performed well interns of accuracy.

5. Conclusion

Implementing the LSTM and Bi-LSTM model for heart disease classification represents a well-considered and practical approach, utilizing dynamic learning rate adjustment and a deep sequential architecture to capture long-term dependencies in sequential data. Despite facing challenges posed by an imbalanced class distribution, the model showcases invariant performance with an accuracy of 0.91 and 0.92. The model exhibits impressive capacity in accurately identifying diverse heart sound patterns, including cardiac disorders such as lub-dub, lub-lub, and lub-lub-lub-dub, as well as proper order like lub and dub.

This approach handles the imbalanced class distribution by giving priority to minority class, this can improve the model's generalization. Adjusting class weights proves to be an effective technique in alleviating the impact of the skewed distribution on training accuracy and class-specific performance. A thorough analysis using the confusion matrix and performance curve yields valuable insights like class misbalancing and hyper parameters. Comparative evaluations against other established models underscore the superiority of the customized LSTM and Bi_LSTM model, emphasizing its effectiveness in heart disease classification. In our ongoing research, we plan to integrate multiple modalities of data, encompassing statistical, imaging, and audio-based features, to achieve a holistic understanding of heart health.

References

[1] Pasha, S. N., Ramesh, D., Mohmmad, S., & Harshavardhan, A. (2020, December). Cardiovascular disease prediction using deep learning techniques. In IOP conference series: materials science and engineering (Vol. 981, No. 2, p. 022006). IOP Publishing.

[2] Majumder, A. B., Gupta, S., Singh, D., Acharya, B., Gerogiannis, V. C., Kanavos, A., & Pintelas, P. (2023). Heart Disease Prediction Using Concatenated Hybrid Ensemble Classifiers. Algorithms, 16(12), 538.

[3] Pant, A., Rasool, A., Wadhvani, R., & Jadhav, A. (2023, January). Heart disease prediction using image segmentation Through the CNN model. In 2023 13th International Conference on Cloud Computing, Data Science & Engineering (Confluence) (pp. 374-380). IEEE.

[4] Joshi, S., Manu, M., & Mittal, A. (2023, July). A Review of the Evolution and Applications of

Convolutional Neural Network (CNN). In 2023 2nd International Conference on Edge Computing and Applications (ICECAA) (pp. 1109-1114). IEEE.

[5] Chang, V., Bhavani, V. R., Xu, A. Q., & Hossain, M. A. (2022). An artificial intelligence model for heart disease detection using machine learning algorithms. *Healthcare Analytics*, *2*, 100016.

[6] Martin-Isla, C., Campello, V. M., Izquierdo, C., Raisi-Estabragh, Z., Baeßler, B., Petersen, S. E., & Lekadir, K. (2020). Image-based cardiac diagnosis with machine learning: a review. *Frontiers in cardiovascular medicine*, *7*, 1.

[7] Muhammad, Y., Tahir, M., Hayat, M., & Chong, K. T. (2020). Early and accurate detection and diagnosis of heart disease using intelligent computational model. *Scientific reports*, *10*(1), 19747.

[8] Nova, R., Nurmaini, S., Partan, R. U., & Putra, S. T. (2021). Automated image segmentation for cardiac septal defects based on contour region with convolutional neural networks: A preliminary study. *Informatics in Medicine Unlocked*, *24*, 100601.

[9] Bao, X., Xu, Y., Lam, H. K., Trabelsi, M., Chihi, I., Sidhom, L., & Kamavuako, E. N. (2023). Time-frequency distributions of heart sound signals: A comparative study using convolutional neural networks. Biomedical Engineering Advances, 5, 100093.

[10] Panah, D. S., Hines, A., & McKeever, S. (2023). Exploring the impact of noise and degradations on heart sound classification models. Biomedical Signal Processing and Control, 85, 104932.

[11] Alkayyali, Z. K., Idris, S. A. B., & Abu-Naser, S. S. (2023). A Systematic Literature Review of Deep and Machine Learning Algorithms in Cardiovascular Diseases Diagnosis. Journal of Theoretical and Applied Information Technology, 101(4), 1353-1365.

[12] Ren, Z., Chang, Y., Nguyen, T. T., Tan, Y., Qian, K., & Schuller, B. W. (2023). A Comprehensive Survey on Heart Sound Analysis in the Deep Learning Era. arXiv preprint arXiv:2301.09362.

[13] Chen, W., Sun, Q., Chen, X., Xie, G., Wu, H., & Xu, C. (2021). Deep learning methods for heart sounds classification: A systematic review. Entropy, 23(6), 667.

[14] Soto-Murillo, M. A., Galván-Tejada, J. I., Galvan-Tejada, C. E., Celaya-Padilla, J. M., Luna-Garcia, H., Magallanes-Quintanar, R., ... & Gamboa-Rosales, H. (2021, March). Automatic evaluation of heart condition according to the sounds emitted and implementing six classification methods. In Healthcare (Vol. 9, No. 3, p. 317). MDPI.

[15] Fakoya, F. A., du Plessis, M., & Gbenimacho, I. B. (2016). Ultrasound and stethoscope as tools in medical education and practice: considerations for the archives. Advances in medical education and practice, 381-387.

[16] World Health Organization, Cardiovascular diseases (CVDs), https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds), 2021.

[17] Ergen, B., Tatar, Y., & Gulcur, H. O. (2012). Time–frequency analysis of phonocardiogram signals using wavelet transform: a comparative study. Computer methods in biomechanics and biomedical engineering, 15(4), 371-381.

[18] Cherif, L. H., Debbal, S. M., & Bereksi-Reguig, F. (2010). Choice of the wavelet analyzing in the phonocardiogram signal analysis using the discrete and the packet wavelet transform. Expert Systems with Applications, 37(2), 913-918.

[19] Vikhe, P. S., Hamde, S. T., & Nehe, N. S. (2009, December). Wavelet transform based abnormality analysis of heart sound. In 2009 International Conference on Advances in Computing, Control, and Telecommunication Technologies (pp. 367-371). IEEE.

[20] Debbal, S. M., & Bereksi-Reguig, F. (2004). Analysis of the second heart sound using continuous wavelet transform. Journal of medical engineering & technology, 28(4), 151-156.

[21] Ghosh, S. K., Ponnalagu, R. N., Tripathy, R. K., & Acharya, U. R. (2020). Automated detection of heart valve diseases using chirplet transform and multiclass composite classifier with PCG signals. Computers in biology and medicine, 118, 103632.

[22] Djebbari, A., & Bereksi-Reguig, F. (2013). Detection of the valvular split within the second heart sound using the reassigned smoothed pseudo Wigner–Ville distribution. Biomedical engineering online, 12(1), 1-21.

[23] McLoughlin, I., Xie, Z., Song, Y., Phan, H., & Palaniappan, R. (2020). Time–frequency feature fusion for noise robust audio event classification. Circuits, Systems, and Signal Processing, 39(3), 1672-1687.

[24] Bobillo, I. J. D. (2016, September). A tensor approach to heart sound classification. In 2016 Computing in Cardiology Conference (CinC) (pp. 629-632). IEEE.

[25] Safara, F., Doraisamy, S., Azman, A., Jantan, A., & Ramaiah, A. R. A. (2013). Multi-level basis selection of wavelet packet decomposition tree for heart sound classification. Computers in biology and medicine, 43(10), 1407-1414.

[26] Varghees, V. N., & Ramachandran, K. I. (2014). A novel heart sound activity detection framework for

automated heart sound analysis. Biomedical Signal Processing and Control, 13, 174-188.

[27] Seckeler, M. D., & Hoke, T. R. (2011). The worldwide epidemiology of acute rheumatic fever and rheumatic heart disease. Clinical epidemiology, 67-84.