

# SEPSIS SEVERITY PREDICTION USING MACHINE LEARNING

Bhumika A<sup>1</sup>, Swathi P<sup>2</sup>, Mridula R<sup>3</sup>, Apoorva<sup>4</sup>, Latha D U<sup>5</sup>

<sup>1,2,3,4</sup>Students, Dept. of Computer Science and Engineering, Vidya Vikas Institute of Engineering and technology college, Mysore, Karnataka, India

<sup>5</sup>Professor, Dept. of Computer Science and Engineering, Vidya Vikas Institute of Engineering and technology college, Mysore, Karnataka, India

\*\*\*

**Abstract** - Sepsis still makes up one of the leading causes of death for patients in the ICU of hospitals. Early and accurate detection of the disease considerably increases the survival rate of the affected patients. Machine learning models offer automated techniques that provide continuous and fast identification of sepsis risk based on recorded vital signs. This study evaluates temporal models, most notably the bidirectional Long-Short Term Memory network, through their prediction performance on various sepsis indications such as positive blood cultures. The classifiers are assessed on the open database and a propriety database originating from the different Hospital's several approaches to sepsis risk estimation are considered, each offering unique characteristics. Their prediction performance and early detection capacity were found to provide distinctive complementary functionality.

**Key Words:** sepsis, Machine Learning, Blood culture, Support Vector Machine(SVM), Logistic Regression, Decision Trees, Temporal Model

## 1. INTRODUCTION

Sepsis is a potentially deadly medical condition that frequently occurs in patients of the Intensive Care Unit (ICU). The disease is one of the leading causes of morbidity and death in the ICU and its occurrence still rises yearly. Sepsis is caused by an excessive response of the body to an infection and can result in tissue damage, organ failure and death. Sepsis can be treated and full recoveries are possible. However, this requires the timely administration of medication. A patient's survival probability decreases by 7.6% for every hour treatment is postponed[1]. Therefore, efficient diagnosis of the disease is of life-saving importance. Blood culture tests identify the occurrence and type of bacteria or fungi in a patient's blood. Because of its association with sepsis, blood cultures are often ordered when suspicion of sepsis arises. However, blood cultures are imperfect indicators for sepsis as 40% to 60% of patients with sepsis exhibit a negative blood culture[2]. Gathering medical data is a prominent process in ICUs.

This collection of data allows the deployment of machine learning techniques. Machine learning models are capable of recognizing complex patterns within data and use those correlations for classification. Therefore, such techniques offer substantial potential for sepsis detection.

Considerable research has been performed that evaluates such models for sepsis prediction, yielding promising results. However, most studies applied models that ignore the temporal nature of the medical data. Temporal evolution within data can offer important information for the occurrence of sepsis. Moreover, exploiting the temporal correlations have been shown to improve the accuracy of classifiers [3]. This work will account for the temporal nature of the data by employing variations of Recurrent Neural Networks, a popular temporal modelling technique. Such networks have been shown to yield considerable potential for modelling sequential correlations [4]. This study will consider several types of sepsis risk assessments. Temporal models will be constructed for both blood culture detection and direct sepsis prediction. The differences between the acquired results will be analysed.

## 2. LITERATURE SURVEY

Sepsis is a potentially deadly medical condition that often occurs in patients of the Intensive Care Unit (ICU) [2]. It is caused by the response of the immune system to an infection. The disease mostly arises in patients with a weakened immune system. Sepsis can lead to septic shock which can induce organ failure, and can come up suddenly and quickly. This makes the disease still one of the leading causes of death in the ICU [3]. In the USA, more people die every year from sepsis than prostate cancer, breast cancer and AIDS combined [4]. Moreover, the amount of sepsis cases is still on the rise. Sepsis can be treated if it is detected in time. Some medical centers have been able to double the sepsis survival rate by identifying and treating the disease faster [5]. Doctors can diagnose the disease by checking the patients for the typical symptoms. These include fever, increased heart rate, and hyperventilation. Additionally, blood tests can be taken to inspect the number of white blood cells. These parameters define the so called Systemic Inflammatory Response Syndrome (SIRS) criteria, However, sepsis has many more variable manifestations that may be hard to notice. Sepsis is divided in three subcategories based on the severity of the disease [6]. Normal sepsis is defined by the fulfillment of the SIRS criteria and the occurrence of an infection.

Sepsis in combination with organ dysfunction is classed as severe sepsis. Finally, septic shock is the most serious form of sepsis, and is defined by sepsis with hypotension. Early diagnosis of sepsis leads to a timely start of the treatment, which could considerably increase the survival probability of

the patient. However, early detection of sepsis is often still a challenge and can require significant resources. Techniques that enable early detection while using safely collected measurements can thus be of life saving importance. Besides the loss of human lives, sepsis brings a significant economic cost. Sepsis has been classified as the most expensive condition treated in hospitals in the US. The costs were estimated at around 20 billion dollars in 2011 while still rising every year. Earlier sepsis detection and better treatment could save 92,000 lives per year and reduce hospital costs by 1.5 billion dollars [7].

## 2.1 Positive Blood Cultures

A blood culture test identifies the presence and type of bacteria and fungi in blood. This makes blood culture tests an important diagnostic tool for the detection of sepsis. Additionally, the specification of the type of bacteria allows for the administration of the most effective antibiotic [8]. A blood culture test is commonly performed in the ICU when indications of sepsis occur in a patient. The test involves taking a blood sample, which is investigated in a lab.

Despite its apparent association with sepsis, blood culture tests are not entirely accurate. A positive blood culture in association with the SIRS criteria precisely indicates sepsis. A negative blood culture test, however, does not completely exclude occurrence of sepsis. Only 40 to 60% of patients with severe sepsis test positive in a blood culture test [9]. The separate investigation of both positive blood culture detection and direct sepsis detection might thus yield diverse results and insights.

## 2.2 Relevant Research

Given its potential, automated sepsis detection is a thoroughly researched subject. Its specific detection with machine learning techniques has been investigated as well. However, the use of time series classification techniques for sepsis detection is a rather unexplored area. These techniques have yielded positive results for classification in other use cases with temporal data. Since the clinical data is of a sequential nature, these techniques could yield favorable results for sepsis and blood culture identification.

## 2.3 Sepsis Detection

A significant amount of research has been done on the employment of machine learning techniques for sepsis detection. The literature shows that usage of such models yields promising results, often exceeding the performance of techniques most commonly used in practice by experts. Furthermore, such classifiers enable fast continuous evaluation of sepsis risk at a low cost.

Ho et al. [10] evaluated different machine learning models for septic shock detection. Logistic regression, Support Vector Machines (SVM) and regression trees were tested as prediction models. The Multiparameter Intelligent Monitoring in Intensive Care (MIMIC)-II database was employed for training and evaluation. The paper further

explores data imputation methods to handle missing data in this dataset and their improvements on the overall prediction accuracy. The findings indicate that missing value imputation techniques did significantly improve the results. The choice of imputation method had relative small impact on the overall performance.

The trained prediction models gave promising results. The best model was achieved by Ho et al. [10] using an SVM in combination with Bayesian Principal Component Analysis (BPCA) imputation, accomplishing an AUC (Area Under the ROC Curve) of  $0.882 \pm 0.190$ .

Guillén et al. [11] apply similar machine learning models to achieve early sepsis prediction. The same MIMIC-II database was used in the research. Features were selected during a period of 24 hours to two hours before the occurrence of severe sepsis. Severe sepsis was defined as having a lactate concentration of at least 4 mmol/L within 24 hours of blood culture acquisition. Data outside this time window was not considered. The K-nearest neighbor technique was used for missing data imputation. The model evaluation concluded that the SVM model slightly outperformed logistic regression and logistic model trees. The SVM model, trained exclusively on a very limited amount of vital sign features (temperature, heart rate, blood pressure and respiratory rate), achieved an AUC of 0.840.

The TREWScore is introduced by Henry et al. [12]. TREWScore is a targeted real-time early warning score, given for septic shock. Septic shock is thus predicted based on this score. The model was trained on the widely used MIMIC-II database. TREWScore assigns a risk prediction of the patient getting septic shock during points in time. It employs two detection criteria based on thresholds. The patient is first identified when the predicted risk exceeds the detection threshold. The patient is later concluded as high risk if the prediction risk remains above the threshold during a predefined time period. This technique gained an AUC of  $0.83 \pm 0.2$ . Furthermore, it achieved a specificity of 0.67 and a sensitivity of 0.85, performing better than the standard screening protocols. A recent paper by Desautels et al. investigates sepsis prediction with machine learning techniques using the MIMIC-III database [13]. The research employs inSight, a sepsis prediction model. The model is trained on widely available patient data such as vital signs, Glasgow Coma Score (GCS), and peripheral capillary oxygen saturation (SpO<sub>2</sub>). Instead of using the available diagnosis of the MIMIC-III database, the study specifies sepsis using certain value thresholds. This definition entails a change in SOFA score of 2 points or higher following an infection. An infection was identified as the combination of an ordered culture lab test and an administration of a dose of antibiotics within a certain time window. Furthermore, not all records of the MIMIC-III database were considered. The medical data in the MIMIC-III dataset is collected by two different measurement systems. The research ministered all records from the least accurate charting system. Moreover, the data was additionally filtered based on the occurrence of all

required measurements and age requirements. The paper compares the performance of the InSight system to other techniques such as SOFA or SIRS diagnoses. It clearly outperformed those techniques, achieving an AUC score of 0.88 when detecting sepsis at the point of diagnosis. Additionally, the prediction power for detection 4 hours in advance reduced to an AUC of 0.75.

### 2.4 Temporal Sequence Classification Techniques

The available literature mostly discusses machine learning techniques that do not account for the sequential nature of the medical data, e.g. SVMs or logistic regression. Specific research on the usage of time series classification techniques for sepsis detection is mostly unavailable. However, the medical data is highly temporal. Accounting for the sequential nature of the data could thus improve the prediction accuracy.

Peer applied time series classification techniques for blood culture prediction [14]. Recurrent Neural Networks (RNN) and Long-Short Term Memory (LSTM) networks were researched and their performance was compared to Feed-Forward Neural Networks (FNN). The findings showed that incorporating the sequential nature of the data improved the predictive ability of the models significantly. The Bidirectional LSTM (BiLSTM) model with an added hidden layer accomplished a prediction accuracy with an AUC of 0.90. When predicting 10 hours before the diagnosis, an AUC of 0.8 was achieved. The AUC further decreased to 0.76 when predicting 24 hours before the blood test. The performance decline with respect to the time before diagnosis is visualized the models were trained with the Ghent University Hospital database, which will be used in this thesis as well.

Autoregressive Hidden Markov Models have been used for Neonatal Sepsis detection [15]. This allowed for real-time predictions and took the temporal aspect into account with promising results. Learning and inference of these models were extensively based on domain knowledge of neonatal sepsis

### 3. METHODOLOGY

Xianchuan wang et.al[20] used a total of 42 sepsis patients with the mean age of 42 are considered from emergency department or ICU of THE SECOND AFFILIATED HOSPITAL of Wenzhou medical university between January 2015 and January 2016.

The patients less than 18 years were excluded. The sample of measurement was fasting blood that was obtained after diagnosis of sepsis. There were 35 healthy controls that were randomly selected in the medical examination centre[16]-[19]

#### 3.1 GC-MS Analysis

Agilent technology 6890N-5975B GC-MS were conducted during analysis the ambient temperature of HP-5 MS column was 80°Celsius for 5 min. The oven temperature increased to

260°C for 10°C/min. Then the data gathered are exported to Microsoft Excel for analysis[20], [21]

#### 3.2 RF-CFOA-KELM

The flow chart of RF-CFOA-KELM represented in fig 1. It is composed of two stages. The first stage includes feature selection and commonly used assessment criteria including Matthews correlation coefficients (MCC), classification accuracy (ACC), sensitivity and specificity were used to evaluate the quality of experiments. ACC is easy to understand where number of samples is divided into the correct and is divided by the number of all samples. The classifier obtained is better when ACC was higher. The feature classification of data is characterized by the MCC. The sensitivity represents the proportion of all positive cases that are correctly classified, which measures the ability of the classifier towards the positive case. Specificity represents the proportion of all negative cases that are classified and it will identify the ability of classifiers towards the negative case.

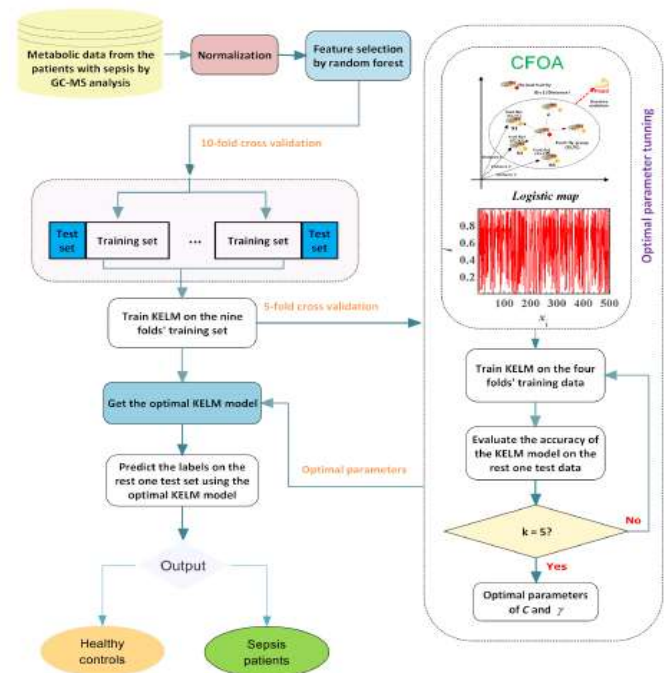


Fig 1. Flowchart of RF-CFOA-KELM.

### 4. CONCLUSION

Efficient techniques for the detection of sepsis remain an important research subject. Sepsis still causes an extensive amount of lost lives in the Intensive Care Units (ICU) of hospitals. It originates from the excessive response of the body to an infection and can lead to tissue damage, organ failure and even death. Despite its fatality, the disease can be treated. However, this requires a timely start of the medical treatment. Therefore, early prediction dramatically increases the probability of survival. Sepsis correlates with several symptoms, some of which are harder to notice than

others. Considering that sepsis mostly occurs in the ICU, some symptoms could be assumed to source from other health complications. Furthermore, a continuous evaluation of a patient's symptoms might be hard to achieve in a practical setting.

## REFERENCES

- [1] A. Kumar, D. Roberts, K. E. Wood, B. Light, J. E. Parrillo, S. Sharma, R. Suppes, D. Feinstein, S. Zano, L. Taiberg et al., "Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock," *Critical care medicine*, vol. 34, no. 6, pp. 1589–1596, 2006.
- [2] R. A. Balk, "Severe sepsis and septic shock: definitions, epidemiology, and clinical manifestations," *Critical care clinics*, vol. 16, no. 2, pp. 179–192, 2000.
- [3] M. Taecker, "Hospitalizations, costs, and outcomes of severe sepsis in the united states 2003 to 2007," *The Journal of Emergency Medicine*, vol. 43, no. 2, pp. 405–406, 2012.
- [4] K. A. Wood and D. C. Angus, "Pharmacoeconomic implications of new therapies in sepsis," *Pharmacoeconomics*, vol. 22, no. 14, pp. 895–906, 2004.
- [5] World Sepsis Day, "Fact sheet sepsis," <http://www.world-sepsis-day.org/>, [Online; accessed 26-March-2017].
- [6] F. B. Mayr, S. Yende, and D. C. Angus, "Epidemiology of severe sepsis," *Virulence*, vol. 5, no. 1, pp. 4–11, 2014.
- [7] A. F. Shorr, S. T. Micek, W. L. Jackson Jr, and M. H. Kollef, "Economic implications of an evidence-based sepsis protocol: can we improve outcomes and lower costs?" *Critical care medicine*, vol. 35, no. 5, pp. 1257–1262, 2007.
- [8] M. Previsdomini, M. Gini, B. Cerui, M. Dolina, and A. Perren, "Predictors of positive blood cultures in critically ill patients: a retrospective evaluation," *Croatian medical journal*, vol. 53, no. 1, pp. 30–39, 2012.
- [9] N. de Prost, K. Razazi, and C. Brun-Buisson, "Unrevealing culture-negative severe sepsis," *Critical Care*, vol. 17, no. 5, p. 1001, 2013.
- [10] J. C. Ho, C. H. Lee, and J. Ghosh, "Imputation-enhanced prediction of septic shock in icu patients," in *Proceedings of the ACM SIGKDD Workshop on Health Informatics*, 2012, pp. 21–27.
- [11] J. Guillén, J. Liu, M. Furr, T. Wang, S. Strong, C. C. Moore, A. Flower, and L. E. Barnes, "Predictive models for severe sepsis in adult icu patients," in *Systems and Information Engineering Design Symposium (SIEDS)*, 2015. IEEE, 2015, pp. 182–187.
- [12] K. E. Henry, D. N. Hager, P. J. Pronovost, and S. Saria, "A targeted real-time early warning score (TREWScore) for septic shock," *Science Translational Medicine*, vol. 7, no. 299, pp. 299ra122–299ra122, 2015.
- [13] T. Desautels, J. Calvert, J. Homan, M. Jay, Y. Kerem, L. Shieh, D. Shimabukuro, U. Cheipally, M. D. Feldman, C. Barton et al., "Prediction of sepsis in the intensive care unit with minimal electronic health record data: A machine learning approach," *JMIR medical informatics*, vol. 4, no. 3, 2016.
- [14] T. Peier, "Early detection of positive blood cultures using recurrent neural networks on time series data," Master's thesis, Universiteit Gent, 2016.
- [15] I. Stanculescu, C. K. Williams, and Y. Freer, "Autoregressive hidden Markov models for the early detection of neonatal sepsis," *IEEE journal of biomedical and health informatics*, vol. 18, no. 5, pp. 1560–1570, 2014.
- [16] Q. Wu et al., "Brain metabolic changes in rats after dextromethorphan," *Latin Amer. J. Pharmacy*, vol. 36, no. 9, pp. 1882–1886, 2017.
- [17] C. C. Wen et al., "Brain metabolomics in rats after administration of ketamine," *Biomed. Chromatogr.*, vol. 30, no. 1, pp. 81–84, 2016.
- [18] M. Zhang et al., "Serum metabolomics in rats models of ketamine abuse by gas chromatography–mass spectrometry," *J. Chromatogr. B*, vol. 1006, pp. 99–103, Dec. 2015.
- [19] C. C. Wen, M. L. Zhang, J. S. Ma, L. F. Hu, X. Q. Wang, and G. Y. Lin, "Urine metabolomics in rats after administration of ketamine," *Drug Des. Develop. Therapy*, vol. 9, pp. 717–722, Feb. 2015.
- [20] xianchuan wang, zhiyi wang, jie weng, congcong wen, huiling chen, and xianqin wang, "A New Effective Machine Learning Framework for Sepsis Diagnosis" vol. 6, pp. 48300 – 48310, Aug. 2018.
- [21] L. Yu, T. Liu, K. Liu, J. Jiang, and T. Wang, "A method for separation of overlapping absorption lines in intracavity gas detection," *Sens. Actuators B, Chem.*, vol. 228, pp. 10–15, Jun. 2016.