TOPICAL REVIEW

Ensemble of Autoencoders for Anomaly Detection in Biomedical Data: A Narrative Review

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ABSTRACT In the context of biomedical data, an anomaly could refer to a rare or new type of disease, an aberration from normal behavior, or an unexpected observation requiring immediate attention. The detection of anomalies in biomedical data has a direct impact on the health and safety of individuals. However, anomalous events are rare, diverse, and infrequent. Often, the collection of anomalous data may involve significant loss of human life and healthcare costs. Therefore, traditional supervised machine and deep learning algorithms may not be directly applicable to such problems. Biomedical data are often collected in the form of images, electronic health records, and time series. Typically, an autoencoder (AE) or its corresponding variant is trained on normal data, and an anomaly is identified as a significant deviation from these data based on reconstruction error or other metrics. An Ensemble of AEs (EoAEs) can serve as a robust approach for anomaly detection in biomedical data by combining diverse and accurate views of normal data. An EoAE can provide superior detection to a single encoder; however, its performance can depend on various factors, including the diversity of the created data, the accuracy of the individual AEs, and the combination of their outcomes. Herein, we perform a comprehensive narrative literature review on the use of EoAEs when using different types of biomedical data. Such an ensemble provides a promising approach for anomaly detection in biomedical data, offering the potential for performance improvement by leveraging the strengths of diverse AEs. However, several challenges remain, such as the need for data specification and determination of the optimal number of AEs in the ensemble. By addressing these challenges, researchers can enhance the effectiveness of EoAEs for anomaly detection in various types of biomedical data. Furthermore, through this review, we highlight the significance of evaluating and comparing the performance of an EoAE with that of single AEs by establishing agreed-upon evaluation metrics and investigating normalization techniques for anomaly scores. We conclude the review by presenting challenges and open questions in the field with for future research.

INDEX TERMS Artificial intelligence, autoencoders, ensemble learning, anomaly detection, healthcare.

I. INTRODUCTION

Anomaly detection is the process of identifying unusual or unexpected observations that vary significantly from normal observations [1]. In the medical field, anomaly detection is important because it can help identify rare diseases, potential aberrations, or unexpected behaviors that can directly affect an individual's health and safety. Detecting anomalies in a timely manner (in medical applications) is of paramount importance as it can save human lives and the enormous cost on the healthcare system [2]. Besides, anomaly detection could also highlight potential measurement errors or noisy information in collecting biomedical data, equipment failure, or other situations that could lead to false or missed diagnoses. Deploying proper anomaly detection systems in regular medical care can help identify deviant patterns and

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alert healthcare professionals for further investigation [3]. Normal data for healthy individuals is abundantly available and can be collected easily, whereas this is not the case with collecting anomalous data. Firstly, the scope and definition of 'anomaly' can vary across different medical conditions, and some of those observations may not have been observed yet. A major challenge to model anomalies is that they are rare, diverse, and infrequent [4]. Collecting insufficient data to train machine/deep learning models for anomalous class could lead to loss of human lives and cost in dollars [5]. Therefore, supervised classification approaches are ill-posed for these situations as they assume an almost equal distribution of data from each class. Supervised classifiers can only model samples from seen classes and cannot model unseen anomalies. Autoencoders are a type of artificial neural network trained in an unsupervised manner on raw or processed data and can learn complex relationships between the features in the data. The general principle of any autoencoder or its variant is that it can learn latent representation through an encoder and decoder architecture by reconstructing the input. During testing, any significant deviation in the reconstruction error can be construed as an anomalous behavior or event [6]. Autoencoders have the advantage of being able to handle various types of data [7], including numerical [8], text [9], image [10], videos [11], timeseries [12], besides the tabular data. Biomedical data comprises multiple modalities, such as imaging (e.g., X-Ray, CT) and time series (e.g., EEG, ECG), and text data [13].

A standard approach to detect anomalies in these types of problems is to train an autoencoder (AE) or its variants (including convolution, sequential and spatiotemporal) on abundantly available normal data and identify significant deviations as anomalies based on reconstruction error or other metrics. Some examples of anomaly detection using AE are abnormal blood test results [14], unusual heart rate patterns [15], or suspicious activity in medical records [16]. However, a single AE could be sensitive to the quality and preprocessing of the data and may not generalize well with noisy inputs.

Ensemble of AEs (EoAE) aims to combine various autoencoders to arrive at a final decision. The general principle of EoAE to detect anomalies is similar to a single AE; however, multiple models can be trained (separately or jointly), and their outcomes combined to arrive at a final decision. The multiple models could represent the multi-modality (e.g., speech and MRI) or multiple views of the same data (raw video and optical flow [17]) to train multiple autoencoders. However, the key challenges in obtaining better EoAE are the creation of diverse datasets presented to various AEs and the combination of the outcomes of individual AEs. EoAE often results in robust and accurate detection of anomalies in comparison to single AE [18]. It has been shown that EoAE can perform better than a single AE in various applications, including network security [19], fall detection [20], fault detection [21], and industrial inspection [22]. There is sparse literature on the

use and benefits of EoAE for various biomedical data. To fill this gap, we perform a comprehensive narrative literature to study the various EoAE approach applied to different types of biomedical data. This review provides valuable insights into the current state of EoAE for anomaly detection in biomedical data and offers guidance for future research directions to advance the field.

MOTIVATION

The increasing availability and diversity of biomedical data have paved the way for innovative approaches to detect anomalies within biomedical data. The early detection of these anomalies could be crucial for identifying rare diseases, potential health risks, or even system inefficiencies. However, the limited availability of anomalous data coupled with its variable definition and scope presents a challenge in modeling and detecting these anomalies. Autoencoders are artificial neural networks, that offer a promising solution to this problem by allowing unsupervised learning of the data and thereby detecting deviations or anomalies based on reconstruction error. Despite the advantages of single Autoencoders, they are sensitive to the quality and preprocessing of the data and may not generalize well with noisy inputs. With the potential to mitigate this issue, EoAE seeks to combine the outcomes of multiple autoencoders to produce a more accurate and robust result. However, the use and benefits of EoAE in the realm of biomedical data have been underexplored in the current literature. This review paper aims to fill this gap by conducting a comprehensive narrative literature review on the application of EoAE for various types of biomedical data.

The main contributions of the research are highlighted below;

- The review paper provides a detailed narrative review of the application of EoAE in detecting anomalies in biomedical data. The sparse literature in this area makes this paper a critical reference for scholars and practitioners in the field.
- We highlight the strengths and weaknesses of various EoAE approaches applied to different types of biomedical data. This assessment provides a deep understanding of the field's current state and informs the choice of the EoAE for a given application.
- We identify and discuss the key challenges in employing EoAE in detecting anomalies in biomedical data. This discussion will guide future research in addressing these challenges and improving the effectiveness of anomaly detection in medical applications.
- The paper ends with open questions in the field and provides pointers for future research directions, contributing to the advancement of the field of anomaly detection in biomedical data using EoAE. This will inspire new lines of inquiry and drive innovation in the field.

The rest of the paper is organized as follows as highlighted in FIGURE 1: Section II provides a background of
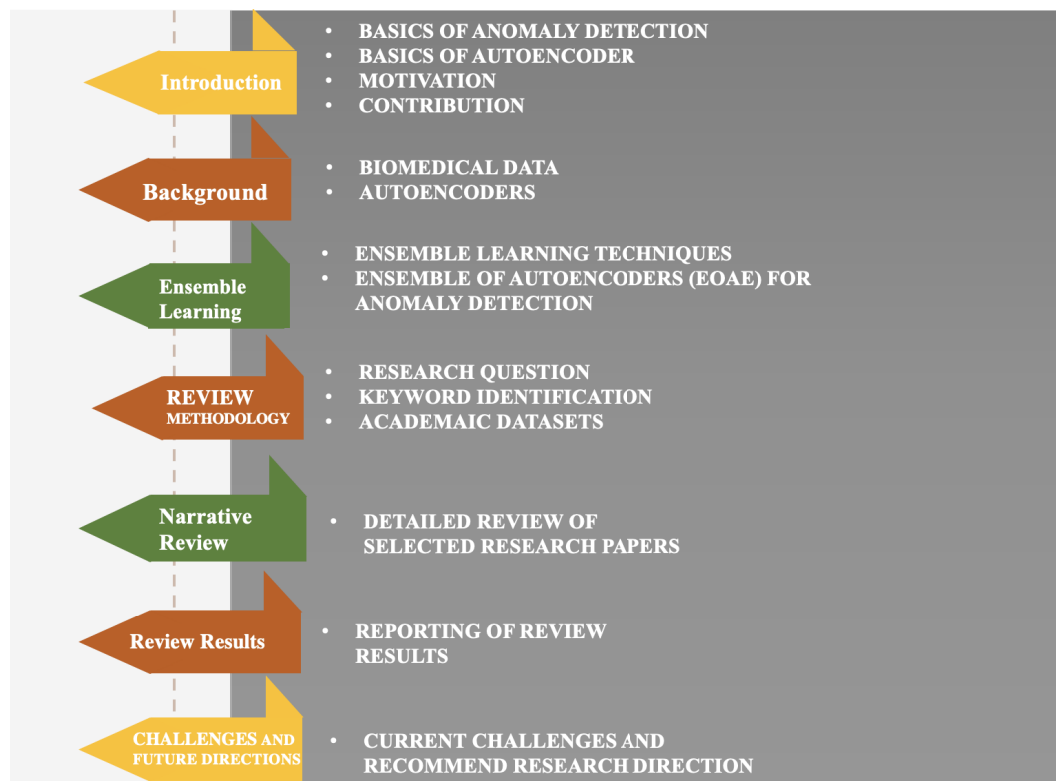
FIGURE 1. Organization of the paper.

biomedical data and autoencoders. The details of EoAE are presented in Section III. Section IV highlights the review methodology and compares this review with other reviews. The narrative review of relevant literature is presented in Section V. Section VI discusses the challenges in employing EoAE in detecting anomalies in biomedical data with open questions in the field and pointers to future direction. Finally, Section VII concludes the research paper.

II. BACKGROUND: BIOMEDICAL DATA AND AUTOENCODERS

This section briefly introduces different biomedical data types and autoencoders and their variants.

A. BIOMEDICAL DATA

biomedical data can be stored within patients' electronic health records or other locations. It can contain physiological data (e.g., blood pressure, electrocardiogram), clinical assessments (e.g., Mini-Mental State Score), clinicians' notes (in unstructured form), imaging data (e.g., X-ray), and others [23]. We briefly mention some of these common biomedical data modalities:

1) TABULAR DATA

Tabular data is organized in a table with rows and columns. The rows represent individual records, while the columns represent the attributes or features associated with each

record [24]. Tabular data can come from various sources, including databases, spreadsheets, and text files. Tabular data can be used to analyze and visualize biomedical data and build machine-learning models.

2) X-RAY

X-rays are a type of radiation that is used to produce images of the inside of the body [25]. X-ray medical images can be used to diagnose and treat various medical conditions [26], such as broken bones, pneumonia, cancer, and heart disease. In addition, advances in x-ray imaging technology have made it possible to create high-resolution x-ray medical images, which can be used to detect and diagnose even the small variations in abnormalities [27].

3) MAGNETIC RESONANCE IMAGING (MRI)

MRI is a medical imaging technique that uses a large magnet and radio waves to produce detailed images of the inside of the body [28]. MRI scans produce high-resolution images of the body's internal structures and can be used to diagnose various medical conditions [29], such as broken bones, cancer, heart disease, and more. MRI can also be used to monitor the progress of a treatment or surgery.

4) COMPUTED TOMOGRAPHY (CT)

CT is a medical imaging technique that uses special X-rays to produce detailed images of the inside of the body [30].

It is often used to diagnose diseases or injuries and to guide medical procedures. CT scans are used to diagnose and monitor a wide range of medical conditions [31], from broken bones to cancer. They can also be used to detect and diagnose minute abnormalities in the body, such as the detection of acute intracranial hemorrhage [32].

5) TIME SERIES

Time series medical data refers to data that is collected over time from patients or medical devices. This data type includes vital signs, lab results, and sensor data from wearable devices [20]. The data is used to track the progression of a patient's condition, monitor treatment efficacy, or identify potential health issues. A common example of time series data is Electrocardiogram (ECG) and Electroencephalogram (EEG). An ECG shows the electrical activity of the heart [33]. It is often used to diagnose heart problems or monitor the heart's health. An EEG is often used to diagnose problems with the brain (e.g. epileptic seizures [34]) or to monitor brain activity [35]. Another type of time series biomedical data is Functional magnetic resonance imaging (fMRI) [36] is a medical imaging technique that uses a magnetic resonance imaging (MRI) machine to measure changes in blood flow to different parts of the brain [37]. It is often used to study brain function and to diagnose brain disorders [38].

Different biomedical data modalities may lead to the discovery of the following (non-exhaustive) list of anomalies, including [39];

- Structural anomalies refer to physical abnormalities or deviations from the body's normal structure, such as birth defects, abnormal growths, or deformities.
- Functional anomalies refer to abnormal functioning of the body's systems, such as abnormal heart rhythms, abnormal blood pressure, or abnormal hormone levels.
- Pathological anomalies are the presence of abnormal cells or tissue in the body, such as cancer or infections.
- Diagnostic anomalies are the discrepancies or inconsistencies in diagnostic testing or imaging, such as false positive or false negative results.
- Behavioral anomalies are the anomalies related to abnormal behavior or changes in behavior, such as changes in appetite, sleep patterns, or mood.
- Cognitive anomalies refer to abnormal cognitive functioning, such as memory loss or impaired decision-making.
- Contextual anomaly is the type of anomaly where the data points are distinguished from whole datasets in terms of some pre-defined context [40]

B. AUTOENCODER

An AE is a neural network that takes an input, goes through bottleneck layers (encoder) represented by Z in FIGURE 2. and repeats the same layers in reverse order (decoder) to reconstruct the input. In the vanilla form, AE optimizes a mean squared error; however, other types of variants are also
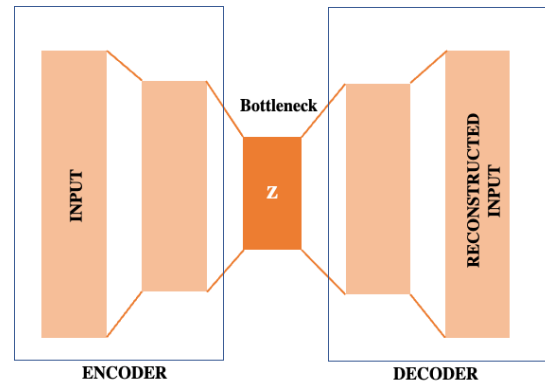

FIGURE 2. Architecture of autoencoder.

possible [41]. If the autoencoder can reconstruct the input with low reconstruction error, it shows that AE has generalized well on the seen data. If an unseen sample gives a high reconstruction error, it could be assumed to vary significantly from the seen samples and be considered anomalous. The ability of AEs to identify such out-of-the-distribution samples is the basis to use for anomaly detection. In these problems, especially in medical data, abundant samples from the normal class (e.g., healthy adults) are easily available, whereas the anomalies are either unknown or very few samples are available for them. If an AE generalizes well on the samples from the normal class, it can be used to identify anomalies [7]. The architecture of an autoencoder is shown in Figure 1. Depending upon the type of training, inputs, and methods, the following are common variants of AE.

1) SPARSE AUTOENCODER

Sparse autoencoder introduces information bottleneck without reducing the number of nodes/neurons. This is usually achieved by introducing a sparsity constraint on the activity of the hidden layer so that a few neurons would fire at a given time [42]. As compared to other neural networks where weights are regularized, in sparse autoencoders, activation layers are not regularized. This allows the network to activate individual hidden layer nodes to specific input data attributes [43]. Whereas a simple autoencoder would use the entire network for every observation, a small autoencoder would be compelled to selectively activate areas of the network based on the input data. Consequently, The network's ability to memorize input data can be limited, which helps to preserve its ability to extract relevant information from the data. The network's regularization and latent state representation can be evaluated and adjusted independently, providing the flexibility to select the optimal combination for a given task. There are different ways to introduce sparsity in the network: L-1 regularization and KL-Divergence [107].

2) DENOISING AUTOENCODER

Denoising autoencoder is the type of autoencoder in which random noise is added to the input of the encoder part

and makes it recover from noise-free data in the decoding part [44]. By doing so, the autoencoder not only maps the input to the output but also removes the random noise, which results in better learning of underlying features.

3) CONVOLUTIONAL AUTOENCODER (CAE)

The AE comprises feed-forward layers only. If the image is flattened, then it can lose its spatial information. CAE can take input as an image, combining convolutional layers and pooling to reduce the dimension (encoder) [45]. Then de-convolution and unspooling layers to increase the image size (decoder) to reconstruct the original input.

4) VARIATIONAL AUTOENCODER

A variational autoencoder learns the probability distribution of parameters instead of learning any deterministic mapping from the input data to the encoded representation [46]. This type of autoencoder tries to generate new data samples from the sample of distribution, which is why it is considered as a generative model. As compared to simple autoencoders where output is mapped to input through bottleneck/latent space, in this case, the actual bottleneck is replaced by the mean and standard deviation of encoder representation and takes sample latent space as a bottleneck.

5) RECURRENT AUTOENCODER

A simple AE, CAE, or VAE cannot be trained on sequential or time-series data, as it can only model tabular or spatial data. To model sequential data, recurrent layers are needed in the encoder and decoder. LSTM is one of the common types of recurrent neural networks that can be used as an AE [47], [48]. Recurrent or LSTM layers allow the model to process sequential data by maintaining a hidden state that is updated at each time step. This allows the model to capture temporal dependencies and patterns in the input data. Recurrent Autoencoders (RAEs) can be trained using a sequence-to-sequence approach. The encoder maps the input sequence to a fixed-length representation, and the decoder generates the output sequence from this representation. RAEs can also be trained using a sequence-to-latent approach. The encoder maps the input sequence to a variable-length representation, and the decoder generates the output sequence from this representation. This variable-length representation can be used for clustering and dimensionality reduction tasks. Additionally, the internal state of the RAE can be used to represent the context in a given input, which can be used to improve the performance of other models.

III. ENSEMBLE LEARNING

Ensemble learning is an approach in machine learning that aims to enhance decision-making results by combining multiple models, often referred to as base models, to create a superior predictive model [49]. As depicted in FIGURE 3. A panel of five neurologists (N1, N2, N3, N4, and N5) is formed to diagnose a critical brain tumor. N1, N3, and N5 classify the patient's MRI as suggestive of a tumor after
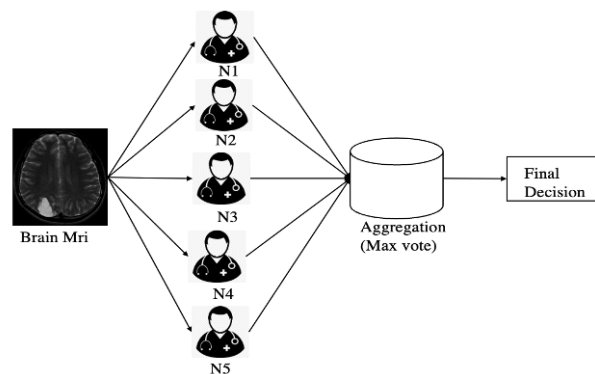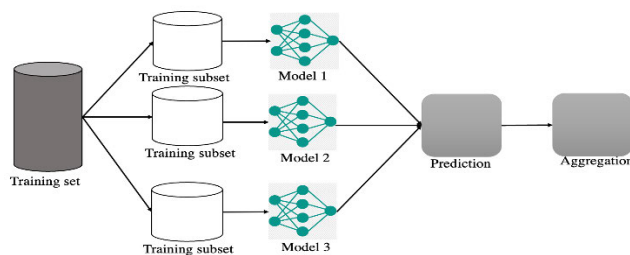

FIGURE 3. Ensemble learning.

FIGURE 4. Schematic overview of bagging.

evaluating it, while N2, N4, and N5 classify it as non-tumorous. Based on the principle of majority voting, the MRI would be considered non-tumorous in this scenario. Similarly, ensemble learning uses multiple models, each of which makes a prediction. Usually, majority voting or some other method of consolidation is used to reach a final decision.

A. ENSEMBLE LEARNING TECHNIQUES

Ensemble learning techniques on the basis of model can be classified into to broad categories i.e., sequential ensemble learning techniques and parallel ensemble learning techniques [50]. Sequential ensemble technique is a technique in which base models are trained in sequence and are dependent on each other. Conversely, Parallel ensemble learning is a technique where base model is trained parallel, and all base models are independent of each other. On the other hand, data-based ensemble approaches include late fusion, early fusion, and joint learning.

1) BAGGING

Bagging or Bootstrap aggregation is a technique in which several week base models are combined to form one strong predictive model [51]. Bagging technique is classified into two subtypes, Bootstrapping and Aggregation. In bootstrapping technique as shown in FIGURE 4, samples are extracted from whole datasets using the with replacement procedure which allow the random selection of samples and then several base models are trained on each sample. On the
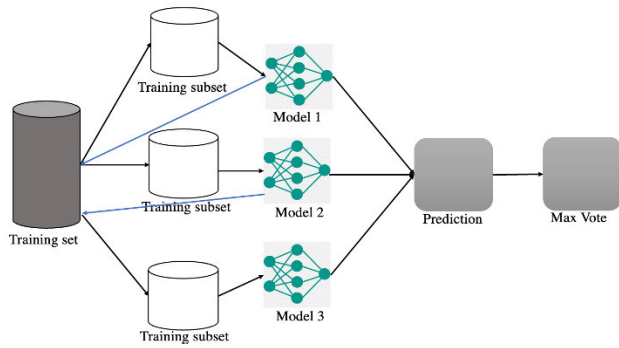
FIGURE 5. Schematic overview of boosting.

other, accurate decision is made in aggregation by taking the average or majority of the task depending on the task. In regression, an average is taken of all the outputs predicted by the individual classifiers; this is known as soft voting. While in hard voting or majority voting [52], the class with the highest majority of votes is accepted for classification problems.

2) BOOSTING

Boosting is an ensemble learning technique that makes the better prediction in a future by learning from previous predictor mistakes [53]. As compared to bagging, which is parallel ensemble technique, this technique is a sequential ensemble technique where several week base models are arranged in a sequence that learns from next base model in a sequence to create optimal predictive model. The general overview of boosting technique is presented in FIGURE 5.

3) STACKING

Stacking is a less commonly used type of parallel ensemble technique and known as a stacked generalization as shown in FIGURE 6. Unlike bagging and boosting, stacking can be used to combine multiple models of different types. In stacking, outputs of sub-models are taken as input and attempts to learn how to best combine the input predictions to make a better output prediction [54]. Stacking is an extended form of the Model Averaging Ensemble technique in which all sub-models equally contribute as per their performance weights and build a new model with better predictions.

4) EARLY FUSION

In early fusion, the input data is combined or preprocessed before being fed into the autoencoders [55]. This can involve feature concatenation or transformation, for example. The primary advantage of early fusion is that it enables the model to learn shared representations and cross-modal features, which can improve performance in tasks involving multiple data modalities or features [56]. However, early fusion may require careful preprocessing and feature engineering, and it may not always be the most effective approach when dealing with complex data structures.
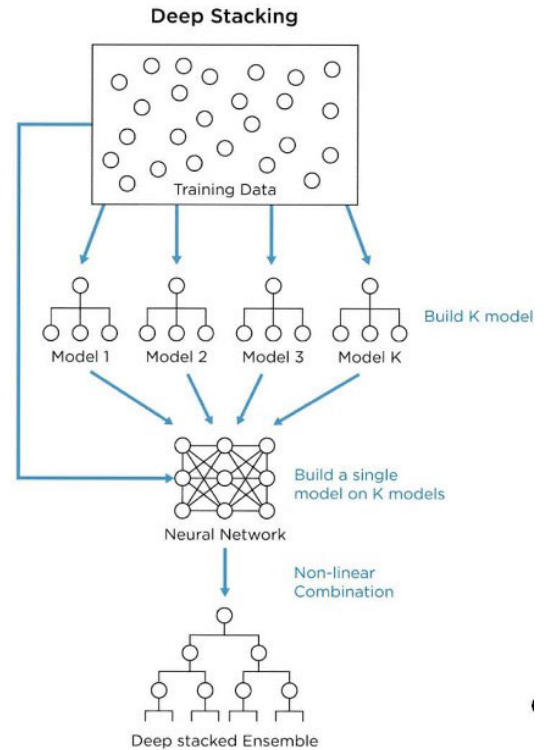

FIGURE 6. Schematic overview of stacking.

5) LATE FUSION

In this technique, autoencoders are trained independently on different parts or representations of the input data [57]. Their output is combined later, typically during the decision-making process. The primary advantage of late fusion is that it allows each autoencoder to learn specialized features from its respective input data [58]. It can be more flexible when dealing with heterogeneous data. However, late fusion may require more computational resources, as multiple autoencoders need to be trained and combined. Additionally, finding the optimal way to combine the outputs of multiple autoencoders can be challenging.

6) JOINT LEARNING

Autoencoders are trained together with shared or connected layers, allowing them to learn features jointly from the input data [59]. This approach can lead to more efficient representation learning, as the models can share knowledge and learn from each other. However, joint learning can be more complex and require more computational resources [60]. Additionally, it may be more sensitive to model hyperparameters, making it harder to find the optimal configuration.

B. ENSEMBLE OF AUTOENCODERS (EOAE) FOR ANOMALY DETECTION

EoAE is a technique that combines multiple autoencoder models to improve the overall performance of anomaly detection tasks [61].

Specifically, biomedical data is complex, with details ranging from patient information to images modalities like X-rays and involves human life. AE can simplify this complex data, making it easier to understand and analyze. When we use EoAEs, it is like having multiple detectives working on a case - they can spot things that one might miss. This is especially important in healthcare, where missing even a tiny detail can have big consequences. So, using a EoAEs helps to make sure nothing is overlooked. However, the ensemble approach works best for complex medical data and might not be as effective for simpler data.

The use of EoAEs for anomaly detection in biomedical data is extremely significant, specifically as it involves important decision-making processes that have a direct effect on human life [48]. Data in the field of biomedical can be complex, exhibiting minute patterns that could point to underlying diseases or newly discovered medical conditions and anomaly may be subjective [40]. EoAE can greatly improve anomaly detection's accuracy and robustness, which lowers the possibility of false positives and false negatives. Different models are able to capture different representations of the data, providing a more comprehensive and all-encompassing understanding. Leveraging ensemble techniques with autoencoders not only increases the reliability of diagnostic processes but also substantiates the trust that patients and healthcare professionals place in cutting-edge technological solutions in the delicate field of healthcare [62], where a mistake or misdiagnosis can have detrimental or even fatal outcomes.

IV. REVIEW METHODOLOGY

This section presents our review methodology for using EoAEs to detect anomalies in biomedical data as shown in FIGURE 7. The research question we address in this paper is "How effective are EoAE for detecting anomalies in biomedical datasets compared to single AE?". We identified relevant keywords to address this research question and ran the criteria on popular academic databases, such as IEEE, Springer, ScienceDirect, and Google Scholar. The search was conducted in February 2023. We took care to search and select most of the relevant papers; however, we did not perform the systematic or scoping review search methodology. Thus, the comprehensibility and reproducibility of the search results cannot be ascertained. Our search keywords contain the terms "ensemble autoencoder" (and its palindrome) and "anomaly detection" in combination with data types, i.e., "medical data," "medical image," "MRI," "X-Ray," "CT scan," "medical record," "electronic health record", "patient data", "medical dataset", "medical imaging", "healthcare data", and "time series medical data". These search keywords yielded 16 peer-reviewed papers from different data repositories.

There have been numerous review papers published on the topic of anomaly detection with deep learning approaches.

Pang et al. [4] reviewed the use of deep learning techniques for detecting anomalies in various data types. The review
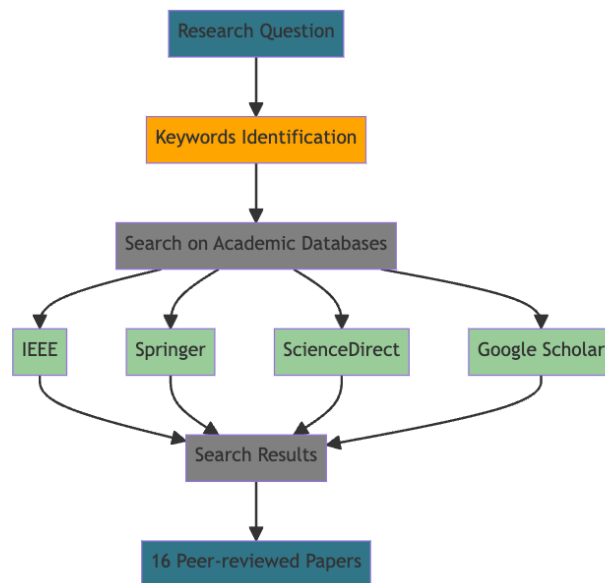

FIGURE 7. Review methodology.

defined anomalies and explained their importance in various applications, such as fraud detection and cybersecurity. It then reviewed different deep learning approaches that have been developed for anomaly detection, including supervised, unsupervised, and semi-supervised. Fernando et al. [63] specifically highlighted the use of deep learning techniques for detecting anomalies in biomedical data. The paper reviewed various approaches, including supervised, unsupervised, and semi-supervised, and provides examples of their successful application in different medical applications. While Fernandes et al. [64] discussed general anomaly detection in biomedical data using various data labeling settings, we are specifically investigating the application of EoAE for detecting anomalies in biomedical data.

V. NARRATIVE REVIEW

In this section, we present different types of EoAE approaches categorized by data type as follows:

A. TABULAR DATA

Anomaly detection in medical tabular data involves identifying datapoints significantly different from most other data points in the electronic health records dataset.

Chaurasia et al. [65] proposed an ensemble autoencoder model for detecting anomalies in electronic health records. Specifically, the proposed ensemble model was composed of customized autoencoders. To create diversity in the ensemble autoencoder, the authors used different initialization values and architectures for each autoencoder in the ensemble. The models were combined by taking the median of their normalized anomaly scores. The two medical datasets used in the experimentation are the Cardio and Ecoli datasets. The evaluation metric used in the experiment was accuracy. The accuracy of the proposed ensemble method was 90.7% and

87.4% on the Cardio and Ecoli datasets [66], respectively. Liu et al. [67] presented an ensemble autoencoder technique for anomaly detection in clinical data. They trained the same autoencoder on a different subset of the data and combined outlier scores by employing the mean function to decide whether a sample was normal or anomalous. Their methods were evaluated on different publicly available datasets, i.e., Cardio, arrhythmia, breast, mammography, thyroid, and antithyroid dataset. Their method achieved an AUC-ROC of 0.9, 0.8, 0.97, 0.84, 0.96, and 0.68 on Cardio, arrhythmia, breast, mammography, thyroid, and antithyroid, respectively.

B. X-RAY

Anomaly detection in X-ray images refers to the process of identifying unusual or abnormal features in the images that may indicate the presence of a disease such as pneumonia, tuberculosis, and cancer.

Paul et al. [68] proposed an ensemble of autoencoders to recognize various abnormalities in chest X-ray images, such as pneumonia, tuberculosis, and lung nodules. The models are trained on a small number of examples for each abnormality. Then the ensemble is trained to combine the outputs of the individual models to make a final prediction. The discriminative ensemble learning approach uses a distance metric to measure the similarity between the input image and the training examples for each abnormality. The proposed method was evaluated on publicly available chest X-ray datasets [69]. The evaluation metric used in the experimentation was F1-score which achieved 19 improved results than previous methods.

Paul et al. [70] proposed an ensemble of autoencoders to identify different diseases from chest X-rays. Using an autoencoder ensemble, the proposed architecture presented a transfer learning approach for disease identification from chest X-ray images. Diversity in the ensemble was created by training autoencoder models on different parts of the training data. The models were then combined to improve disease identification performance. The model outcomes were combined using a weighted voting scheme based on the performance of each individual model. The authors used two publicly available chest X-ray datasets for their experiments: the Montgomery and Shenzhen datasets [71]. Their method generated a recall, precision, and F1-score of 0.51, 0.43, and, 0.48, respectively. Similarly, for Montgomery, they achieved a recall, precision, and F1-score of 0.48, 0.39, and 0.42, respectively. While recall, precision, and F1-score of 0.48, 0.44, and 0.45 were achieved on Shenzhen datasets.

Addo et al. [72] performed an extensive experiment to diagnose Covid-19 from X-ray datasets using EoAE. The method performed the diagnosis in two steps by proposing three different variational autoencoder models. In the first step, various representations of variational autoencoders were applied to extract the chest X-ray's general characteristics. In the second step, model results were combined for the final diagnosis. The ensemble of models was combined by assigning weights/votes to the output of each autoencoder. Their method was evaluated on the Chest X-ray datasets [69], which are publicly available on Kaggle datasets. The evaluation metrics used in the experimentations were accuracy, precision, recall, and F1-score.

C. MRI

Anomaly detection in MRI can be useful for identifying a wide range of medical conditions, including brain tumors and strokes.

Chen et al. [73] proposed an EoAE approach for anomaly detection and localization of MRI. They trained various autoencoder models on the MRI dataset, each with different architecture, weight initialization, and training methods. The outputs of the individual models are combined to obtain a final detection. Different architectures for the autoencoder models, including feedforward neural networks with different numbers of hidden layers and nodes, were used to create diversity in the ensemble. The MRI data contained 253 images in total, 155 of which are of a normal brain and 98 of brain images with tumors. These regions of hemorrhage and tumors were considered anomalies that must be detected. The evaluation metrics used are the AUC-ROC. The results showed that the autoencoder ensemble approach outperformed the single autoencoder approach and achieved an AUC-ROC of 0.9581.

An EoAEs was employed by Zhang et al. [74] to extract the anomalous region in MRI and address the limitations of single autoencoder models. The diversity of the models in the ensemble is created by randomly initializing the weights and biases of each model. The autoencoder models were trained on a large dataset of normal brain MRI images and were then used to detect anomalies in new MRI images. The outputs of the individual models are combined by calculating the average reconstruction error of each image. If the reconstruction error of an image is higher than a pre-determined threshold, the image is considered to be anomalous. The proposed method is evaluated on an ADNI publicly available dataset of brain MRI images [75]. The results show their method's effectiveness in detecting anomalies in brain MRI images. The proposed autoencoder ensembles achieved an AUC-ROC of 0.96 and an accuracy of 0.93 on ADNI datasets.

D. CT SCAN

Anomaly detection in CT refers to identifying unusual or abnormal features in the images that may indicate the presence of medical conditions, such as lung cancer, pneumonia, and emphysema [76].

A dual-layer architecture to protect medical devices from anomalous instructions, focusing specifically on insulin pumps as a case study. The main goal of the architecture is to detect anomalous medical device instructions that could potentially harm patients Mahler et al. [77]. An ensemble of

recurrent autoencoders in the anomaly detection layer detects anomalies in the device's CT scan data. The authors trained multiple recurrent autoencoders on different subsets of the data, each with different initializations. Then the second layer utilizes a rule-based system to analyze the detected anomalies and filter out false alarms. The evaluation was performed on computed tomography (CT) using 8,277 CT instructions that they recorded privately. The maximum F1-score achieved on the proposed was 98.8%.

Almulhim et al. [78] presented a two-stage approach to identify anomalies in CT scans. At a pre-training stage, a convolutional neural network (CNN) was trained to learn a representation of the CT scan. Then, an ensemble of autoencoders is trained to identify anomalies in the latent representation. Finally, the ensemble is combined to form a final anomaly score, which can be used to classify a scan as normal or anomalous. They trained multiple autoencoder models with different architectures, the number of hidden layers, and different learning rates. Then, the outputs from these autoencoder models were combined to produce a final decision. The combination of the model outcomes was done using a majority voting approach, where the final decision was based on most of the outputs from the individual autoencoder models. The proposed approach is evaluated on two publicly available datasets, i.e., the non-small-cell lung cancer (NSCLC) data [79] and the Prostate Cancer Research International Active Surveillance (PRIAS) datasets [80]. The experimental results showed that the proposed method outperforms existing anomaly detection methods and achieved accuracy, precision, recall, an F1 score, and Matthews Correlation Coefficient (MCC) of 99.71%, 99.72%, 99.61%, 99.67%, 99.59% respectively.

E. ECG

Anomaly detection in ECGs refers to the process of identifying deviations from normal heart function, such as irregular heartbeat, a heart attack, or coronary artery disease [81].

An EoAE technique was presented by Campos et al. [82] for anomaly detection in different time series datasets. Diversity among the models in the ensemble was created by using different architectures and training methods for each model. The models in the ensemble were convolutional neural networks, which are trained on the same time series data but with different random initializations and hyperparameters. The outputs of the individual models in the ensemble were combined by taking a median of outlier scores. The datasets used in the experimentation were ECG readings for seven patients, represented as a 2-dimensional time series with 3,700 to 5,400 observations each. The evaluation metrics used in the experiments were precision, recall, f1-score, PR, and AUC-ROC and achieved values of 0.2522, 0.4924, 0.2521, 0.1887, and 0.5715, respectively.

Kieu et al. [83] proposed a deep learning-based anomaly detection system for ECG time series data using an ensemble of sparse autoencoders. The encoder part of the model is a recurrent neural network. In particular, two ensemble frameworks, the independent (IF) and the shared (SF), utilize multiple sparsely connected RNN autoencoders. The IF trained each autoencoder separately, while the SF, drawing on the concepts of multi-task learning, trained all autoencoders together by sharing a common feature space. The diversity in the ensemble was created by training multiple autoencoders with different architectures and hyperparameters. The autoencoder models were combined by taking the median function after arranging the outlier score in ascending order. The proposed approach was evaluated on two real-world time series repositories, the univariate time series repository Numenta Anomaly Benchmark (NAB) [84] and the multivariate time series repository ECG [85], and achieved an average AUC-ROC and AUC-PR of 0.97 and 0.777 respectively.

Kieu et al. [86] presented an EoAE approach to detect anomalies in ECG signals. They employ multiple variants of CAE for feature extraction and anomaly detection. Diversity was created by training multiple CAE models with different hyperparameters on ECG datasets containing 2-dimensional electrocardiogram time series collected from seven patients, each with 3,700 to 5,400 observations. The autoencoder models were combined by taking the median of the reconstruction errors for models. Experimental results on the ECG datasets demonstrate that the ensemble autoencoders approach outperforms the other approaches. The ensemble autoencoders achieved AUC-PR and AUC-ROC of 0.15 and 0.58, respectively.

F. EEG

Anomaly detection in EEG refers to identifying deviations from normal brain function in an EEG [87], such as epilepsy, a sleep disorder, or a brain tumor [88].

Ferariu and Mihalachi [89] presented an EoAE to detect seizures in EEG datasets. Diversity was created in the ensemble by training stacked autoencoder models on different subsets of the dataset. The authors then combine the outputs from each autoencoder model to produce a final anomaly score for each EEG signal. The datasets used in the experimentation include The Unit of Neurology and Neurophysiology at the University of Siena collected EEG recordings from 14 patients, totaling 30 GB of data [90]. This included recordings from 8 male patients with ages ranging from 25 to 71 and 6 female patients with ages ranging from 20 to 58. The maximum accuracy of the proposed method was 0.95.

Zheng et al. [91] proposed an EoAE approach for workload detection in EEG data. In their method, diversity was created in the ensemble by applying stacked denoising autoencoders on the EEG data of the different patients. The model outcomes were combined by taking average Q-statistics. The performance of their method was evaluated on private datasets collected in the laboratory of two cases. The evaluation metrics used in the experimentation were
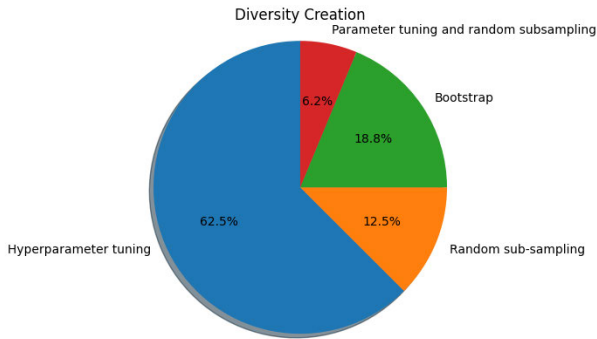
FIGURE 8. Percentage of methods used to create diversity in the reviewed EOAEs.

FIGURE 9. Percentage of combination methods used in the reviewed EoAEs.

accuracy. The highest accuracy of the CEM-AE obtained by 170 EEG features are 0.6353 and 0.6747 on case 1 and case2 respectively

G. FMRI

Anomaly detection in fMRI [92] refers to the process of identifying deviations from normal brain function in an fMRI scan that may indicate a brain disorder, such as epilepsy, a brain tumor, or a stroke [93].

Guanget al. [94] presented an EoAE framework for schizophrenia detection using resting state FMRI datasets. A total of five deep autoencoders were combined to form the ensemble. Specifically, different hyperparameters and random initializations in each autoencoder were employed to create diversity in the ensemble. The outcomes of the final anomaly score were calculated as the average of the scores of all the autoencoders. The proposed method was evaluated on two publicly available fMRI datasets: the OpenNeuro dataset [95] and the ABIDE dataset [96]. The evaluation metrics used in experimentation were the ROC-AUC, the accuracy, and the specificity. The authors performed a 10-fold cross-validation experiment to evaluate the performance of their proposed model. They reported a ROC-AUC score of 0.979, an accuracy of 0.967, and a specificity of 0.971.

Zafar Iqbal et al. [97] proposed an EoAE approach for anomaly detection in resting-state fMRI data. Diversity among the models was created by training each deep autoencoder on a different randomly selected subset of the training data. The autoencoder models were combined by taking the mean of the reconstruction error for each sample generated by each individual autoencoder. They compared their approach to existing anomaly detection methods for resting-state fMRI data. The dataset used for this research was the Human Connectome Project (HCP) dataset [98] consisting of resting-state fMRI scans from healthy adults. The evaluation metrics were root mean square error (RMSE), reconstruction loss, and mean absolute error (MAE). The autoencoder achieved an RMSE of 0.03, a reconstruction loss of 0.04, and an MAE of 0.009.
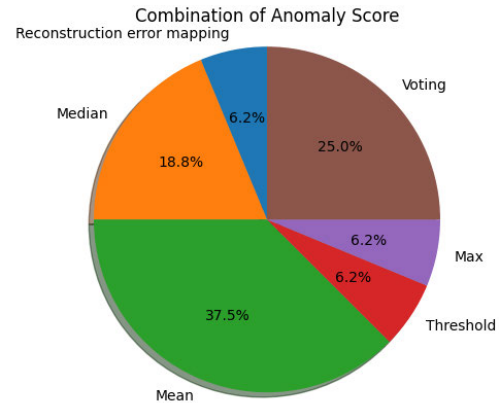
VI. REVIEW RESULTS

As shown in FIGURE 8 The largest sector of the chart, accounting for 62.5% of the total, corresponds to Hyperparameter tuning. This indicates that most of the techniques employed in the biomedical dataset focus on optimizing model parameters to improve performance. The second-largest sector, comprising 18.75% of the total, is dedicated to the Bootstrap technique. Random sub-sampling constitutes 12.5% of the pie chart, representing the third most common technique. Finally, the smallest sector, at 1/16 or 6.25% of the total, represents Parameter tuning and random subsampling.

The pie chart in FIGURE 9 displays the distribution of six different methods for combining anomaly scores in a biomedical dataset. The largest sector of the chart, representing 37.5% of the total, is dedicated to the Mean method. This suggests that, in most cases, the average of the anomaly scores is used to determine the final score and identify potential anomalies in the biomedical data. The second-largest sector, accounting for 25% of the total, is the Voting method. This approach involves combining the decisions of multiple algorithms or models to reach a final consensus, which can improve the overall performance and robustness of the anomaly detection system. At 18.75%, the Median method constitutes the third most common technique. The Max, Threshold-based, and Reconstruction error mapping methods each make up 6.25% of the pie chart, indicating that they are less frequently used for combining anomaly scores.

The bar chart in FIGURE 10 represents the usage frequency of six different types of autoencoders in EOAE. The most frequently used autoencoder is the Deep AE, with a count of seven. This indicates that Deep AE, which consists of multiple layers to learn complex representations, is the preferred method for solving EOAE-related tasks in different biomedical data. The second most common type is the Convolutional AE, with a count of 3. Convolutional AE leverages convolutional layers, which are particularly effective in handling image and grid-like data, to learn hierarchical features. Vanilla AE and Stacked AE both have a count of 2, making them moderately popular choices in the
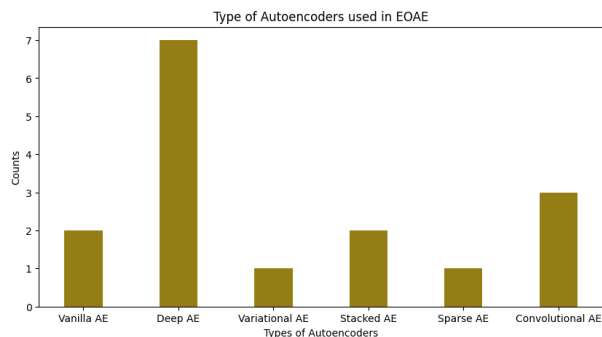
FIGURE 10. Number of AEs used in reviewed EOAE by AE type.

biomedical dataset. Variational AE and Sparse AE each have a count of 1, indicating that they are the least frequently used autoencoders in the biomedical dataset.

VII. CHALLENGES AND FUTURE DIRECTIONS

This section challenges, future direction, and recommendations based on the review.

A. DIVERSITY CREATION

Diversity creation in an autoencoder ensemble refers to the process of training multiple autoencoder models on different subsets of the data to create a diverse set of models that can make more accurate predictions [82]. Creating diversity in an autoencoder ensemble can improve the ensemble's performance by reducing the risk of overfitting, which occurs when a model is too closely fitted to the training data and performs poorly on new data [99], [100].

By training multiple autoencoder models on different subsets of the data, the ensemble can learn a more diverse set of features and be better able to generalize to new data. There are several approaches to creating diversity in an autoencoder ensemble [101]. One approach is to use different types of autoencoders with different architectures and better suited to different types of data. Another approach is to use different subsets of the data to train each autoencoder, such as random subsets or stratified subsets. Out of sixteen research papers, ten research papers create diversity in EoAE by performing hyperparameter tuning.

However, diversity can also be created by proposing different structures of autoencoders [102]. Different architectures, numbers of layers, activation functions, and regularization techniques can all contribute to the diversity of the ensemble. They can be used to automatically discover the optimal structure of autoencoders for a given dataset.

While creating diversity in an ensemble for anomaly detection, the practitioners' major problem is computational expensiveness, especially if the individual models in the ensemble are complex and require a lot of computational resources to train [103], such as autoencoder. This is because each autoencoder in the ensemble must be trained separately, which can be time-consuming and require a large

amount of data and computational resources. Numerous strategies can be used to reduce the computational expense of ensemble learning. One strategy is to use simpler models in the ensemble, which may be easier to train and require fewer resources. However, it could lead to underfitting. Another approach is to use parallelization techniques, such as distributing the training process across multiple GPUs or CPUs [104], to speed up the training process. It is also possible to use ensemble learning techniques that are more computationally efficient, such as bagging or boosting, which involve training multiple models on different subsets of the data or at different stages in the learning process.

Although ensemble methods may improve anomaly detection, [40] shows that they are not always able to capture all relevant anomalies. The study emphasizes the critical role that context and data representation play in active ensemble learning under minimal supervision. The integration of ensemble techniques and supervised context may redefine the standards for anomaly detection accuracy as future directions develop.

B. BETTER EXPERIMENTAL PRACTICES

It is observed that most of the cited research papers performed an EoAE without comparing it with simple autoencoders. Without a comparison, it is hard to determine whether the ensemble truly provides improved performance or adds complexity without any real benefit. Another issue is that it can be hard to justify the added computational cost of using an ensemble over a single autoencoder if the performance benefits are not clearly demonstrated. Additionally, not comparing the ensemble with a single autoencoder can make it hard to identify the specific factors that contribute to the improved performance of the ensemble, making it difficult to optimize the ensemble for specific data or problems.

Additionally, the reason behind an optimal number of autoencoders to use in EoAE is not well-defined in most of the research and can vary depending on several factors [105]. These factors include the size and complexity of the dataset, the level of outliers present in the data, and the availability of computational resources. While using more autoencoders in an ensemble can potentially improve anomaly detection accuracy, it also comes with a higher computational cost and longer training time [82]. Hence, finding the right balance between accuracy and efficiency is crucial when deciding on the number of autoencoders to use in an ensemble.

It is also observed that most of the trained EoAE models for anomaly detection are not publicly available or open source. It would be beneficial if more pre-trained EoAE models for anomaly detection were publicly available. This would enable researchers and developers to use these models as a starting point for their own work, which could save time and resources as well.

C. DATA SCALABILITY

As the biomedical datasets grow in size and complexity, the ability to scale becomes paramount for any machine learning

system [106]. Scalability does not merely involve handling more data but doing so efficiently without compromising on performance. In the context of EoAE, dividing the data among multiple autoencoders seems like a practical solution to handle vast datasets [107]. This division allows different autoencoders to specialize and learn fine features from various subsets of the data.

However, this approach has its challenges. For one, splitting data means that each autoencoder might work with a fraction of the information, potentially missing out on broader patterns. More critically, as data multiplies, the storage and computational demands surge [108]. Efficient storage solutions are essential, not just to house the data but also to ensure quick retrieval and processing. Training multiple autoencoders on vast datasets demands advanced computational infrastructure, often involving parallel processing, specialized hardware like GPUs, and distributed computing environments.

Furthermore, while the initial idea behind ensembles is to improve accuracy by leveraging multiple models, there is a risk of increased redundancy as data grows, leading to inefficiencies. Optimization techniques [109], both at the model and infrastructure level, are needed to ensure that as EoAE scales, it optimizes resources efficiently.

D. EXPLAINABILITY/INTERPRETATION

In the intricate world of medical diagnostics and treatment, the stakes for making accurate and timely decisions are exceptionally high. As machine learning models, specifically EoAE, find their place in aiding such decisions, the black-box nature of these models becomes a pressing concern [110]. Interpretability is not just about a model making a prediction. It is also about understanding the 'why' behind that prediction. For medical professionals, this 'why' is critical. A doctor is not just looking for a diagnosis; they need the reasoning behind it to make informed treatment choices and to communicate effectively with patients.

The EoAE complicates this further. While prediction of a singular model might be challenging to interpret, an ensemble, that combines the outputs of multiple autoencoders, introduces several layers of complexity. Each autoencoder in the ensemble might base its predictions on different facets of the data, making the collective decision-making process even more opaque [111].

However, the very strength of EoAE can also be leveraged for better interpretability. Techniques that highlight the contribution of each autoencoder, or even subsets of neurons within them, can shed light on which features or patterns were deemed most critical for a given prediction. Therefore, utilizing model agnostic tools like LIME or SHAP [112]. Integrate attention mechanisms within autoencoders to visually highlight significant features influencing predictions.

E. DATA PRIVACY AND SECURITY

The promise of EoAE to enhance diagnostic and predictive capabilities is appealing [113]. However, this progress comes with the weighty responsibility of securing sensitive patient data. Medical records are more than just numbers and data points. They are a collection of intimate details about an individual's health history, making them a valuable resource that, if mishandled, could lead to serious privacy violations.

The challenge of using biomedical data for better predictions while protecting individual privacy is a complex one. Traditional anonymization techniques may not be enough to protect privacy in the era of deep learning [114], where models can learn and reveal personal details even from anonymized data. This is where approaches like differential privacy [115] come into the limelight. By introducing a degree of randomness during model training, differential privacy ensures that the model's output cannot be traced back to any single data entry, effectively providing a protective cloak around individual data points. This method holds great potential for EoAE models, ensuring that while the ensemble learns from the collective wisdom of the data, the identity and specifics of individual patients remain shielded.

F. DOMAIN ADOPTATION

In biomedical data analysis, EoAE is a promising new technique that can improve anomaly detection by combining the strengths of multiple models. However, a critical challenge lies in the domain specificity of the data [116]. Just as a physician trained in one country may at first struggle with the details of healthcare procedures in another, EoAE models trained on data from a specific hospital or region may not perform as well when exposed to data from a different source.

The root of this challenge is the inherent variability in biomedical data. Differences can arise from numerous factors such as the demographics of the patient population, variations in equipment and techniques, or even divergent diagnostic conventions and practices [117]. These differences mean that a model optimized for one dataset may misinterpret or overlook variation in another, potentially compromising its diagnostic accuracy [118].

This underlines the vital importance of domain adaptation in the deployment of EoAE models. To ensure widespread applicability and maintain the trust of medical professionals, models must be designed to quickly adapt to new datasets without requiring exhaustive retraining [119]. Techniques like transfer learning, where models leverage knowledge from one domain to aid performance in another [120], or domain-adversarial training [121], where models are trained to be agnostic to domain-specific features, can be pivotal in this endeavor.

G. LIMITATION OF PRACTICAL APPLICATION

The computational intensity of EoAE models is one of the primary concerns. The requirement to train multiple autoencoders at the same time necessitates significant computational resources and processing time, which can be a limiting factor, particularly in time-critical medical situations. Furthermore, the efficacy of EoAE is heavily dependent

TABLE 1. EOAE algorithm for anomaly detection in different datasets.

Data Types	Ref No.	Anomaly Type	AE Type	Datasets	Diversity creation	Combination of Outlier score	Normalization function	Strength	Evaluation Metrics	Number of Autoencoders
Tabular Data	[65]	Behavioral anomaly	Vanilla Autoencoders	Cardio and Ecoli [66]	Hyperparameter tuning	Median function	Not mentioned	allows for the detection of anomalies with high accuracy	Accuracy	25
	[67]	Behavioral anomaly	Vanilla Autoencoders	Cardio, arrhythmia, breast, mammography, thyroid, and antithyroid [66]	Parameter tuning and random subsampling	Mean function	Not mentioned	Real-time detection of anomalies in addition to subtle anomalies detection	AUC-ROC	2
X-ray	[70]	Pathological anomaly	Deep Autoencoder	Chest X-ray [69]	Bootstrap	Voting	Not mentioned	Efficiently creating diversity in the model by self-organize the detection of anomalies	F1-score	20
	[68]	Pathological anomaly	Deep Autoencoders	Montgomery and Shenzhen datasets [71]	Bootstrap	Voting	Not mentioned	Fast method by training only the classifier on novel classes (anomaly classes)	Recall, precision, F1-score	20
	[72]	Pathological anomaly	Variational Autoencoders	Chest X-ray datasets publicly available on kaggle [69]	Hyperparameter tuning	Max function	Softmax function	Flexibility for diagnosis more diseases	accuracy, precision, recall and F1-score	2
MRI	[73]	Pathological anomaly	Deep Autoencoder	Private MRI datasets	Hyperparameter tuning	Mean function	Not mentioned	In addition to detection the proposed localize the anomaly precisely	F1-score	3
	[74]	Pathological anomaly	Deep Autoencoders	ADNI [75]	Hyperparameter tuning	Threshold based	Not mentioned	Efficiently Reduce latent space loss which is common in AE	AUC-ROC	3
CT Scan	[77]	Pathological anomaly	Deep Autoencoder	Private CT scan	Hyperparameter tuning	Reconstruction error mapping	Not mentioned	Easy to train and has faster convergence and higher accuracy	F1-score	5
	[78]	Pathological anomaly	Convolutional autoencoders	INCLCC, PRIAS [79]	Hyperparameter tuning	Voting	Not mentioned	Handle overfitting issue efficiently	Accuracy, precision, recall and F1-score	Not Mentioned
ECG	[82]	Functional anomaly	Convolutional Autoencoder	Private ECG datasets	Hyperparameter tuning	Median	Not mentioned	Unsupervised algorithm for efficient anomaly detection in ECG	Precision, Recall, F1-score, AUC-PR and AUC-ROC	20
	[83]	Pathological anomaly	Sparse autoencoders	NAB, and private multivaratie ECG datasets [84]	Hyperparameter tuning	Voting	Not mentioned	Complete framework for end-to-end anomaly detection in ECG	AUC-ROC and AUC-PR	10, 20, 30 and 40 for different experimentation
	[86]	Pathological anomaly	Convolutional autoencoders	Private ECG datasets	Hyperparameter tuning	Median Function	L2 norm	Efficient feature extraction for anomaly detection in ECG datasets	AUC-ROC and AUC-PR	2

TABLE 1. *(Continued.)* EOAE algorithm for anomaly detection in different datasets.

EEG	[89]	Functional anomaly	Stacked Autoencoder	Private datasets	Random sub-sampling	Mean	Not mentioned	Clearly addresses an imbalanced issue	Accuracy	29
	[91]	Cognitive anomaly	Stacked Autoencoder	Private datasets	Random sub-sampling	Mean function	Not mentioned	Improve model robustness when there is an imbalance between normal and abnormal data	Accuracy	14
FMRI	[94]	Cognitive anomaly	Deep Autoencoder	OpenNeuro dataset [95] and the ABIDE dataset [96]	Hyperparameter tuning	Mean	Not mentioned	accurately identify subjects with and without schizophrenia	AUC-ROC	8
	[97]	Functional anomaly	Deep autoencoder	Open-source HCP datasets [98]	Bootstrap	Mean function	Not mentioned	superior performance as compared to existing methods	RMSE	10

on the quality and quantity of available data. When medical data is scarce or unbalanced, the performance of these models can suffer significantly. Another challenge is integrating EoAE systems into existing medical data infrastructure, which necessitates alignment of these advanced models with the current technological ecosystem in healthcare settings. This integration necessitates not only technical compatibility but also adherence to medical data privacy and security regulations.

H. REVIEW METHODOLOGY AND ITS LIMITATION

The methodology chosen for the review is effective but it also has limitations. Our narrative review approach differs from systematic or scoping review methodologies in terms of both the scope of literature covered and the analytical depth we were able to achieve. The narrative style enabled a thorough investigation of ensemble of autoencoders in biomedical anomaly detection, delving into both theoretical concepts and practical applications. However, there are some disadvantages of the method. The narrative review approach have an impact on the reproducible of our findings and introduces the possibility of subjectivity in the selection and interpretation of literature. Therefore we propose that future studies incorporate systematic review methodologies. This would not only supplement the findings of our narrative review, but would also ensure a more methodologically diverse and balanced examination of the subject.

VIII. CONCLUSION

To conclude, this review highlights the effectiveness of using an EoAE for anomaly detection in biomedical data. In today's medical diagnostics and treatment, integrating technology with clinical procedures has shifted from being a trivial enhancement to an essential requirement. This paper delves into the profound capabilities and inherent challenges

posed by EoAE in the analysis of biomedical data. Ranging from the challenges of scalability to the crucial demand for interpretability, and from navigating data privacy concerns to ensuring domain relevance, the integration journey of EoAE in healthcare is detailed yet holds immense promise. The patient is the central focus of this discussion. They are the ones who provide the data for these models, and they are the ones who will benefit the most from their predictions. As we push the boundaries with advanced EoAE models, we must ensure that patient well-being, confidentiality, and trustworthiness are always prioritized. Our anticipated future endeavors, characterized by interdisciplinary partnerships and a focus on clarity and adaptability, chart a path to unlock the responsible potential of EoAE.

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