

SALIVA-BASED EARLY GASTRIC CANCER CLASSIFICATION USING DEEP SPARSE AUTOENCODERS

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Abstract

Gastric cancer (GC) continues to represent a significant global health challenge, being one of the primary contributors to cancer-associated mortality. Its poor prognosis is largely attributed to the absence of clear early-stage symptoms and the shortage of reliable biomarkers. Consequently, there is a critical demand for rapid, accurate, and non-invasive diagnostic methods that can support early detection, prognosis, and clinical decision-making. Saliva has recently emerged as a valuable biofluid due to its non-invasive collection and diverse molecular composition. In this work, we introduce a deep learning framework designed to classify individuals into three categories: patients with early gastric cancer (EGC), those with advanced gastric cancer (AGC), and healthy controls. Our dataset consists of 300 saliva samples, including 90 from EGC patients, 100 from AGC patients, and 110 from healthy volunteers. The findings demonstrate that the proposed approach effectively differentiates EGC and AGC cases from healthy individuals, highlighting its strong potential for clinical translation. The FC-DSAE + SMC neural network achieved outstanding performance, yielding an accuracy of 99%, selectivity of 98.9%, sensitivity of 100%, specificity of 99.57%, detection rate of 99.76%, and an Fmeasure of 99.5% for the EGC category.

INTRODUCTION

Gastric cancer (GC) is considered a highly aggressive malignancy, ranking as the fourth most prevalent cancer worldwide and the second leading contributor to cancer-related mortality. Its early-stage detection remains particularly challenging [1–3]. GC is closely associated with genetic, lifestyles, and the environment [4]. According to the

previous studies, northeast Asia has the highest incidents of GC. China has been severely affected by GC, where the number of GC cases accounts for 42% of the worldwide cases [5]. Generally, GC is divided into two stages, which are the early gastric cancer stage (EGC) and the advanced gastric cancer stage (AGC). The survival rate is closely

related to cancer stages [6]. If the cancer is diagnosed in the early stages, the mortality rate can be reduced to a great extent. The five-year survival rate is nearly 83% for EGC patients, whereas it is as low as 24% for AGC patients [7]. Only Japan has a reasonable survival rate for EGC patients which is more than 90%, this can achieve through early screening of cancer [8]. Therefore, achieving an early prognosis is crucial for enhancing patient survival rates. Although several new clinical techniques for cancer screening have been introduced in recent years [9–14], there remains a pressing need for approaches that can identify early gastric cancer (EGC) cases through methods that are non-invasive, user-friendly, rapid, and potentially suitable for self-testing at home. Saliva is a complex mixture that not only contains proteins, but also VOCs, DNA, RNA, fatty acids, and microorganisms, including important biomarkers associated with diseases, can reflect real-time human health status. Saliva diagnosis is a noninvasive, simple, fast, safe, and home self-diagnosis method that owns clinical translational prospect [15]. In our earlier study, specific amino acid biomarkers identified in human saliva were utilized to differentiate gastric cancer patients from healthy individuals [16]. Statistical evaluation was conducted using the Mann-Whitney U test to compare metabolic variations between the two groups, and a diagnostic model was subsequently developed through logistic regression. This approach demonstrated promising performance, yielding a specificity of 87.7% and a sensitivity of 80% [16]. Nevertheless, improving both sensitivity and specificity for gastric cancer detection remains a significant challenge. To address this limitation, we explored the application of deep learning methods to establish a model capable of accurately and efficiently classifying GC patients. For biomarker detection, we employed a Surface-Enhanced Raman Scattering (SERS) sensor [17–18]. However, Raman signal analysis is often complicated by spectral noise, including interference from background fluorescence, sample contaminants, and cosmic rays, which can distort the baseline [19–20]. Therefore, appropriate preprocessing techniques are required to mitigate these issues. Artificial intelligence (AI) has

increasingly been integrated into the field of medical diagnostics, with machine learning (ML) approaches reported to enhance cancer detection accuracy by approximately 15–20% [21]. The remarkable progress in this area is largely attributed to the development of deep neural networks (DNNs) [22]. DNNs consist of multiple layers of interconnected neural units and include models including architectures such as multilayer perceptrons (MLPs), convolutional neural networks (CNNs), restricted Boltzmann machines (RBMs), and autoencoders (AEs). MLPs are typically employed for classification tasks [23], while CNNs, inspired by the structure of the human visual cortex, are primarily used in image recognition [24]. RBMs, on the other hand, are probabilistic models designed to capture the distribution of input data [25]. Autoencoders, which exist in various forms, are widely applied to generate compact representations of data [26]. Their applications span a broad range, including latent feature extraction from text, image quality enhancement, dimensionality reduction, tomographic reconstruction in positron emission tomography, and hash function-based data mining [27–31].

In recent years, computational approaches have been increasingly employed to support pathologists in the interpretation of microscopic images [32–33]. Deep neural networks, in particular, have exhibited outstanding performance in the domains of pattern recognition and computer vision, achieving cutting-edge accuracy in image classification and recognition [34]. For example, Oikawa et al. [35] developed a multistage gastric cancer detection system using pathological images, which achieved a false-positive rate of 14.1%. Similarly, Xu et al. [36] applied convolutional neural network (CNN)-based segmentation and classification to histopathological images by separating them into epithelial and stromal regions, where CNNs were used to identify specific image patches. Wang et al. [37] proposed a CNN-based method for breast cancer detection that followed a comparable patch-based approach. Li et al. [38] also designed a patch-based deep learning framework for gastric cancer diagnosis, incorporating both shallow and deep networks for

classification. Beyond image-based studies, Daniel et al. [39] introduced a technique that classified gastric cancer using breath analysis, employing single- and multi-layer networks with the Resilient algorithm to achieve 92.54% accuracy. In another direction, Guyon et al. [40] presented a gene-selection-based approach for cancer detection, applying support vector machines with recursive feature elimination (RFE) and reporting an accuracy of 86% using the baseline model. More recently, Aslam et al. [41] give an idea of deep learning framework that utilized breath samples to distinguish early gastric cancer from advanced gastric cancer, and healthy individuals, achieving an overall accuracy of 97.3%.

In this work, to extract communal features from the Raman based salivary samples, we propose here a deep neural network comprises of Deep Sparse Autoencoder (DSAE) and SoftMax Classifier (SMC). DSAE constructed a Deep Neural Network (DNN), which was used as a classifier to discriminate between cancer-diagnosed patients and healthy subjects. In the proposed deep neural network, DSAE reconstructed the input by learning hierarchal features from the unlabeled

Raman data. Once the deep sparse autoencoder has learned the features, a layer of these autoencoders is connected to an additional classifier. In this way, a cascaded deep neural network was formed. Lastly, we used this trained deep neural network as a classifier to predict the class labels of the input data. The proposed system for gastric cancer classification yields an accuracy of 99%. Moreover, the proposed FC-DSAE+SMC based neural network has distinguished 98%, 98.9% and 100% AGC, EGC and Healthy person respectively.

2. MATERIALS AND METHODS

Deep Sparse Autoencoder (DSAE): Machine learning (ML) techniques are broadly categorized into supervised and unsupervised approaches. Autoencoders fall under the unsupervised learning paradigm, as they are designed to capture correlations within high-dimensional input data to generate more effective feature representations. An autoencoder is an asymmetric, multilayer feed-forward neural network trained through backpropagation to reproduce its input at the output layer. As illustrated in Figure 1,

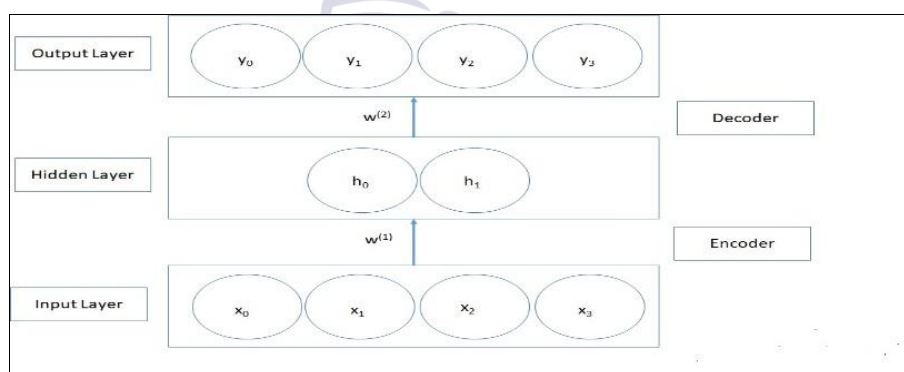


Figure 1. Basic structure of an autoencoder showing the encoder, hidden layer (h), and decoder, where input (x) is reconstructed as output (y) with weights $w(1)$ and $w(2)$.

a basic autoencoder consists of input, hidden, and output, with neurons connected via synapses. Its structure is typically divided into two main components— The encoder functions by mapping the input into a latent representation, whereas the decoder utilizes this representation to reproduce the initial data. In the figure, x denotes the input, h the hidden layer representation, and y the reconstructed output. Extending this concept, by

stacking successive sparse autoencoders, a deep autoencoder is obtained, where the output of each preceding layer is utilized as the input for the succeeding one. In this study, a fully connected deep sparse autoencoder (FC-DSAE) was developed to classify gastric cancer using salivary Raman spectra. The overall framework for feature-communal learning based on FC-DSAE combined

with a SoftMax Classifier (SMC) is depicted in

Figure 2

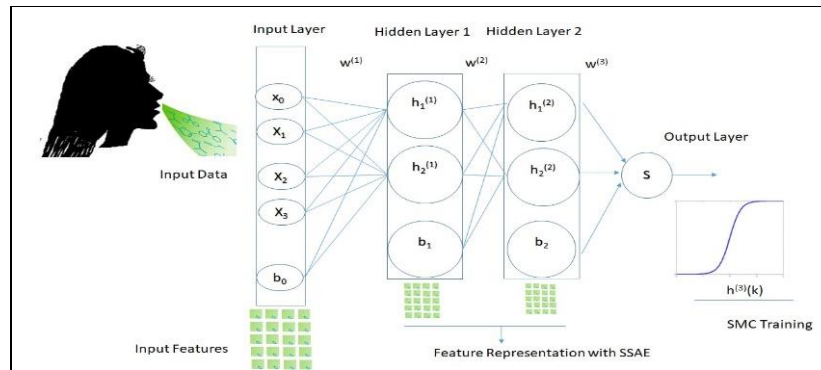


Figure2. Gastric cancer classification using FC-DSAE + SMC neural network from saliva samples

SoftMax Classifier (SMC):

The SoftMax classifier belongs to the supervised learning algorithm, which is represented as the following equation.

$$f_W = 1/(1 + \exp(-xW^T))$$

Where $f(.)$ is the sigmoid function, SMC is used to classify the data of multiple classes. SMC is the advanced and generalized version of logistic regression (42).

Clinical Sample Verification: In conducting this study, compliance with the Reporting

Recommendations for Tumor Marker Prognostic Studies guidelines was ensured. A total of 220 saliva samples were analyzed using Surface-Enhanced Raman Spectroscopy (SERS) technology. The dataset, obtained from Horiba Ltd., Shanghai, China, was categorized into three groups: patients with early gastric cancer (EGC), patients with advanced gastric cancer (AGC), and healthy individuals. For model development, the dataset was split into training and testing subsets, with 70% allocated for training and 30% reserved for evaluation. The detailed distribution of samples across the three groups is presented in Table I.

Table I. The clinical characteristics of volunteers

Group	Number of Volunteers	Age (Years)	Gender (M:F)
AGC	100	60 ± 9	61:39
EGC	90	53 ± 8.6	56:34
Healthy	110	35 ± 10	57:43

Feature Communal Learning based on Deep Sparse Autoencoder + SoftMax Classifier (FC-DSAE+SMC):

This model comprises of Feature Communal Learning based on Deep Sparse Autoencoder with SoftMax Classifier. The DSAE was initially assigned a set of hyper-parameters. These parameters include the network parameters, the weight of SMC, and the regularization term. For evaluation, the proposed model is tested on the validation dataset, and the classification outcomes are used to optimize the hyperparameters. The training framework is organized into three distinct steps

In the first step, SAE was employed to the Raman data of the saliva sample in training set X , to learn the basic representations of the $h(1)(x)$ on the data by updating all the weights $w(1)$.

These primary representations are then fed to the sparse autoencoder to find the secondary representation $h(2)$ by adjusting the weights $w(2)$.

These secondary representations now act as the input to the SMC, and it was trained for mapping the $h(2)$ by adjusting the weights $w(3)$.

These three layers were integrated to construct the FC-DSAE+SMC model, which demonstrated the

capability to classify cancerous from non-cancerous data. The FC-DSAE component was trained in a bottom-up manner using an unsupervised approach, followed by the SMC module, which applied a supervised learning strategy to train the top layer and fine-tune the overall architecture.

Ethical Approval: The study was approved by the Ethical Committee of Shanghai Jiao Tong University (Shanghai, China), and informed consent was obtained from all patients in line with clinical research guidelines.

3. EXPERIMENTAL RESULTS AND DISCUSSION

Performance Evaluation: The effectiveness of the proposed Feature Communal Learning model based on DSAE + SMC was assessed by comparing its

performance with existing methods using multiple evaluation metrics. The assessment was conducted through standard quantitative parameters, including sensitivity, specificity, selectivity, detection rate, and F-measure. In addition, performance was measured in terms of precision (Pr), recall or true positive rate (TPR), false positive rate (FPR), and F-measure.

For these calculations, True Positive (TP) and True Negative (TN) represent the number of cases correctly classified as malignant and benign, respectively. Conversely, False Positive (FP) refers to benign cases incorrectly identified as malignant, while False Negative (FN) corresponds to malignant cases misclassified as benign. The formulas used to compute these evaluation metrics are given as follows:

$$\text{Sensitivity} = \frac{TP}{TP + FN} * 100 \%$$

$$\text{Specificity} = \frac{TN}{TN + FP} * 100 \%$$

$$\text{Selectivity} = \frac{TP}{TP + FP} * 100 \%$$

$$\text{Detection rate} = \frac{\text{Sensitivity} + \text{Specificity}}{2} * 100 \%$$

$$F - \text{measure} = 2 \left(\frac{\text{Selectivity} * \text{Sensitivity}}{\text{Selectivity} + \text{Sensitivity}} \right) * 100\%$$

Computational Considerations: In this study, we have used a CPU Intel (R) Core (TM) i3, with 2.3GHz processor and 8GB of RAM for the implementation of all the stated machine learning algorithms. The implementation of all the algorithms of machine learning was performed on MATLAB 2017a, LabSpec. The training+ validation data set consists of 255 samples, and test dataset consist of 45 samples. The test set included 10 samples of EGC, 13 samples of AGC and 22 samples of healthy persons.

Artificial Neural Network (ANN): We also developed an ANN using scaled conjugate backpropagation technique. This method also used to analyze the performance of the systems. We trained the model; after completing the training we tested the developed model on our dataset. Again, we keep the testing dataset to 15% of the total dataset, whereas, the remaining dataset was used for training and validation.

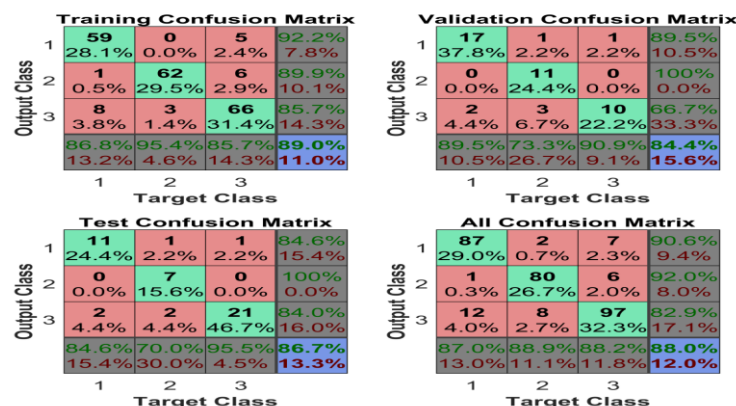


Figure 3 Confusion Matrix for ANN based Classification of AGC, EGC and Healthy Persons

Figure 3 shows the results in form of confusion matrix and receiver operating characteristics for the classification of EGC, AGC and healthy persons using ANN based system. In this technique, the model has distinguished 87, 80 and 97 samples correctly as AGC, EGC and Healthy persons. The training dataset has an accuracy of 89%, validation

dataset has an accuracy of 84.4% and test dataset has an accuracy of 86.7%. The ANN based neural network produced an accuracy of 88%, selectivity 88.8%, sensitivity 91.95%, specificity 95.19%, detection rate 93.57% and F-measure 90.34%. All these parameters were calculated for EGC class.

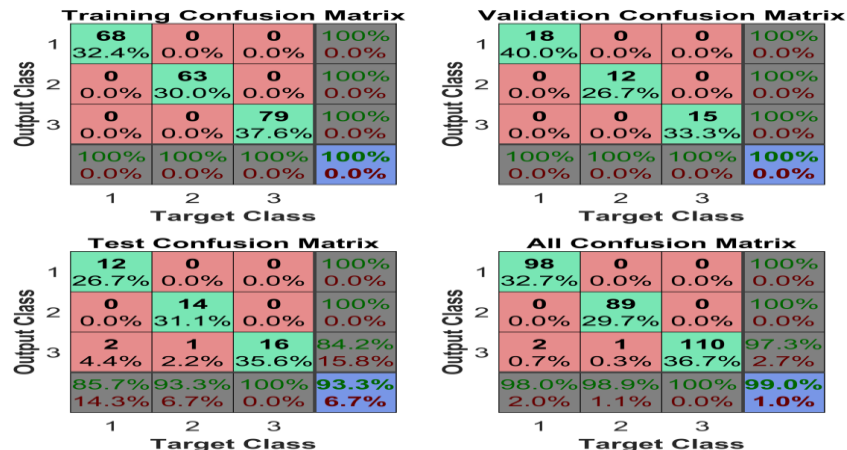


Figure 4 FC-DSAE + SMC based Classifier System for AGC, EGC and Healthy Persons

Figure 4 show the result of the developed FC-DSAE + SMC based classifier, which distinguishes the AGC, EGC and Healthy samples more accurately. This model produces an overall accuracy of 99% on the complete dataset. This model misclassified only 3 samples in the test data out of 45 samples. This model produced an accuracy of 93.3% on the test dataset. In the training phase, the FC-DSAE + SMC has distinguished all the AGC, EGC and Healthy

samples accurately producing an accuracy of 100%. This model has misclassified 2 samples in AGC and 1 sample from the EGC class. Moreover, this method has distinguished all the healthy samples accurately. The FC-DSAE + SMC based neural network produced an accuracy of 99%, selectivity 98.9%, sensitivity 100%, specificity 99.57%, detection rate 99.76% and F-measure 99.5%. All these parameters were calculated for EGC class.

Table II. Comparison of FC-DSAE+SMC with ANN, in terms of Accuracy, Selectivity, Specificity, Sensitivity, Detection Rate, F-Measure

Method	Accuracy	Selectivity	Specificity	Sensitivity	Detection Rate	F-Measure
ANN	88.0%	88.8%	95.19%	91.95%	93.57%	90.34%
FC-DSAE+SMC Classifier	99%	98.9%	99.52%	100%	99.76%	99.5%

Table II summarizes the result of this study. This table indicates that our developed model is better in predicting the GC and non-GC samples with very high efficiency. The FC-DSAE+SMC based neural network has the highest accuracy, selectivity, sensitivity, specificity detection rate, and F-measures when compare to all state of art strategies shown in Table II. However, ANN based neural network has the low accuracy, selectivity, specificity, detection rate, and F-measures. Therefore, we can say that our proposed model using deep neural network architecture has achieved higher accuracy, higher precision, higher recall for the gastric cancer classification, and the method has outperformed all other existing techniques.

4. Conclusions

In this study, we have developed a deep neural network model using sparse auto encoder architecture. This model was used to detect gastric cancer by using saliva samples. The proposed model used the unsupervised technique to capture the high-level feature representation of the Raman data. The classifier works very well with very high accuracy by utilizing these high-level feature representations. From the qualitative analysis and quantitative analysis, we can conclude that the deep sparse autoencoder with the combination of SoftMax classifier has outperformed the other state of art methods in terms of efficiency, accuracy, selectivity, sensitivity, and classification which have been used in this study. The proposed model has accurately distinguished the gastric cancer patients from healthy persons.

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