## RESEARCH



# **Deep Learning Based Entropy Controlled Optimization** for the Detection of Covid-19

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Received: 30 July 2023 / Accepted: 16 April 2024 / Published online: 23 May 2024 © The Author(s), under exclusive licence to Springer Nature B.V. 2024

Abstract Emerging technological advancements open the door for employing deep learning-based methods in practically all spheres of human endeavor. Because of their accuracy, deep learning algorithms can be used in healthcare to categorize and identify different illnesses. The recent coronavirus (COVID-19) outbreak has significantly strained the global medical system. By using medical imaging and PCR testing, COVID-19 can be diagnosed. Since COVID-19 is highly transmissible, it is generally considered secure to analyze it with a chest X-ray. To distinguish COVID-19 infections from additional infections that are not COVID-19 infections, a deep learning-based entropy-controlled whale optimization (EWOA) with Transfer Learning is suggested in this paper. The created system comprises three stages: a preliminary processing phase to remove noise effects and resize the image, then a deep learning architecture using a pre-trained model to extract features from the

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Department of Information Systems, College of Computer Engineering and Sciences, Prince Sattam bin Abdulaziz University, 16273 Al-Kharj, Saudi Arabia pre-processed image. After extracting the features, optimization is carried out. EWOA is utilized to combine and optimize the optimum features. A softmax layer is used to reach the final categorization. Various activation functions, thresholds, and optimizers are used to assess the systems. Numerous metrics for performance are utilized to measure the performance of the offered methodologies for assessment. Through an accuracy of 97.95%, the suggested technique accurately categorizes four classes, including COVID-19, viral pneumonia, chest infection, and routine. Compared to current methodologies found in the literature, the proposed technique exhibits advantages regarding accuracy.

**Keywords** COVID-19 · Deep learning · Classification · Transfer learning · Chest X-rays, features optimization

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## 1 Introduction

The COVID-19 coronavirus may represent the most significant hazard to people in the 21st century. A global health issue has emerged because of the COVID-19 pandemic since the disease's breakout in December 2019. In January 2022, there were approximately 365 million verified COVID-19 infections, leading to almost 5.5 million fatalities, based on statistics from the World Health Organization (WHO) [1]. SARS-CoV-2, also known as COVID-19, is an infection that causes severe acute respiratory syndrome, also known as SARS. COVID-19 is a member of the virus family that includes the Middle East respiratory syndrome (MERS-CoV) and severe acute lung disease [2, 3]. Prevention of health facilities and the population from COVID-19 dissemination is necessary due to the advent of disease transfer and an increase in death in various nations.

The limits imposed by authorities to prevent individuals' transmission of this dangerous sickness hurt every aspect of life worldwide [4, 5]. From minor ailments to severe and life-threatening conditions, COVID-19-related illnesses can be categorized. COVID-19 can cause pneumonia. The Greek term pneumonia, which means lung, is where the word pneumonia gets its name. Thus, lung disease and pneumonia are connected. Infection in the lungs brought on by pneumonia makes breathing difficult [6]. Additional causes of pneumonia include food aspirations and contact with chemicals. As was previously discussed, pneumonia results in pulmonary inflammation, which causes the alveoli in the lungs to become sticky or viscous.

Pneumonia can be brought on by various infectious agents, including viruses, fungi, and bacteria, and each pneumonia is handled similarly. Antibiotics are used to treat pneumonia caused by bacteria. Antiviral medications are employed for treating viral pneumonia, whereas antifungal medicines are utilized to cure fungi-caused pneumonia [7, 8]. Numerous methods are used to diagnose respiratory infections, including CT scans, chest X-rays, sputum tests, total blood counts, blood gas analyses, and more. Reverse transcription-polymerase chain reaction (RT-PCR) screening is regarded as trustworthy, despite its limitations, for identifying COVID-19. SARS-CoV-2 genetic data is found in the upper respiratory system using a test called RT-PCR [9]. A method that can aid medical personnel in determining the presence of COVID-19 must be developed. By delivering essential medical care promptly, quickly identifying COVID-19 may prolong a patient's life. Deep learning is currently one of the methods that may be employed for solving photographic problems. It was discovered that it has significant effects in a variety of industries, such as satellite imagery [10, 11], farming [12], and medicine [13, 14]. It is employed in medical practice to diagnose and categorize many illnesses, such as skin conditions [15, 16], various ulcer kinds, and cancer [17].

Main motivation behind this research is to predict the diseases accurately. Recently deep learning models achieves more accuracy in diagnosis. The coronavirus pandemic (COVID-19) has posed up till now unseen difficulties for the global healthcare system, exposing crucial weaknesses in our capacity to promptly identify and treat highly transmissible illnesses. The role of technical innovation has come to light during this crisis, especially in the area of deep learning, where it has opened up new avenues for improving treatment plans and diagnostic techniques. The pressing need to supplement established diagnostic techniques, including PCR testing and medical imaging, with more effective, precise, and scalable alternatives is what drove this research.

The main contribution of the proposed method is given below:

- The novelty of the proposed method is increasing COVID-19 detection by applying deep learning-based entropy-controlled whale optimization (EWOA).
- The extraction of features stage of the suggested pipeline uses the pre-trained model based on Transfer Learning.
- Entropy control Whale optimization attempts to regulate or control the degree of entropy in a particular dataset during optimization after the feature extraction.
- Using deep learning algorithms to identify various diseases can also reduce human error.
- To determine that the deep learning-based entropy-controlled whale optimization algorithm offers the best efficiency with the fewest losses, we analyzed different activations of the layers and function activation.

The rest of our research article is written as follows: Section 2 discusses the related work on COVID-19 Detection and Classification and deep learning methods. Section 3 shows the proposed work's algorithm process and general working methodology. Section 4 evaluates the implementation and results of the proposed method. Section 5 concludes the work and discusses the result evaluation.

#### 2 Related Works

The author [18] suggested a deep learning-based method for classifying pneumonia infections and COVID-19. Using CovXNet, a deep CNN approach, characteristics are recovered. A publicly available dataset of 305 samples of COVID-19 pneumonia and 1493 samples of non-COVID-19 pneumonia is used for learning. With an accuracy of 96.9%, the model correctly distinguished between COVID-19 pneumonia and non-COVID-19 pneumonia. The author proposed an approach for the binary categorization of COVID-19 [19]. 7232 chest X-ray pictures from a publicly accessible dataset are utilized for the technique's training and evaluation. In the present investigation, four models for deep learning are contrasted. The results are validated using a variety of evaluation factors.

To identify COVID-19 infection from CXR images, an author [20] presented a generative adversarial network (GAN)-based technique. Their dataset included 307 photos split into COVID-19, typical pneumonia caused by bacteria, and viral pneumonia classes. As TL, they employed the AlexNet, GoogleNet, and ResNet18 methods. Their predictive accuracy on four classes (GoogleNet), three classes (AlexNet), and two classes (GoogleNet) was 80.6%, 85.3%, and 100%, respectively. The writer [21] used TL and the Xception pre-trained system similarly. Their algorithm successfully classified 4 and 3 classes with 89.6% and 95% accuracy, respectively. The researcher [22] used the DCNN transfer learningbased pipeline, Inception V3, to identify COVID-19 in infected patients utilizing chest X-ray scans.

The local binary pattern was employed for obtaining texture characteristics, and a Gaussian filter was applied for pre-treatment. Afterward, to enhance performance, the extracted characteristics of LBP are combined with the CNN model InceptionV3. Multi-layer perceptrons are used for the categorization. The model's accuracy was 94.08% when validated using an X-ray dataset. The author [23–25] suggests a method based on convolutional neural networks in which COVID-19 and standard photos were classified using a 24-layer CNN model. This model's creator gave it the moniker nCOVnet. The initial development of nCOVnet utilized the X-ray dataset. The model achieves up to 97% accuracy. The segmentation-based method of classification is presented by the author [26]. The U-Net [27] is trained on CT images to create lung masks.

Convolutional Neural Networks (CNNs) have been extensively utilized for processing medical images recently because of the rapid growth of computational intelligence, and more specifically, technology for deep learning and their potent depiction of features and extracting capabilities. Numerous CNN-based strategies have been released, demonstrating promising results in cases involving the diagnosis of various diseases, such as cancer and others [28–30], and they should be equally feasible for this innovative pneumonia detection method. Deep learning techniques can classify and segment biomedical image data to recognize abnormalities and regions of interest (ROIs). CNN and Unet-based structures are the researchers' most promising and well-liked options [31].

Shahin [32] and colleagues present a smartphonebased application designed for early skin disease prognosis. Their work addresses the potential of computer-based vision in lean healthcare systems. The application leverages smartphone cameras and image analysis to provide early diagnosis and monitoring of skin diseases. The study highlights the potential of mobile technology in improving healthcare accessibility and facilitating timely medical intervention for skin conditions. The article [33] contributes to the field of medical image analysis and retrieval, which is crucial for diagnosing and monitoring pulmonary diseases. The article discusses the application of deep learning in managing and retrieving medical image data, emphasizing its potential in enhancing the diagnosis and treatment of lung-related conditions. The healthcare diagnosis prefers deep learning model for better results [34–36]. The research [37] contributes to the development of more accurate and robust diagnostic models for infectious diseases, which is particularly valuable in healthcare settings. The covid 19 detection is accurately detected using deep learning models [32–43]. The transfer learning provides extraordinary learning capacity to the deep learning model for achieving accurate results [44, 45].

#### **3** Proposed Methodology

The proposed method for the detection of COVID-19 by using Deep Learning entropy-controlled whale optimization (EWOA) with Transfer Learning (TL). Initially, the dataset is collected, and then the collected dataset is given into the pre-processing step. Next, the pre-processed data is passed into the normalization process. After normalization, the features are extracted using entropy-controlled whale optimization. Finally, the proposed EWOA-TL method is used to classify COVID-19 and classifies the results as chest infections, COVID-19, Pneumonia, and Normal. Figure 1 shows the architecture of the proposed method.

### 3.1 Dataset Collection

The dataset utilized for the suggested technique's training and evaluation is accessible to the public on Kaggle [46, 47]. The dataset used in this study was

obtained from Kaggle following three changes to the original dataset. The dataset comprises several subdatasets that fall into four categories: COVID-19, lung transparency, regular, and pneumonia caused by viruses. As the used dataset is created by combining other datasets, it is crucial to detail its structure. Each category is produced by combining various subdatasets. There are 3616 photos in the class COVID-19, gathered from four distinct sources. With 2473 pictures, the BIMCV-COVID19+[48] collection significantly contributes to the COVID-19 dataset. It serves as one of the largest, freely accessible, distinct databases. The German Medical School dataset [49], containing 183 chest X-ray images, and the 560 chest X-ray images obtained from SIRM, GitHub, Kaggle, and Twitter [50-53], are additional datasets that contribute to the COVID-19 collection. A further set with 400 combined chest X-ray pictures is additionally accessible on GitHub [38].

Another well-known chest X-ray dataset is the RSNA pneumonia test dataset [39]. The RSNA dataset includes normal (healthy) lungs and other lung pathologies. The anomalies include everything from various infections of the lungs to lung cancer. The collection is divided into three main groups and includes 26,684 chest X-ray pictures in the Dicom format.



Fig. 1 Architecture of Proposed Method

The most extensive of these groups has 11,821 photographs of various lung infections, 6012 labeled as non-COVID-19 lung infections (lung opacity), and 8851 pictures of regular lung function. The healthcare record is also considered during the assessment, as it is crucial to know if a person has encountered any linked infections before. Medical specialists analyze the dataset based on key indications. The data set has been widened by adding 1345 chest X-ray images from viral pneumonia and 1341 standard chest X-ray images, all of which come from [40]. Figure 2 displays representative photos from the dataset that was used. Table 1 also shows the dataset's makeup.

## 3.2 Data Normalization

Obtaining datasets for deep learning model training is complex because they are not always easily accessible. Deep learning models need high-quality datasets with lots of samples for practical training. The dataset has been normalized between 0 and 1. Every picture pixel in the data set has its size doubled by a ratio of 1/255. This was done to ensure that the dataset's intensity of pixels was constant. The dataset gathered has a class imbalance since it has varying amounts of photos in each class. These data sets cannot be used to effectively train deep learning models since they are skewed towards one or more courses, significantly impacting the model's accuracy. Additionally, deep learning systems need a sizable dataset for learning; alternatively, overfitting may contribute to the model's accuracy decline [41, 42].

The picture enhancement method is used to solve both issues. In addition to expanding the dataset, image augmentation aids in creating an even data class. The picture augmenting mode allows adding more instances to classes that initially had fewer examples, improving the quality and dimension of the initial data set, substantially impacting how well the model performs. Here are numerous methods for enhancing images. Techniques for image enhancement are applied following needs. The picture dataset is utilized in the present study for training.

The COVID-19 group, pneumonia caused by viruses, and lung opacity are the three classes for which data augmentation is done to tackle the difficulty of class imbalance. Image augmentation refers to the numerous sorts of boosts done to images. Among the varieties are random elimination, color

space alteration, blending pictures, and geometric or positional enlargement [39]. Several sorts of geometric enhancement exist, including rotating, translational, expanding, trimming, and flipping. Figure 3 shows the different types of Geometric augmentation used in the proposed method.

# 3.3 Feature Extraction and Classification Using Entropy-Controlled Whale Optimization Based Transfer Learning

In the proposed method, the Chest X-ray features are extracted by MobilenetV2, and then the extracted data is given into Entropy Controlled Whale Optimization [43] based on Transfer Learning. In the following section, it is described. MobilenetV2, a pre-trained deep learning model, is utilized for feature extraction from Chest X-ray images. This model has learned to recognize various features and patterns from a vast dataset, making it capable of capturing rich information from images. When a Chest X-ray image is passed through MobilenetV2, it undergoes a series of convolutional and pooling layers. These layers transform the input image into a set of feature vectors that represent different aspects of the image's content. Each vector captures specific features like edges, textures, shapes, and patterns present in the X-ray image. The resulting feature vectors form a high-dimensional representation of the image's content. These vectors can be thought of as a structured numerical description of the image's characteristics. MobilenetV2's early layers are designed to capture low-level features, such as edges, contours, and gradients [44, 45]. These features help identify sharp changes in pixel values and edges within the image. They are essential for detecting boundaries between anatomical structures in X-ray images.

#### 3.3.1 Transfer Learning

A previously learned and used model is the basis for an entirely novel assignment and framework in transfer learning. As an optimization to boost efficiency, the model employed for one task may be applied to other tasks. Transfer learning allows the model to be trained using a small amount of data. Saving time and getting quality outcomes are both benefits.

With the transfer learning method, we convert the origin chest X-ray data into target images



Fig. 2 Sample Images Used for Proposed Method [1]

Table 1COVID-19Dataset Used for Evaluation

Categories	BIMC- COVID19+	German Medical School	SIRM,GitHub, Kaggle, and Twitter	GitHub	RSNA	Kaggle
COVID-19	2473	183	560	400	-	-
Lung Transparency	-	-	-	-	6012	-
Normal	-	-	-	-	8851	-
Pneumonia	-	-	-	-	-	1341



Fig. 3 Geometric Augmentation Used in Proposed Method

 $I_T$ . The target classifier Tc (Mt) is being developed using the input Chest X-ray image. It is to the desired picture  $I_T$  to obtain a classifier's forecast for CCPN<sub>i</sub>, or Chest Infections, Covid-19, Pneumonia, and Normal. It uses a transfer layer to extract the features. While the other classifier layers remained frozen, the top layer retrained the new target classes.

$$CCPN_i = T_c(M_i) \tag{1}$$

The transfer learning approach is utilized for extracting the features from MobilenetV2. Multiple knowledge classes have been combined into four classes in Fig. 4.

# 3.3.2 Entropy Controlled Whale Optimization Algorithm (EWOA)

Whale individuals are utilized in the community to investigate the possibilities for a workable solution to the issues in the search space. WOA carries out all three duties of surrounding, shrinking, and hunting. Whereas the hunting function is utilized in the exploration stage, the surrounding and shrinking operations are used in the exploitation phase.

The i<sup>th</sup> person in the  $c^{t\bar{t}}$  generation's methods is employed to discover the optimum answer to the dimension optimization problems (DO). The WOA guidelines are being followed.

Encircling Operation

$$ESH_{ij}(c+1) = ESH_{*j}(c) - BO_{ij}(c)$$
<sup>(2)</sup>

• Shrinking Operation

$$ESH_{ij}(c+1) = ESH_{*j}(c) + g^{et} \cdot \cos(2\pi t) \cdot O_{ij}^{\dagger}(c) \quad (3)$$

Hunting Operation

$$ESH_{ij}(c+1) = ESH_{kj}(c) - BO_{ij}^{*}(c)$$
(4)

$$B = 2\left(1 - \frac{c}{c_{max}}\right).(2rd - 1) \tag{5}$$

The most effective positive vectors are denoted by ESH(c), the random integer in the range [0, 1] is given by (rd), the current number of iterations is given by c, and the maximum number of iterations is characterized by  $c_{max}$ .

The exploitation phase, readily subject to neighborhood optimization and minimizes population diversity,



Fig. 4 Architecture of Transfer Learning

provides the WOA with the best current solution. The method's convergence rate is disrupted by the random individual learning operation's partial blindness and the lack of adequate information exchange between groups during the exploration phase. To lessen these problems, the WOA must be modified. A new method called EWOA is suggested. The control parameter B is utilized to balance the exploration and exploitation capabilities of the WOA. WOA's exploration chance is just 0.1535 in the repeated steps of the way. The EWOA's growth and exploration process is controlled by gradually raising the probability. When individuals in an animal's large group learn from the best other people in the group, their individuality increases. Distinctive neighborhoods are created by adaptable social learning processes that draw on societal position, societal impact, and the development of social networks. The flexible social network strategy is utilized to create a network of adaptable whales, enhance group communication, and raise the accuracy of the EWOA computation. The new system is suggested based on area, which will broaden the demographic range.

It was a calculated decision to use MobilenetV2 as the pre-trained deep learning model for feature extraction. This model is well known for its efficacy and efficiency while processing image data, especially because of its lightweight architecture and capacity to extract a large number of features with a small amount of CPU power. By applying a model that has already been pretrained on a large dataset to a new job with sparse data, transfer learning increases the effectiveness of the suggested strategy. This methodology plays a key role in improving the model's capacity to accurately identify chest X-ray pictures into four categories: viral pneumonia, COVID-19, chest infection, and normal cases. The method saves time and computational resources while preserving high-quality results by adjusting the MobilenetV2's learnt characteristics to the target task instead of starting from scratch.

#### 4 Result Analysis

The chest X-ray sample with four different categories was obtained from Kaggle, as was already described. The planning phase of the dataset addressed the issue of unbalanced classes. This is a crucial step since an unbalanced dataset will bias the algorithm's training process in favor of any number of categories. The data set is then divided into three separate sets, with the ratios of testing, training, and validation being 70:20:10, correspondingly. The test data set is utilized to assess the system whenever the algorithms have been

trained. The studies use an Intel Core I7 with 16 GB of RAM.

The NVIDIA GTX 1070 Ti is also compatible with the operating system. To verify that the findings of the suggested technique EWOA-TL are accurate, the results are analysed using a variety of assessment factors. In this study, accuracy, precision, F1-score, sensitivity, and specificity were employed as evaluation criteria. The proposed EWOA-TL method is compared with three existing methods such as ResNet50, DCNN and MEWOM.

#### 4.1 Accuracy

It is used to evaluate the classification of Chest X-Ray images accurately for the detection of COVID-19.

$$accuracy = \frac{TP + TN}{TP + TN + FP + FN} X100$$
(6)

#### 4.2 Sensitivity

It is used to evaluate sensitive to measure how much COVID-19 are identified.

$$Sensitivity = \frac{TP}{TP + FN}X100$$
(7)

#### 4.3 Specificity

It is used to evaluate the rate between True Negative (TN) and True Positive (TP)

$$Specificity = \frac{TN}{TN + FP} X100$$
(8)

4.4 Precision

$$precision = \frac{TP}{TP + FP} X100 \tag{9}$$

The results are evaluated and presented in Table 3. The Proposed EWOA-TL outperforms greater compares with other methods used. It attains the accuracy of 97.95%, precision of 95.15%, Specificity of 93%, F1-score of 94.85% and Sensitivity of 92.87%. In Fig. 5 shows the classification result of various methods. The proposed method is compared with existing methods such as DCNN, ResNet50 and MEWOM. The DCNN attains the accuracy of 93%, precision of 89.25%, Specificity of 89%, F1-score of 91% and Sensitivity of 89.15%. The ResNet50 attains the accuracy of 89.30%, precision of 91.75%, Specificity of 90.12%, F1-score of 92.75% and Sensitivity of 87%. The MEWOM attains the accuracy of 90.25%, precision of 92.25%, Specificity of 87.23%, F1-score of 91.75% and Sensitivity of 86.75%.

In Figs. 6 and 7 displays the training diagrams for the proposed model, EWOA-TL. The accuracy of the validation and training plots is shown in Fig. 6. The system's accuracy for validation is attained on the 14th epoch, and its training and validation error plots are shown in Fig. 7. The learning process proceeds until the 14th epoch, while the least validation loss is reached on the 14th epoch. However, after the 12th epoch, the loss continued to decrease.

The receiver operating characteristics (ROC) curve is also used to demonstrate and verify the precision and durability of our deep learning algorithm, along with accuracy measures. Utilizing the true positive and false positive rates

Table 3 Comparison of Different Method's Accuracy

References	Year	No of Classes Used	Accuracy
Khan et al. [28]	2020	4	89.45%
Abbas et al. [24]	2021	3	93.1%
Rahman et.al. [47]	2021	3	96.27
Proposed	2023	4	97.95%

Table 2Classificationresult of variousclassification methods	Methods Used	Accuracy	Precision	Specificity	F1-score	Sensitivity
	ResNet50	89.30%	91.75%	90.12%	92.75%	87%
	DCNN	93%	89.25%	89%	91%	89.15%
	MEWOM	90.25%	92.25%	87.23%	91.75%	86.75%
	EWOA-TL	97.95%	95.15%	93%	94.85%	92.87%











at different classification thresholds, ROCs represent a model's categorization output. The area under the curve (AUC) of a ROC is a quantitative evaluation metric frequently used in classification systems. The ROC curve is shown in Fig. 8.

In the above Fig. 8 shows the evaluation result of ROC curve. It uses four classes for the evaluation. Class 0 is Chest Infections, Class 1 is COVID-19, Class 2 is

Pneumonia and Class 3 is Normal. The proposed model's COVID-19 classification performance metrics depend on the various deep learning techniques is shown in Fig. 8.

In Table 3 makes it quite evident that EWOA-TL outperforms various other models about accuracy and other metrics. With the aid of a confusion matrix, these findings are also verified. In Fig. 9, the confusion matrix is displayed. The proposed method



Fig. 8 ROC curve of proposed method



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Fig. 9 Confusion matrix for Four Different classes

accurately classifies the COVID-19 infections, Pneumonia, Chest Infections and Others.

Three distinct models are trained in this study and compared using the suggested methodology. It has been noted that using methods of regularization considerably enhances the efficiency of all four models. Even though EWOA-TL works well in both situations, regularization procedures greatly enhance EWOA-TL's efficiency. It is evident that the proposed EWOA-TL outperformed the other strategy in both cases. Additionally, Table 3 displays an analysis of performance with recent research given in the available literature.

The model's generalizability across various imaging devices and procedures, the computational complexity of the optimization process, and the reliance on the quality and variety of the training data are some potential obstacles. Furthermore, although novel, the incorporation of EWOA necessitates meticulous calibration to guarantee that the phases of exploration and exploitation are optimally balanced for every distinct dataset, a procedure that can be intricate and time-consuming.

#### 5 Conclusion

A deep learning-based method is suggested for classifying various chest illnesses. The current COVID-19 coronavirus outbreak has significantly burdened the world's healthcare infrastructure. COVID-19 can be identified through PCR testing and medical imaging. Since COVID-19 is highly contagious, a chest X-ray is typically accepted as a reliable method of diagnosis. This research proposes a deep learning-based entropy-controlled whale optimization (EWOA) with Transfer Learning to differentiate COVID-19 infections from other infections that are not COVID-19 infections. A preliminary analysis step to remove the impact of noise and compress the picture is the first of three stages that make up the developed system. Next, a deep learning architecture employing a trained model is used to extract characteristics from the pre-processed photo. The features are extracted, and then optimization is done. The best characteristics are combined and optimized using EWOA. The final categorization is achieved using a softmax layer. The systems are evaluated with different functions for activation, limits, and optimizers. The efficacy of the provided approaches for assessment is evaluated using a variety of performance criteria. The suggested method correctly divides four classes into COVID-19, viral pneumonia, chest infection, and normal, with an accuracy of 97.89%. The proposed strategy shows advantages in terms of accuracy when compared with the present techniques identified in the existing literature.

Acknowledgements Aisha M. Alqahtani from Princess Nourah bint Abdulrahman University Researchers Supporting Project number (PNURSP2024R52), Princess Nourah bint Abdulrahman University, Riyadh, Saudi Arabia.

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**Data Availability** The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

#### Declarations

Ethics Approval and Consent to Participate Not applicable.

Consent for Publication Not applicable.

**Competing Interests** The authors declare no competing interests.

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