A Comparative Analysis of CNN and Transfer Learning Algorithms in Predicting Alzheimer's Disease Stages using Neuroimaging

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***Abstract:*** **Alzheimer's disease (AD) prediction plays a critical role in early detection and intervention, allowing for better patient care and management. This paper investigates the predictive capabilities and state-of-art of Convolutional Neural Networks (CNN) and transfer learning models, including Inception V3, Resnet-18, and Resnet-50, for the progression of Alzheimer's disease (AD). The Alzheimer's disease Neuroimaging Initiative (ADNI) dataset used in this study, which includes multimodal neuroimaging, clinical, genetic and demographic data, the research aims to provide accurate predictions at various stages of the EA. This dataset enables robust training and evaluation of deep learning algorithms to predict AD progression. The data undergoes pre-processing and feature engineering to prepare a robust data set. Evaluations covering accuracy, precision, recall and F1 score, using k-fold cross-validation, are performed to measure the performance of the chosen algorithms. CNN and Inception V3 demonstrate remarkable performance with an accuracy of 93.75% and 94%. Comparative analyzes include exploration of Inception V3, Resnet-18, and Resnet-50, shedding light on their individual contributions to AD prediction. This paper contributes to the development of reliable and efficient deep learning approaches for early prediction and diagnosis of AD, with the potential to improve patient outcomes. Comparing the predictive capabilities of CNNs and transfer learning models provides valuable insights into their effectiveness in modeling AD progression.**

**Keywords:** Alzheimer’s disease, convolutional neural network, transfer learning models AD progression, early detection, intervention, confusion matrix**.**

# Introduction

Alzheimer's disease (AD) presents an imposing challenge to healthcare systems worldwide, standing as the predominant form of dementia that progressively impacts cognitive abilities, memory, and behavior [1]. This degenerative condition manifests a spectrum of symptoms, ranging from mild instances such as forgetfulness and word-finding difficulties to more severe stages marked by profound memory loss, disorientation, and communication impediments. Presently lacking a definitive cure, the treatment of AD primarily revolves around medication to alleviate its progression, underscoring the crucial importance of accurate and early diagnosis for effective intervention. The significance of predictive models in addressing the challenges of AD cannot be overstated, particularly given the absence of a cure and the imperative for timely interventions. Precise prediction of disease progression empowers healthcare professionals to tailor treatment plans, provide appropriate support, and enhance the overall quality of life for individuals and their caregivers. As a leading cause of cognitive decline, addressing these challenges necessitates cutting-edge technologies capable of delivering accurate and timely information, rendering AD an ideal subject for exploration through advanced neural network models.

In recent years, the convergence of artificial intelligence and medical diagnosis has yielded promising results, with Convolutional Neural Networks (CNNs) emerging as a powerful tool. The intricacies of neuroimaging data make CNNs particularly adept at extracting meaningful patterns and features [2]. Their ability to discern subtle nuances in medical images not only aids in early diagnosis but also facilitates a deeper understanding of the disease's evolution.

Furthermore, the integration of transfer learning, particularly from well-established databases such as ImageNet, enhances the efficiency and generalization capabilities of CNN models. Transfer learning leverages pre-existing knowledge from extensive datasets, enabling the model to adapt and excel in new domains with limited labeled data. This approach accelerates model training and strengthens the performance of the neural network in accurately classifying the stages of Alzheimer's disease. This paper boards on a comprehensive exploration of the application of a fully layered CNN model alongside transfer learning, utilizing pre-trained models, namely Inception-V3, ResNet-18, and ResNet-50[3]. These models are meticulously applied to neuroimaging data, specifically magnetic resonance imaging, facilitating the classification of Alzheimer's disease into distinct stages: non-demented, very mildly demented, mildly demented, and moderately demented. As we delve deeper into this comparative analysis, the goal is not only to delineate the effectiveness of these models in classifying Alzheimer's disease but also to contribute to the growing body of knowledge seeking innovative solutions for early detection and intervention. The synthesis of advanced neural network architectures and transfer learning strategies holds the promise of revolutionizing our approach to understanding and managing Alzheimer's disease, paving the way for more targeted and timely interventions [4]. This research strives to bridge the gap between cutting-edge technology and clinical applications, fostering advances that have the potential to make a substantial impact on the lives of those affected by this debilitating condition.

The rest of the paper is structured as follows: Section 2 reviews previous work related to the prediction of Alzheimer's disease. In Section 3, we present a detailed explanation of the methodology. Section 3 is further divided into seven subsections. Section 3.1 describes the components used in building a CNN. Sections 3.3 to 3.6 describe the steps taken to prepare the training data for the classification task. Section 3.3 delves into the mathematical model, while subsequent Section 3.6 explains the application of transfer learning in classification.

Moving forward, Section 4 compiles the experimental results, including accuracy and loss function plots of our classification model, along with comparisons with other existing techniques. Finally, Section 5 provides concluding remarks on the method, emphasizing its practical applications and describing possible future developments.

# RELATED WORK

Medical imaging data is diverse and encompasses various modalities, such as structural or functional MRI, diffusion tensor imaging (DTI), positron emission tomography (PET), and computed tomography (CT). These scans, in various forms, have been used with different machine learning algorithms in previous efforts for early diagnosis and disease detection.Most early diagnosis methods for Alzheimer's disease (AD) have traditionally been based on the classification of features extracted from brain images. These features aim to accurately capture variations in brain anatomical structures associated with AD. Typically, these features are input into classic machine learning algorithms such as support vector machines (SVM), random forest classifiers, or feed forward networks for classification purposes.

Ghaffari et al. [5] investigated into the application of transfer learning to gray matter analysis derived from T1-weighted MRI scans within the ADNI dataset. The study employed three pre-trained Convolutional Neural Network (CNN) models – ResNet101, Xception , and InceptionV3 – and also trained them from the ground up for the sake of performance evaluation[3].The results indicated that transfer learning-based CNN models surpassed their counterparts trained from scratch, showing the highest accuracy of 93.75% achieved by the pre-trained InceptionV3 model in binary classification.

Soliman et al. [6] conducted a series of experiments using a dataset comprising medical images from two primary sources. The first type of scans, 18F-FDG-PET scans, was obtained from the European DLB (EDLB) Consortium, while the second type consisted of scans collected from the ADNI database. The authors evaluated the performance of pre-trained InceptionV3[13], VGG16, and ResNet50 [11] models, as well as a 3D VGG model trained from scratch using the 18F-FDG-PET scans. The experiments yielded the following optimal results: ResNet50 achieved a validation accuracy of 89% for the binary classification task (AD vs. CN), while the 3D model achieved a validation accuracy of 87% for the 3-way classification task (AD vs. CN vs. DLB) and a validation accuracy of 73% for the 4-way classification task (AD vs. CN vs. DLB vs. MCI).

In the study by Sharma et al. [7], introduced a modified Inception model using transfer learning. This model was trained on a Kaggle dataset containing images of four different classes: CN, very mild AD, mild AD, and moderate AD. The proposed model achieved an impressive classification accuracy of 94.92 %.

On the topic of preprocessing techniques, Druzhinina et al. [8] investigated how skull removal affects the accuracy of Alzheimer's disease (AD) classification results. They found that skull removal significantly influenced the performance of the classification models by aiding model convergence. However, the authors also noted that skull removal could lead to image corruption and loss of information, which could be critical for an accurate diagnosis of AD. Skull extraction is a common preprocessing step in neuroimaging research for brain extraction and has been used in several studies, including those by Pan et al. [9] and Dhinagara et al. [10]. Both studies employed skull extraction on MRI images from the ADNI data set, and Dhinagara et al. specifically using the HD-BETCPU implementation for this purpose.

# Materials and Methods

## Data description

The dataset employed in this paper was sourced from the Alzheimer's disease Neuroimaging Initiative (ADNI), established in 2003 through a collaborative effort led by principal investigator Michael W. Weiner, MD. The primary goal of ADNI is to investigate the combination of serial magnetic resonance imaging (MRI), positron emission tomography (PET), various biological markers, and clinical and neuropsychological assessments. Additionally, MRI images capturing Alzheimer's disease were obtained from Kaggle, an open source platform. The data set covers a total of 6,400 MRI images representing four stages of the disease: no dementia (3,200 images), very mild dementia (2,240 images), mild dementia (896 images), and moderate dementia (64 images). Each image in the dataset has a resolution of 176 × 208 pixels.

## Methodology

Deep learning, a subset of machine learning, draws on structural and functional aspects of the human brain, often implemented using algorithms called “neural networks.” An important type of deep learning algorithm is the convolutional neural network (CNN), which leverages convolution operations for transformations [2]. CNNs are particularly adept at processing data with a known grid-like topology.First introduced by Lecun, Bottou, Bengio, and Haffner in 1998, CNNs represent a specialized class of neural networks designed for processing grid-like data. In at least one of their layers, CNNs employ convolution operations instead of general matrix multiplication. The fundamental layers and operations used in building a CNN are as follows:

### Convolution layer

The convolutional layer serves as a cornerstone in the architecture of a convolutional neural network (CNN), assuming a fundamental role in performing most computational tasks. Its functionality is defined by sets of learnable filters or kernels that act as parameters. These filters are strategically applied to the input data with the main objective of extracting features relevant and essential for the network learning process.

To derive the feature map values, a specific equation is employed, where the input image is denoted as 'f' and the kernel as 'h'. The row and column indices of the resulting matrix are symbolized by 'm' and 'n' respectively. The row and column indexes of the resulting matrix are denoted by m and n respectively [10].

G[m, n] = (f\*h)[m, n] = [j, k] f [m-j, n-k] (1) The dimensions of the output matrix, considering padding and stride, can be determined by using the following equation:

= (2)

### Pooling layer

### Reducing the dimensions of an input image can be achieved using two approaches: convolution layers with a step greater than 1 and pooling layers. It is common practice to incorporate pooling layers between consecutive convolutional layers in convolutional neural network (CNN) architecture[11]. The main goal of the Pooling layer is to systematically decrease the spatial dimensions of the input image.The Max-pooling operation, a key feature of the Pooling layer, involves extracting the maximum value within a defined region of the image. This region has size h × w in an image with dimensions h × w, using a kernel of size k and a step of size s. This process helps simplify the representation of the input data, contributing to the overall efficiency of the CNN.

The output produced is of size of ×

### Fully-connected layer

Fully-connected layers comprise neurons with assigned weights and biases. These layers establish connections between neurons across distinct layers, commonly positioned preceding the output layer within a Convolutional Neural Network (CNN) architecture. The flattened input derived from preceding layers is transmitted to this particular layer. At this juncture, the classification process initiates. Subsequently, the output of the fully connected layer undergoes processing through a softmax layer, yielding a probability distribution for each class.

### Activation layer

Convolutional layers are typically followed by activation functions, which play a crucial role in determining the data to be utilized during the forward process and those to be excluded towards the network's conclusion. In earlier times, activation functions like sigmoid and tanh enjoyed widespread usage. However, contemporary preferences lean towards activation functions such as the rectified linear unit (ReLU) and its diverse variants, including leaky ReLU, Noisy ReLU, and ELU [12].

ReLU activation function and its variants are expressed mathematically as:

(3)

(4)

(5)

Equation (3) is for Simple ReLU, (4) for Leaky ReLU, (5) for Exponential LU (ELU).

### Dropout layer

The utilization of the dropout layer serves the purpose of mitigating over fitting, a phenomenon wherein the model excels on the training dataset but falters when applied to testing data. This layer selectively omits random neurons from the neural network during the training process, thereby diminishing the overall size of the model [13]. Within a neural network, dropout involves setting the output of certain neurons in a hidden layer to 0, determined by a specified dropout ratio. In the event that this ratio is set to 1 for a particular hidden layer, all neurons within that layer will output 0.

## Image Pre-processing

*1. Size Standardization and Normalization:*

Fig. 1(a, b) shows two images taken from the dataset. A resizing operation was applied to conform all images to a consistent size of 176 × 176 × 3, ensuring uniformity in input dimensions for the model. The original RGB images were transformed from 176 × 208 × 3 to the specified dimensions. The scaling operation involved dividing pixel values by 255.0, thereby constraining them within the normalized range of [0, 1].

*2. Data Augmentation:*

The dataset underwent augmentation to reinforce the model's generalization capabilities. Two augmentation techniques were employed. Firstly, smaller cropped square images were horizontally flipped and then expanded to the desired size through the incorporation of horizontal reflections. Secondly, random adjustments were made to the brightness of the images. The augmentation process resulted in an augmentation factor of 2, doubling the initial dataset from 6400 to 12800 images.

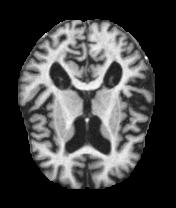
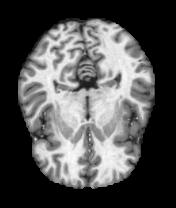
 

Fig. 1a. Moderate Demented Fig. 1b. Non-Demented

*3. Oversampling Technique:*

Addressing class imbalance issues within the dataset (non-demented: 3200 images, very mild demented: 2240 images, mild demented: 896 images, moderate demented: 64 images), the Synthetic Minority Over-sampling Technique (SMOTE) was employed. SMOTE duplicates images from the minority class, generating synthetic data points and achieving a balanced distribution of 3200 images per class.

*4. Splitting into Training and Test Sets:*

The balanced dataset, comprising 6400 images, underwent a randomized shuffle and subsequent division into training and testing sets with a 70:30 split ratio. Further partitioning of the testing set occurred, resulting in a 50:50 split ratio for validation and an additional test set. Class labels 0, 1, 2, and 3 corresponded to Mild Demented, Moderate Demented, Non-Demented, and Very Mild Demented classes, respectively. Table I summarizes the resulting sets.

## Classification using CNN

In the image classification task, each input image with dimensions 176 × 176 × 3 undergoes processing through a Convolutional Neural Network (CNN). The CNN model comprises a total of 32 layers, encompassing convolutional layers, max-pooling layers, dropout layers, batch normalization layers, and fully connected (dense) layers. This architecture is detailed as follows:

*Input Layer:*

The input layer receives images with dimensions 176 × 176 × 3. The images have a height and width of 176 pixels and three input channels representing RGB color.

*First Convolution*

The first convolutional layer involves a Convolution2d layer with 16 filters, a 3 × 3 kernel size, ReLU activation function, and padding set to 'same.'

*Second Convolution:*

Similarly, the second convolutional layer employs a Convolution2d layer with 16 filters, a 3 × 3 kernel size, ReLU activation function, and padding set to 'same.'

*Max-Pooling:*

A MaxPool2d layer follows with a stride of 2 × 2.

*First Convolution Block*

This block consists of two Convolution2d layers with 32 filters each, a 3 × 3 kernel size, ReLU activation function, and padding set to 'same.' Batch normalization is applied, followed by a MaxPool2d layer with a stride of 2 × 2.

*Second Convolution Block*

Similar to the first, this block contains two Convolution2d layers with 64 filters each, a 3 × 3 kernel size, ReLU activation function, and padding set to 'same.' Batch normalization is followed by a MaxPool2d layer with a stride of 2 × 2.

*Third Convolution Block*

TABLE I. TRAINING, TESTING AND VALIDATION SET SIZES.

|  |  |  |  |
| --- | --- | --- | --- |
| **Class label** | **Training set size** | **Test set size** | **Validation set size** |
| 0 | 2240 | 480 | 480 |
| 1 | 2240 | 480 | 480 |
| 2 | 2240 | 480 | 480 |
| 3 | 2240 | 480 | 480 |
| Total | 8960 | 1920 | 1920 |

This block involves two Convolution2d layers with 128 filters each, a 3 × 3 kernel size, ReLU activation function, and padding set to 'same.' Batch normalization is applied, followed by a MaxPool2d layer with a stride of 2 × 2.

*Dropout Layer (Rate: 0.2)*

A dropout layer with a dropout rate of 0.2 is introduced.

*Fourth Convolution Block*

Similar to previous blocks, this one comprises two Convolution2d layers with 256 filters each, a 3 × 3 kernel size, ReLU activation function, and padding set to 'same.' Batch normalization is applied, followed by a MaxPool2d layer with a stride of 2 × 2.

*Dropout Layer (Rate: 0.2) and Flatten Layer*

Another dropout layer with a rate of 0.2 is introduced, followed by a flatten layer to transform the pooled feature map into a one-dimensional matrix vector.

*First Normalization Block*

This block includes a dense layer with 512 units, ReLU activation function, batch normalization, and a dropout layer with a rate of 0.7.

*Second Normalization Block*

A dense layer with 128 units, ReLU activation function, batch normalization, and a dropout layer with a rate of 0.5 are incorporated in this block.

*Third Normalization Block*

The third normalization block consists of a dense layer with 64 units, ReLU activation function, batch normalization, and a dropout layer with a rate of 0.3.

*Softmax Layer*

A dense layer with 4 units for the 4 classes and a softmax activation function is employed.

*Optimization*

The Adam optimizer is utilized for model optimization, employing two gradient descent methodologies to minimize losses.

*Loss Function*

The Categorical Cross-Entropy loss function, widely used in multi-class classification tasks with softmax activation, is expressed mathematically as:

(6)

In this, are the true labels for class j for instance i and  is the predicted probability for class j for instance i [14].

## Classification using transfer learning

In machine learning, transfer learning is like recycling a smart model used for one task to kick start another task. We applied Inception-V3, ResNet-50, and ResNet-18 models to classify Alzheimer's disease as shown in Figure1. These models had already learned from lots of images in the ImageNet database. We ditched the fully connected layers from the original model, where the output was set up for 1000 different classes in ImageNet. After removing the last fully connected layers, the following layers were added to the transfer learning models:

*Dropout layers: Dropout ratio of 0.5*

*Global average pooling 2d: stride of 2 × 2 size.*

*Flatten layer*

*Batch Normalization*

*Dense layer: 512 units or neurons, ReLU activation function*

*Dense layer: 256 units or neurons, ReLU activation function*

*Dense layer: 128 units or neurons, ReLU activation function*

*Dense layer: 64 units or neurons, ReLU activation function*

# Results and discussion

Our classification model, implemented with Keras and Tensorflow, underwent training for 4-way classification on an 8960-sample dataset. With a batch size of 250 and 100 epochs, the training and validation processes consumed approximately 5 hours, yielding a commendable test set accuracy of 93.75% and an auc of 0.9986. The "metrics" parameter for evaluation was specified as 'accuracy' and also included 'auc-roc' during compilation.

Table II shows the accuracy and auc-roc for different classification models used for 4-way classification Transitioning to multi-class classification, Inception-V3, ResNet-50, and ResNet-18 transfer learning models were applied to the same dataset.

Trained with a batch size of 280 over 50 epochs, Inception-V3 emerged as the top performer, boasting an accuracy of 94.06% and an auc of 0.90. ResNet-50 showcased robust performance as well, achieving an 88.33% accuracy and a 0.90 auc. However, ResNet-18 exhibited a modest 50% accuracy and 80% auc, potentially attributed to its simple design.In summary, our classification and transfer learning models demonstrated promising results, with Inception-V3 leading the way in effective feature extraction and model performance.

Using Python's matplotlib library, accuracy, AUC, and loss metrics of four classification models on training/validation sets were visualized in Fig. 2(a,b,c,d). Confusion matrices were computed, and precision, recall, and F1-Score were derived to assess model performance. Table III presents an overall classification report for the models.

# CONCLUSION AND FUTURE SCOPE

In conclusion, this research explores the predictive capabilities of Convolutional Neural Networks (CNN) and transfer learning models (Inception V3, Resnet-18, Resnet-50) for Alzheimer's disease (AD) progression using the Alzheimer's disease Neuroimaging Initiative (ADNI) dataset. Demonstrating outstanding accuracy, CNN and Inception V3 achieved rates of 93.75% and 94%, respectively. The comparative analysis highlights the unique contributions of each model, offering valuable insights for AD prediction.

This study contributes to reliable deep learning approaches, aiming for enhanced early prediction and diagnosis of AD to improve patient outcomes. For future work, refining and expanding datasets, exploring diverse neural network architectures, and optimizing hyperparameters are suggested. Additionally, integration of real-time patient data, continuous model training, and collaboration with healthcare professionals can enhance practical utility and impact on patient care, addressing challenges like data imbalance and ethical considerations in AI applications for healthcare.

TABLE II. ACCURACY AND AUC ROC VALUES OF DIFFERENT MODELS

|  |  |  |
| --- | --- | --- |
| **Model name** | **Accuracy (%)** | **Area under ROC curve** |
| CNN model | 99.75 | 0.99 |
| Inception-V3 | 94.06 | 0.99 |
| ResNet-50 | 88.33 | 0.96 |
| ResNet-18 | 50.83 | 0.80 |

TABLE III. CLASSIFICATION REPORT FOR DIFFERENT MODELS

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Model name** | **Class label** | **Precision** | **Recall** | **F1-score** |
| CNN model | 0 | 1 | 0.81 | 0.90 |
| 1 | 1 | 1 | 1 |
| 2 | 0 | 1 | 0 |
| 3 | 0 | 1 | 0 |
| Inception-V3 | 0 | 0.97 | 0.99 | 0.98 |
| 1 | 1 | 1 | 1 |
| 2 | 0.91 | 0.87 | 0.89 |
| 3 | 0.88 | 0.90 | 0.89 |
| ResNet-50 | 0 | 0.97 | 0.99 | 0.98 |
| 1 | 1 | 1 | 1 |
| 2 | 0.92 | 0.62 | 0.74 |
| 3 | 0.71 | 0.92 | 0.80 |
| ResNet-18 | 0 | 0 | 0 | 0 |
| 1 | 1 | 1 | 1 |
| 2 | 0 | 0 | 0 |
| 3 | 0 | 0 | 0 |

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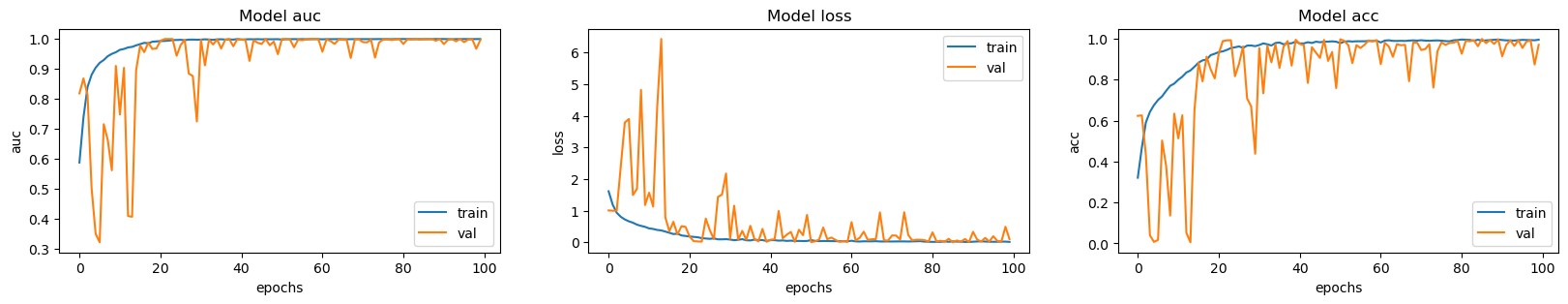


Fig. 2a. AUC-ROC, Loss, Accuracy plots for CNN model

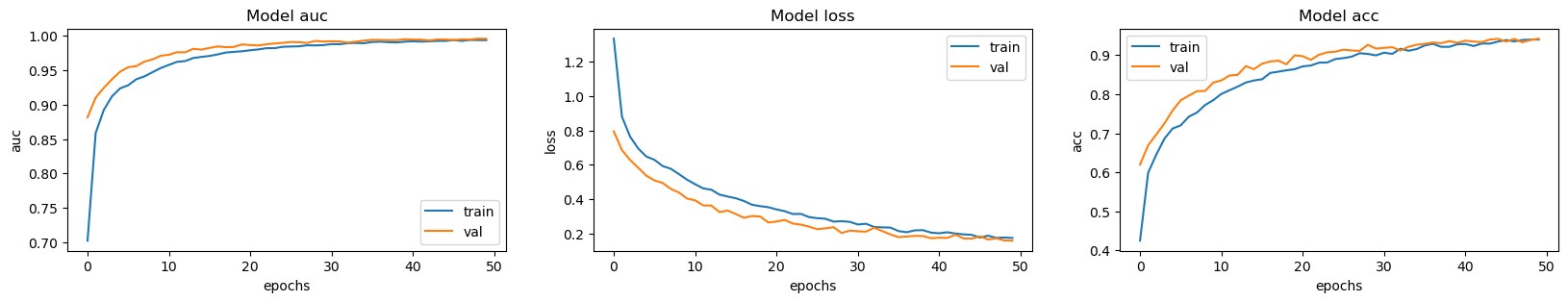


Fig. 2b. AUC-ROC, Loss, Accuracy plots for Inception-V3 model

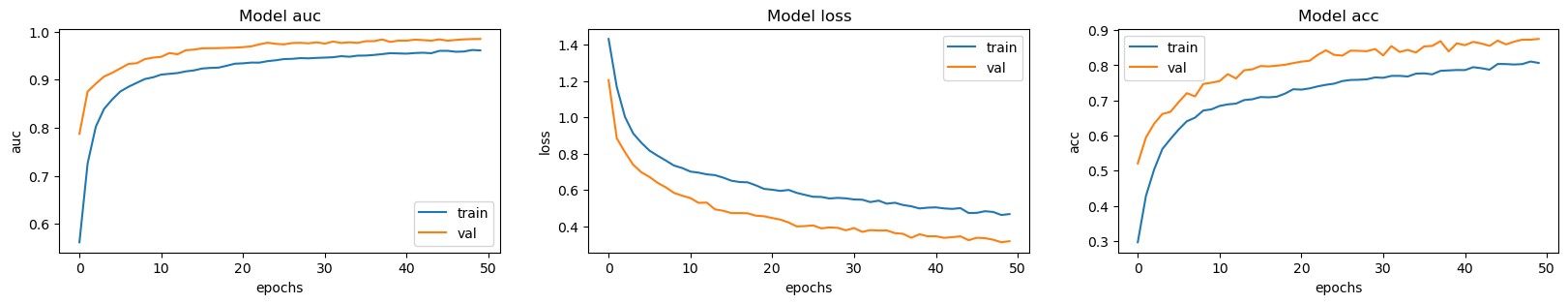


Fig. 2c. AUC-ROC, Loss, Accuracy plots for ResNet-50 model

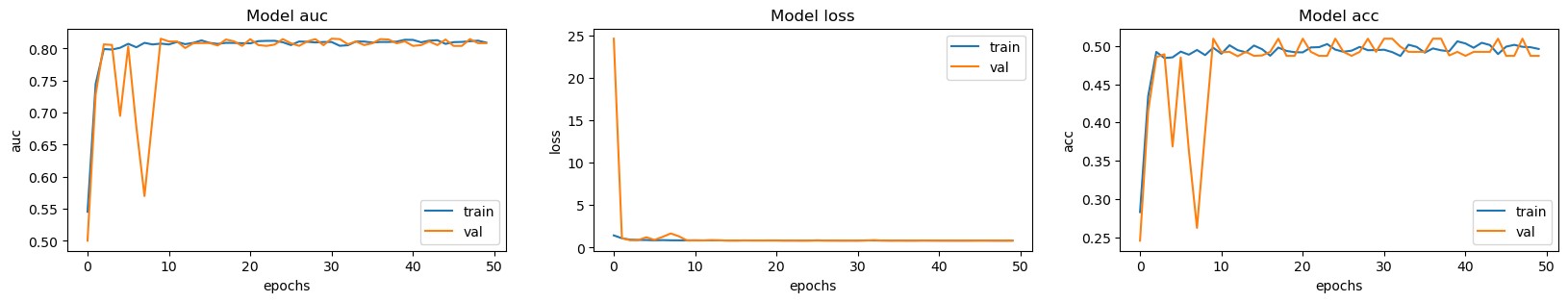


Fig. 2d. AUC-ROC, Loss, Accuracy plots for ResNet-18 model