Fine-tuned Generative Adversarial Network-based Model for Medical Images Super-Resolution

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Abstract

In medical image analysis, low-resolution images negatively affect the performance of medical image interpretation and may cause misdiagnosis. Single image super-resolution (SISR) methods can improve the resolution and quality of medical images. Currently, Generative Adversarial Networks (GAN) based super-resolution models have shown very good performance. Real-Enhanced Super-Resolution Generative Adversarial Network (Real-ESRGAN) is one of the practical GAN-based models which is widely used in the field of general image super-resolution. One of the challenges in the field of medical image super-resolution is that, unlike natural images, medical images do not have high spatial resolution. To solve this problem, we can use transfer learning technique and fine-tune the model that has been trained on external datasets (often natural datasets). In our proposed approach, the pre-trained generator and discriminator networks of the Real-ESRGAN model are fine-tuned using medical image datasets. In this paper, we worked on chest X-ray and retinal images and used the STARE dataset of retinal images and Tuberculosis Chest X-rays (Shenzhen) dataset for fine-tuning. The proposed model produces more accurate and natural textures, and its outputs have better details and resolution compared to the original Real-ESRGAN outputs.

Keywords: Super-resolution, Deep learning, Generative adversarial network, Medical images, Transfer learning, Fine-tune
1. Introduction

Medical images are used to diagnose various diseases and analyze and retrieve important information. [3] In fact, there is a strong need for higher details and resolution in medical images. Usually, better diagnosis is achieved if fine textures and important details are preserved in the image. Unfortunately, capturing high-resolution images is expensive and challenging because it requires complex and expensive equipment, trained manpower, and a lot of time. [1] To address these issues, we can recover high-resolution (HR) images from low-resolution (LR) ones using medical image super-resolution models as a post-processing step to enhance the resolution of the medical images. [2]

The following challenges exist in the field of medical image super-resolution:

- **Importance of details.** Small details and fine textures in medical images contain important information and play an important role in diagnosing diseases and analyzing medical images. For example, in retinal images, there are very small textures that are used in diagnostics (retinal images are in the results section), and also in brain MRI images, small details are used to identify tumors, etc. [1] A very important point that we must pay attention to in the field of medical image super-resolution is that super-resolution models should not remove important details or produce unrealistic and artificial details because it may have an adverse effect on diagnosis. It is clear that this issue is less important in other fields such as general image super-resolution, but in the field of medical image super-resolution, attention should be paid to preserving fine details.

- **Lack of medical data.** Another challenge that exists in the field of medical image super-resolution is the small number of data in most datasets. To solve this problem, the number of data was increased with the help of data augmentation techniques. Transfer learning also helps to solve this problem.
- **Quality of medical images.** The datasets we choose for training or fine-tuning super-resolution models should contain high-resolution images. Finding medical datasets that contain high-quality images is one of the challenges in the field of medical image super-resolution. To solve this problem, datasets containing high-quality images have been used as much as possible.

Traditional image super-resolution includes interpolation-based, reconstruction-based, and machine learning-based methods. Interpolation-based methods such as linear, bicubic, and lanczos often fail to reconstruct fine details and textures, and produce blurred edges. Reconstruction-based and machine learning-based methods have better performance than interpolation-based methods. But they are not very effective in the field of medical image super-resolution.

Medical image super-resolution models based on deep learning can help us to reconstruct the textures and high-frequency information of a low-resolution medical image and also increase its resolution and quality. These models have better performance than traditional models. At first deep learning-based single image super-resolution (SISR) models only used Convolutional Neural Networks (CNN). The super-resolution outputs produced by Convolutional Neural Network-based models often lack rich texture details and have blurred edges. [3] This issue makes them useless in the field of medical image super-resolution.

Nowadays, Generative Adversarial Networks (GANs) [13] are widely used in general and medical image super-resolution fields and perform well in generating high-quality images. The GAN models are more realistic in performance and usually faster than CNN models. Generative Adversarial Network-based super-resolution models have shown significant improvement among deep learning-based models. GAN-based super-resolution models usually use perceptual loss, adversarial loss, and content loss functions to overcome the limitations of previous models. [1] General GAN-based super-resolution models have good super-resolution output, but medical images have different structures and features when compared to natural images. Therefore, a model trained on general datasets does not
perform well in the field of medical image super-resolution. [3] Real-Enhanced Super-Resolution Generative Adversarial Network (Real-ESRGAN) [4] is an effective GAN-based super-resolution model which is used to increase the quality and resolution of general images. This model generates more realistic images with better details and resolution compared to previous models.

These reasons motivated us to modify the Real-ESRGAN model for use in the field of medical image super-resolution. In this work, we fine-tune the pre-trained Real-ESRGAN model with medical image datasets so that it performs better in enhancing the resolution and quality of medical images.

The rest of this paper is organized as follows. We go through some related literature in Section 2. The section 3 includes datasets and preprocessing methods, the structure of generator and discriminator networks of the Real-ESRGAN model, the importance of using the transfer learning technique, and a review of the method and details of the fine-tuning process. The section 4 is devoted to the review and analysis of the results, and Conclusion remarks and future works are given in Section 5.

2. Related Work

In this section, medical and general image super-resolution models are reviewed separately. As we said, small details and fine textures are more important in the field of medical image super-resolution.

2.1. Medical image super-resolution models

Yuhua Chen et al proposed an efficient and accurate GAN-based super-resolution model called mDCSRN [5]. mDCSRN is a 3D multi-level densely connected super-resolution network for enhancing the resolution of brain MRI images. The proposed model has better accuracy and performance in generating high-quality images and also runs 6x faster. This model produces realistic images with high resolution. [5]
MedSRGAN [6] is one of the effective models in the field of medical image super-resolution. In that work, Residual Whole Map Attention Network (RWMAN), as a generator network, extracts useful information and focuses more on meaningful areas. Also, a combination of content loss, adversarial loss, and adversarial feature loss functions is used to create a multi-task loss function. The proposed model generates more realistic images with more natural and accurate textures. [6]

In the field of multimodal medical image super-resolution, Fayaz Ali Dharejo et al proposed Multi-Attention Network with Wavelet Transform. [3] They presented a GAN network with deep multi-attention modules to learn high-frequency information. In that work, they used transfer learning, too. They first trained their proposed model on natural image datasets and then fine-tuned the pre-trained model on medical datasets. Combination of wavelet transform (WT) and GANs in their model overcomes some limitations in reconstructing the details of medical image textures. They used multi-attention GAN loss and perceptual loss functions. Finally, using transfer learning and provided loss functions improved the performance of their model. [3]

2.2. General image super-resolution models

SRGAN [7] was the first GAN-based super-resolution model. The SRGAN generator is a ResNet34 architecture with skip-connection. Christian Ledig et al enhanced the resolution of the LR image with two trained sub-pixel convolution layers. One of the main improvements proposed by this model was providing a new perceptual loss function. The presented perceptual loss function includes both adversarial loss and content loss functions. For the content loss function, they used a loss function that is closer to perceptual similarity rather than pixel-wise losses. The adversarial loss used in this model helped them to use their model for natural images. This model can reconstruct natural textures from LR-degraded images. [7]

In the SRGAN model, details are often associated with unpleasant artifacts. Following that work, many improvements were applied to the SRGAN model. Xintao
Wang et al improved network architecture, adversarial loss, and perceptual loss of the SRGAN model, to create an Enhanced SRGAN (ESRGAN). [8] They proposed the Residual-in-Residual Dense Block (RRDB) without batch normalization. Removing the batch normalization layer improved the performance of the traditional SRGAN architecture and also reduced computational complexity. In the ERSGAN model, the standard SRGAN discriminator was replaced by a relativistic discriminator [17]. Unlike the SRGAN model, they also created more effective perceptual loss by constraining features prior to activation. According to these improvements, the ESRGAN model produces more natural and accurate textures than SRGAN and generates images with better quality and resolution. [8]

In the field of single image super-resolution, much research has been done on different degradation processes applied to images. Researchers have tried to increase the resolution of low-quality images that have been degraded by complex and unknown degradations. But in the real world, more complicated and diverse degradations are applied to images; sometimes several stages of degradation may be applied to images. In the Real-ESRGAN [4] model, a high-order degradation modeling process is used to solve these problems. In this process, more complex and unknown real-world degradations are applied to the images. One of the things that have been paid attention to in the high-order degradation process is the ringing and overshoot artifacts. The ringing and overshoot artifacts are usually generated by JPEG compression, etc. In this model, a sinc filter is used to synthesize these artifacts. [4]

It should be noted that the use of the Residual-in-Residual Dense Block (RRDB) in the ESRGAN model increases computational complexity. In the Real-ESRGAN model, most calculations are done in a smaller space, which makes the computations faster. In this model, a U-Net discriminator [10] with spectral normalization [11] is used to improve the performance of the discriminator network in distinguishing between the generated output and ground truth image. Also, spectral normalization is used to stabilize the dynamics of the training. [4] Due to these improvements and the excellent performance of the Real-ESRGAN model in the field of general image super-resolution, we fine-tuned this model to improve the resolution of medical images.
3. METHODOLOGY

In this section, the proposed method is explained. The first sub-section includes the important points in dataset selection, the datasets used, and the preprocessing technique. The structure of Real-ESRGAN model and its improvements compared to previous models are reviewed in sub-section 2. Transfer learning and the benefits of using it in the field of medical image super-resolution have been discussed in the third sub-section. In the next sub-section, the methods used for fine-tuning and generating degraded images have been explained. Also, the parameters and details of the fine-tuning process are described in the last sub-section.

3.1. Datasets and Preprocessing

One of the important steps in fine-tuning is choosing the right dataset. The following points are considered in choosing the right dataset for fine-tuning Generative Adversarial Network-based super-resolution models:

- The selected dataset should contain high-quality images.
- The dataset we choose should contain images related to our application.
- We use Generative Adversarial Networks, so a relatively large amount of data is required to fine-tune the model.

Retinal images dataset. STARE (STructured Analysis of the Retina) dataset is one of the most commonly used datasets in the field of medical image super-resolution. This dataset contains just 397 images with good quality, so we need data augmentation techniques to compensate for the shortage of data.

Chest X-ray images dataset. Tuberculosis Chest X-rays (Shenzhen) dataset contains high-quality photos that are very suitable for our application. The total number of images in this dataset is 662, and we need data augmentation techniques to compensate for the shortage of data.
As we said, GAN-based models require a relatively large amount of data for training or fine-tuning, and we need data augmentation techniques to compensate for the small number of images in dataset of the chest X-ray and retinal dataset. So we generated multiscale images. In this step, the high-quality images are down-sampled to get several ground truth images at different scales, and then these images are combined with the original images. Finally, for each type of medical data (chest X-ray and retinal images), the number of images was increased fivefold.

3.2. Networks Architecture

In this part, the generator and discriminator networks of the Real-ESRGAN model are investigated separately.

3.2.1. Generator:

Xintao Wang et al used a deep neural network with several residual-in-residual dense blocks (RRDB) same as ESRGAN [8] generator. RRDB uses a deeper and more complex structure than the residual block in SRGAN. This generator has 23 residual-in-residual dense blocks (RRDB) and each of these RRDBs has three Residual-Dense-Blocks. Residual-Dense-Blocks include five convolutional layers with Leaky-RELU layers. An up-sampling block and two convolution layers come after RRDB blocks. In addition, residual scaling technique is used to make network training easier. [4] In the Real-ESRGAN model, the pixel-unshuffle operation [12] is used first before entering the inputs into the generator, and most calculations are done in a smaller space. [4]

3.2.2. Discriminator:

For better performance of the generator in producing high-quality images, the discriminator in the Real-ESRGAN model needs more discrimination power. One of the main improvements of the Real-ESRGAN model is the use of a U-Net discriminator [10] with spectral normalization [11]. This is a relativistic discriminator [17] that predicts relative
realness rather than the absolute values. [8] This discriminator can provide accurate feedback of each pixel, and also generate realness values for each pixel. [4] As we said, in the field of medical image super-resolution, our model should not remove important details or produce artifact details. Spectral normalization is useful for reducing overly sharp and unpleasant artifacts. [4] This technique is very useful in enhancing the resolution of medical images.

3.3. Transfer Learning

Training the Real-ESRGAN model from scratch with medical data requires powerful hardware resources, huge number of images, and a lot of time. In fact, the main Real-ESRGAN model was trained with four NVIDIA V100 GPUs on DIV2K [14], Flickr2K [15], and OutdoorSceneTraining [16] datasets.

Transfer learning is very useful in medical applications. In our proposed approach, transfer learning is the process of taking a model that has been already trained for general image super-resolution, and then fine-tune it on a second similar task on a smaller dataset (medical image super-resolution). Using a previously designed and trained neural network allows us to use what the model has already learned without having to develop it from scratch. In this regard, transfer learning technique is used to improve the performance of Generative Adversarial Networks in generating high-quality medical images by using knowledge learned from general image datasets. Using the high-frequency information from general image datasets improves our model’s performance to enhance the resolution of medical images. In addition, transfer learning helps the model to converge faster. [3]

3.4. Methods

We can fine-tune the Real-ESRGAN model in two ways:

1- Generating LR degraded images by Real-ESRGAN model during fine-tuning.
2- Using our pair of data, i.e. HR (high resolution) and LR (low resolution) sets.
Depending on the application and the datasets we have, we may choose one of these methods, or in some cases, it may be better to examine both methods. As we said, one of the improvements of the Real-ESRGAN model is that in this model, a high-order degradation modeling process is used to generate LR degraded images. [4] So in this work, the first method has been used to fine-tune the Real-ESRGAN model.

We need to generate degraded images during the fine-tuning process. The degradation process is similar to the process explained in the Real-ESRGAN paper. [4] The classic degradation process usually includes blurring, applying various noises, down-sampling, and jpeg compression. Xintao Wang et al extended the classical degradation model to a high-order degradation process to apply more complex and unknown degradations. To synthesize ringing and overshoot artifacts, they used a 2D sinc filter that cuts off high frequencies. [4] Finally, two degradation processes are applied to the images and the final degraded images are produced.

Another point that should be noted is that the structure and texture of chest X-ray and retinal images are different, so we fine-tuned the model separately for each of them.

3.5. Fine-tuning Details

Medical image datasets have not been used to train the Real-ESRGAN model. Also, our new data is very different from the original datasets that the model was trained on, so a higher number of epochs is needed.

It usually takes a lot of time to train or fine-tune GAN networks. To solve this problem, we can use stronger systems. We used google colab pro GPU to fine-tune the model. In this work, at first, the weights of the pre-trained generator and discriminator networks of the Real-ESRGAN model are loaded. In the next step, the Adam optimizer is used to optimize the weights of the networks. In the Real-ESRGAN model, the RRDB network has 16,697,987 parameters and the discriminator network has 4,376,897 parameters. Similar to training the Real-ESRGAN model, L1 loss, perceptual loss (content and style losses), and GAN loss functions are used for fine-tuning. We set the learning rate
to 0.0001 and adopted exponential moving average (EMA) for more stable fine-tuning and better performance.

The number of required epochs is obtained empirically. In this way, we started with a lower epoch number and changed the number according to the result we were getting. For retinal images, we passed 10000 iterations which are approximately equal to 50 epochs, and for chest X-ray images we passed 16600 iterations which are approximately equal to 50 epochs.

4. Results

We need LR-degraded images to test the performance of our model. To generate the degraded images, we often used blurring, down-sampling, and heavy jpeg compression. To better compare the performance of the models, the original image, LR degraded image, Real-ESRGAN output, and fine-tuned Real-ESRGAN output are shown in figures 1 and 2 on retinal images and figures 3 and 4 on chest X-ray images.

4.1. Retinal images

![Retinal images](image)
Figure 1. Columns 1–4 are the high-resolution ground truth images, LR degraded images, the outputs of the original Real-ESRGAN, and the outputs of the fine-tuned Real-ESRGAN for three different retinal images. As one can see, the pictures in the last column have more details regarding the thinner veins.

In the following, the magnified regions of the above images are shown to better compare the fine textures in the retinal images. As we said, these textures play an important role in diagnosing diseases.
Figure 2. (a) high-resolution ground truth image. (b) LR degraded image. (c) the output of the original Real-ESRGAN. (d) the output of the fine-tuned Real-ESRGAN. The fine-tuned model produces more accurate and natural textures, and its outputs have more realistic details compared to the original Real-ESRGAN outputs.

4.2. Chest X-ray images

| Ground truth | Input | Real-ESRGAN | Fine-tuned Real-ESRGAN |
|-------------|-------|-------------|------------------------|
| ![Ground truth](image1.jpg) | ![Input](image2.jpg) | ![Real-ESRGAN](image3.jpg) | ![Fine-tuned Real-ESRGAN](image4.jpg) |
| ![Ground truth](image5.jpg) | ![Input](image6.jpg) | ![Real-ESRGAN](image7.jpg) | ![Fine-tuned Real-ESRGAN](image8.jpg) |
| ![Ground truth](image9.jpg) | ![Input](image10.jpg) | ![Real-ESRGAN](image11.jpg) | ![Fine-tuned Real-ESRGAN](image12.jpg) |

Figure 3. Columns 1–4 are the high-resolution ground truth images, LR degraded images, the outputs of the original Real-ESRGAN, and the outputs of the fine-tuned Real-ESRGAN for three different chest X-ray images. As one can see, the output images of the fine-tuned model are close to the original ones.
Figure 4. Magnified regions of chest X-ray images to better compare small details. (a) high-resolution ground truth image. (b) LR degraded image. (c) the output of the original Real-ESRGAN. (d) the output of the fine-tuned Real-ESRGAN. The fine-tuned model has increased the resolution and quality of chest X-ray images, and has not removed important details or generated artificial details.

As we said before, we need high-quality data to train or fine-tune super-resolution models. It is clear that if we use more quality data and also if we have more data, we will probably have better outputs.

5. Conclusion and future directions

This work focused on increasing the resolution and quality of medical images. For this, we used the pre-trained Real-ESRGAN model and fine-tuned it with medical image datasets. The outputs of the fine-tuned model are more realistic than the original model and have more accurate and natural textures. In addition, our model has not removed important details or generated artificial details.

In this paper, we worked on chest X-ray and retinal images. The original Real-ESRGAN model can also be fine-tuned for MRI and CT scan images. For further work, if LR subset has appropriate degraded images, one can use the second method mentioned in the methods section. One of the future directions is to use the A-ESRGAN [9] model and fine-tuned it to increase the resolution of medical images. A-ESRGAN is an improved version of the Real-ESRGAN model that uses an attention U-Net-based, multi-scale discriminator.
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