Classification of Medical Images and Illustrations in the Biomedical Literature Using Synergic Deep Learning

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Abstract—The Classification of medical images and illustrations in the literature aims to label a medical image according to the modality it was produced or label an illustration according to its production attributes. It is an essential and challenging research hotspot in the area of automated literature review, retrieval and mining. The significant intra-class variation and inter-class similarity caused by the diverse imaging modalities and various illustration types brings a great deal of difficulties to the problem. In this paper, we propose a synergic deep learning (SDL) model to address this issue. Specifically, a dual deep convolutional neural network with a synergic signal system is designed to mutually learn image representation. The synergic signal is used to verify whether the input image pair belongs to the same category and to give the corrective feedback if a synergic error exists. Our SDL model can be trained ‘end to end’. In the test phase, the class label of an input can be predicted by averaging the likelihood probabilities obtained by two convolutional neural network components. Experimental results on the ImageCLEF2016 Subfigure Classification Challenge suggest that our proposed SDL model achieves the state-of-the-art performance in this medical image classification problem and its accuracy is higher than that of the first place solution on the Challenge leader board so far.

Keywords—Medical image classification; Synergic deep learning model; Dual deep convolutional neural network

I. INTRODUCTION

The indispensable role of digital medical imaging in the modern healthcare has led to the fast growth of digital images in all types of electronic biomedical publications. This fast growth poses great challenges for image retrieval, review and recruiting data for clinical care and research settings. Hence, there have been a large number of image classification researches aiming to improve the data mining ability in this area\textsuperscript{2,5,7}. The ImageCLEF2016 Subfigure Classification Challenge\textsuperscript{3}, recognizing the increasing complexity of images in biomedical literatures, contains figures with sub-figures that produced by multiple imaging modalities and illustrations drawn from analysis of medical data.

Image classification has been thoroughly studied during the past decades with a huge number of solutions being published in the literatures\textsuperscript{11,12,24,25,30}. These solutions usually consist of the handcrafted feature extraction and classifier learning process. Despite of their success, it is difficult to design the handcrafted feature that is optimal for a specific classification task. Recently, with the deep learning methods being introduced, medical image analysis has experienced a rapid development. Especially, due to the fact that deep learning models can overcome the need for manual feature design and have superior classification capabilities, the medical image detection, classification\textsuperscript{22,27} and segmentation\textsuperscript{11,14} enjoyed a performance boosting. For example, Xu et al.\textsuperscript{28} adopted a deep convolutional neural network to minimize manual annotation and produce good feature representations for colon cancer classification using histopathology images. Shen et al.\textsuperscript{21} developed a multi-crop pooling strategy and applied it to a convolutional neural network to capture object salient information for lung nodule classification in CT images.

Although deep learning-based approaches outperform the state-of-the-art in a number of medical image analysis tasks in the field, substantial challenges still remain. For example, the issues with medical image datasets, including small datasets and anatomical variations, still restrict the effectiveness of classifying medical images and illustrations in the literature. The first issue usually relates to the work that required in acquiring the image data and then in image annotation\textsuperscript{26}. Pre-trained deep convolutional neural network (DCNN) models have been used to address this issue, due to the strong transfer learning ability of the DCNN, i.e. learned from large-scale datasets like ImageNet, could be transferred to solving generic small-data visual recognition problems\textsuperscript{15,17}. Koitka et al.\textsuperscript{8} extracted the activation values from the last FC1000 layer in a pre-trained ResNet-152 model and adopted them to train a custom network layer using the pseudo inverse method\textsuperscript{18}. Kumar et al.\textsuperscript{2} proposed to integrate two different pre-trained CNN architectures and ensemble the results from multiple models into one high-quality classifier.

The second issue is the intra-class variation and inter-class similarity\textsuperscript{29}, which poses even greater challenges for classi-
fying medical images according to the different modalities, by which they were produced. A typical example that highlights the difficulty is shown in Figure 1, in which the brain CT and pleural CT images in the top row looks dissimilar due to viewing different anatomical structures although they belong to the same category; whereas the brain CT and MRI CT images in the left column look very similar but belonging to different categories. Although deep neural networks have enough capacity to forcibly remember all training samples [31], the ambiguity produced by intra-class variation and inter-class similarity may tease a neural network and make it fall into confusion. The neural network makes right decision with the low confidence level and the results may even completely opposite if adding small fluctuations in the input.

In this paper, synergic deep learning (SDL) is presented to enhance the distinguishing ability of deep neural networks, especially for those confusing samples. The basic learning strategy of SDL is to use a synergic signal to bridge several neural networks so that they can guide and benefit from each other. We specifically design a SDL model that consists of a dual deep convolutional neural network (dual-DCNN) and a synergic signal system in this paper to solve the medical image classification problems. It’s advisable to initialize our dual-DCNN with the pre-trained DCNN, whose parameters were derived from the ImageNet dataset [4] and further fine tune it with our image dataset. However, to break the independence between dual DCNNs, an additional synergic signal, serving as an information bridge between two DCNNs, is used to verify whether the input pair belongs to the same category or not. The wrong decision made by a DCNN will be highlighted with the low confidence level and the results may even completely opposite if adding small fluctuations in the input.

The dual-DCNN is an important module in our SDL model that contains two complete learning units, namely DCNN-A and DCNN-B. In principle, any DCNN with arbitrary structure can be embedded in our SDL model. Here, due to the strong representation capability of the famous residual network [6], we employ a pre-trained residual neural network (ResNet-50, as shown in Figure 3) as the initialization of our DCNN-A and DCNN-B. It is composed of 50 learnable layers, and its parameters have been converged by training on the ImageNet dataset, for an image classification task. It’s worth to note that two parameter sets of the DCNN-A and DCNN-B, denoted by \( \theta^A \) and \( \theta^B \), are not shared. To adapt the ResNet-50 model to our image dataset, we replace all fully connected (\( FC \)) layers with a \( FC \) layer of 1024 neurons (\( FC1024-A/B \)), a \( FC \) layer of \( K \) neurons (\( K \)-class classification) and a softmax layer, and then fine tune the parameters of ResNet-50 by using our own training data. The weights of new \( FC \) layers are initialized by uniform distribution \( U(-0.05, 0.05) \). The cross-entropy loss function of each DCNN is defined as

\[
 l(\theta) = \frac{1}{M} \sum_{i=1}^{M} \left[ \log \left( \sum_{j=1}^{K} e^{\theta^T_j x^{(i)}} \right) - \theta^T_{y^{(i)}} x^{(i)} \right] 
\]

where \( M \) is the number of training data. The mini-batch stochastic gradient descent (mini-batch SGD) algorithm is used to optimize \( \theta \).

Both DCNN-A and DCNN-B accept input from a pair of images, aiming to supervise the training process in each learning unit with the true labels of corresponding input sequences. and the experimental results show that our proposed SDL model is the state-of-the-art on the medical classification problem.

II. The Synergic Deep Learning Model

Our proposed SDL model consists of three main components, i.e. a data pair input layer, a dual-DCNN and a synergic signal system, as shown in Figure 2. Different from the one by one input mode of conventional deep models, our SDL model accepts a pair of inputs that are randomly selected from the training set. A dual-DCNN, including DCNN-A and DCNN-B, is the main learning module with two input sequences. Both DCNN-A and DCNN-B are pre-trained residual neural networks and fine-tuned with the supervision of the true labels of outputting sequences. Besides, a synergic signal system is used to verify whether the input pair belongs to a same category or not, and gives the corrective feedback if a synergic error exists. For instance, in Figure 2, the first pair of images with high structure similarity actually belong to different classes. The second pair comes from the same class, but visually they are different. It’s easy for a weak DCNN to make false decision under the contrast. The error generated from synergic signal system will further modify the dual-DCNN to have a stronger ability to distinguish these confusing samples.

We discuss the details of our proposed SDL model in the following sections.

A. The Dual Deep Convolutional Neural Network

The dual-DCNN is an important module in our SDL model that contains two complete learning units, namely DCNN-A and DCNN-B. In principle, any DCNN with arbitrary structure can be embedded in our SDL model. Here, due to the strong representation capability of the famous residual network [6], we employ a pre-trained residual neural network (ResNet-50, as shown in Figure 3) as the initialization of our DCNN-A and DCNN-B. It is composed of 50 learnable layers, and its parameters have been converged by training on the ImageNet dataset, for an image classification task. It’s worth to note that two parameter sets of the DCNN-A and DCNN-B, denoted by \( \theta^A \) and \( \theta^B \), are not shared. To adapt the ResNet-50 model to our image dataset, we replace all fully connected (\( FC \)) layers with a \( FC \) layer of 1024 neurons (\( FC1024-A/B \)), a \( FC \) layer of \( K \) neurons (\( K \)-class classification) and a softmax layer, and then fine tune the parameters of ResNet-50 by using our own training data. The weights of new \( FC \) layers are initialized by uniform distribution \( U(-0.05, 0.05) \). The cross-entropy loss function of each DCNN is defined as

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\]
Fig. 2: Architecture of the SDL model, which consists of a dual deep convolutional neural network and an additional synergic signal system. The input is a pair of images which are sampled from the training set.

Fig. 3: Architecture of ResNet-50 model.

Although each DCNN has the ability to predict the label class of an input image, we creatively embed the activations from last two fully connected layers in both DCNNs into a synergic signal system to break the learning independence of the dual DCNNs.

B. Synergic Signal System

In our SDL model, a synergic signal system is designed to supervise the learning from the input pairs and bridge the gap between dual DCNNs. The architecture of this system is shown in Figure 4. Image representations need to be input into the synergic signal system in pairs. We randomly select image pairs from the training data and denote the property of a pair \((x_A, x_B)\) as

\[
S(x_A, x_B) = \begin{cases} 
1 & \text{if } y_A = y_B \\
0 & \text{if } y_A \neq y_B
\end{cases}.
\]  

(2)

where \(x_A\) and \(x_B\) are outputs of FC1024-A and FC1024-B, \(y_A\) and \(y_B\) are true labels of \(x_A\) and \(x_B\), respectively. Here, ‘\(S = 1\)’ is a positive pair and ‘\(S = 0\)’ is a negative pair. Image pairs are selected from each min-batch. To avoid the unbalance data problem, the number of positive pairs in a batch is about 45%–55%. \(x_A\) and \(x_B\) are concatenated together into an embedding layer followed by a FC layer with 2 neurons. It’s convenient to monitor the synergic signal by adding another softmax layer and using the following cross-entropy loss

\[
L^S(\theta^S) = \frac{1}{M} \sum_{i=1}^{M} \log \left( \sum_{j=1}^{K'} e^{\theta^T_{y^i_{(j)}} (x_{T_{(i)}^A} - x_{T_{(i)}^B})} - \theta^T_{y^i_{(j)}} T_{(i)}^A - T_{(i)}^B \right) 
\]

(3)

where \(\theta^S\) is the ensemble of parameters of the synergic signal system. The detailed learning process of our proposed model is summarized in Table 1.

C. Test Phase

In the test phase, for a test image \(x\), the DCNN-A and DCNN-B give predictions \(P^A = (p_1^A, p_2^A, ..., p_K^A)\) and \(P^B = (p_1^B, p_2^B, ..., p_K^B)\), which are activations in last FC layer. The additional synergic signal is abandoned for final classification results in the test phase. The predicted label of the input \(x\) is denoted as

\[
\text{argmax}_i \{ (p_1^A + p_1^B), ..., (p_i^A + p_i^B), ..., (p_K^A + p_K^B) \}
\]

(4)
Table I: Learning process of the synergic deep learning model.

| Step1: | Concatenate two input features FC1024-A and FC1024-B into a combined one, which is denoted as \((x_A, x_B)\). The labels of these three supervisions are \(y_A, y_B, y_S\). |
| Step2: | Update parameters \(\theta^A, \theta^B\) and \(\theta^S\) by using back-propagation algorithm. |

Compute loss: \(l^A(\theta^A), l^B(\theta^B)\) and \(l^S(\theta^S)\),

Compute gradient:

\[
\frac{\partial l^A(\theta^A)}{\partial \theta^A_k} = \frac{1}{m} \sum_{i=1}^{m} x_A^{(i)} \left[ e^{\theta^A_k^T x_A^{(i)}} \sum_{j=1}^{K} e^{\theta^A_j^T x_A^{(i)}} - \delta_{k y_A^{(i)}} \right], \\
\frac{\partial l^B(\theta^B)}{\partial \theta^B_k} = \frac{1}{m} \sum_{i=1}^{m} x_B^{(i)} \left[ e^{\theta^B_k^T x_B^{(i)}} \sum_{j=1}^{K} e^{\theta^B_j^T x_B^{(i)}} - \delta_{k y_B^{(i)}} \right], \\
\frac{\partial l^S(\theta^S)}{\partial \theta^S_{i}} = \frac{1}{m} \sum_{i=1}^{m} \left( x_A^{(i)} \cdot x_B^{(i)} \right)^T \left[ e^{\theta^S_{i}^T (x_A^{(i)} \cdot x_B^{(i)})} \sum_{j=1}^{K} e^{\theta^S_{j}^T (x_A^{(i)} \cdot x_B^{(i)})} - \delta_{k y_S^{(i)}} \right],
\]

\(
\Delta^A = \frac{\partial l^A(\theta^A)}{\partial \theta^A_k} + \lambda \frac{\partial l^S(\theta^S)}{\partial \theta^S_{i}}, \quad \Delta^B = \frac{\partial l^B(\theta^B)}{\partial \theta^B_k} + \lambda \frac{\partial l^S(\theta^S)}{\partial \theta^S_{i}},
\)

where \(\delta_{k y_A^{(i)}} = \begin{cases} 1 & k = y_A^{(i)} \\ 0 & k \neq y_A^{(i)} \end{cases}\) and \(\lambda\) is a weighting factor of synergic signal.

Update parameters:

\(\theta^A = \theta^A - \eta(t) \cdot \Delta^A\) and \(\theta^B = \theta^B - \eta(t) \cdot \Delta^B\).

Fig. 5: A simple convolutional neural network (LeCNN) architecture used in MNIST experiment.

III. EXPERIMENTS

A. A toy example

In this section, a toy example on the MNIST dataset is presented. Based on the classical LeNet-5 model, we designed a simple convolutional neural network called LeCNN, shown in Figure 5, as the architecture of DCNN-A and DCNN-B modules. Thus, the SDL model is composed of two LeCNNs and a synergic signal system. To simply evaluate the effectiveness of our SDL model, we set the \(\lambda = 1\). Figure 6 shows the loss and accuracy curves obtained on the training and testing sets during the training progress. It suggests that using the synergic signal system does lead to performance improvement, as our SDL model has lower loss and higher accuracy than the LeCNN model.

B. Dataset

We evaluated our SDL model on the ImageCLEF2016 Subfigure Classification Challenge dataset [3], which consists of 6776 training images and 4166 testing images collected from the PubMed Central (PMC) [16]. These images are divided into 30 categories, including 12 categories of medical diagnostic images, such as CT images, MRI images and PET images, and 18 categories of illustrations, such as figures, tables and flow charts. The abbreviations and details of each image category were listed in Table 2. The aim of our experiment is to classify medical diagnostic images according to the modality they were produced and classify illustrations according to their production attributes.

*http://www.ncbi.nlm.nih.gov/pmc/

Fig. 6: Comparison of LeCNN and proposed SDL on the MNIST dataset.

C. Parameter Settings

To leverage the overfitting issue in deep learning, we utilized several data augmentation strategies, including rotation, translation and random scaling, to enlarge our dataset 10 times. We designed the following variable learning rate

\[
\eta(t) = \frac{\eta(0)}{1 + 10^{-4} \times t}
\]

where \(t\) is the index of iteration and \(\eta(0) = 0.00005\). We set the maximum epoch number to 80 and adopted the minibatch stochastic gradient descent with a batch size 64 as the optimizer. To stop the training process when the model falls into overfitting, 20% of training data were randomly selected to form a validation set, which was used to monitor the performance of our model. We evaluated our proposed model with different values of the hyper parameter \(\lambda\). The performance shown in Figure 7 reveals that our model achieves the lowest loss and highest accuracy when \(\lambda = 40\). Hence, we empirically set the value of \(\lambda\) to 40 in our experiments.
TABLE II: Category abbreviations and details in the ImageCLEF2016 classification hierarchy.

| No. | Abb.               | Det.                  | Training |
|-----|--------------------|-----------------------|----------|
| 1   | D3DR               | 3D reconstructions    | 201      |
| 2   | DMEL               | Electron microscopy   | 208      |
| 3   | DMFL               | Fluorescence microscopy | 906    |
| 4   | DMLI               | Light microscopy      | 696      |
| 5   | DMTR               | Transmission microscopy | 300    |
| 6   | DRAN               | Angiography           | 17       |
| 7   | DRCO               | Combined modalities in one image | 33 |
| 8   | DRCT               | Computerized Tomography | 61     |
| 9   | DRMR               | Magnetic Resonance    | 139      |
| 10  | DRPE               | PET                   | 14       |
| 11  | DRUS               | Ultrasound            | 26       |
| 12  | DRXR               | X-ray, 2D Radiography | 51       |
| 13  | DSEC               | Electrocardiography   | 10       |
| 14  | DSEE               | Electroencephalography | 8      |
| 15  | DSEM               | Electromyography      | 5        |
| 16  | DVDM               | Dermatology, skin     | 29       |
| 17  | DVEN               | Endoscopy             | 16       |
| 18  | DVOR               | Other organs          | 55       |
| 19  | GCHE               | Chemical structure    | 61       |
| 20  | GFIG               | Statistical figures, graphs, charts | 2954 |
| 21  | GFLO               | Flowcharts            | 20       |
| 22  | GGEL               | Chromatography, Gel   | 344      |
| 23  | GGEM               | Gene sequence         | 179      |
| 24  | GHDR               | Hand-drawn sketches   | 136      |
| 25  | GMAT               | Mathematics, formulate | 15     |
| 26  | GNCP               | Non-clinical photos   | 88       |
| 27  | GPLI               | Program listing       | 1        |
| 28  | GSCR               | Screenshots           | 33       |
| 29  | GSYS               | System overviews      | 91       |
| 30  | GTAB               | Tables and forms      | 79       |

D. Results and Analysis

We evaluated our proposed SDL model against the standard ResNet-50 model with the same experiment settings, including the same training set, validation set, initial parameters and learning rate scheme. Figure 8 shows the loss and accuracy curves of both models on the validation dataset. The smaller loss and higher accuracy achieved by the SDL model indicate that our model outperforms ResNet-50 on the validation set.

The classification accuracies of the ResNet-50 model, each component of our model i.e. DCNN-A or DCNN-B, and our SDL model on the validation set were displayed in Figure 9. It shows that, after incorporating the synergic signal system into the dual-DCNN architecture, each component of our model, which is also ResNet-50, achieves more than 2% accuracy improvement, as compared to the standard ResNet-50. Moreover, jointly using those two component in an ensemble learning manner can further improve the classification accuracy.

The F-scores [19] of our SDL model and ResNet-50 model were calculated on each category of the test dataset and were depicted in Figure 10, in which a red arrow indicates an increased accuracy when applying our model to that category of test data, whereas a blue arrow suggests a decreased accuracy. It shows that our model achieves higher classification accuracy than ResNet-50 on most categories.

Next, we evaluated our SDL model on the ImageCLEF2016 test set. Figure 11 gives the confusion matrix of the classification results obtained by using our SDL model. The x-axis is the predicted label, and y-axis is the true label. A higher intensity value represents higher classification accuracy. Since this is a highly imbalanced classification problem, we let the size of each rectangle in this figure be proportional to the number of training images in each class. The confusion matrix shows that component of our model i.e. DCNN-A or DCNN-B, and our SDL model on the validation set were displayed in Figure 9. It shows that, after incorporating the synergic signal system into the dual-DCNN architecture, each component of our model, which is also ResNet-50, achieves more than 2% accuracy improvement, as compared to the standard ResNet-50. Moreover, jointly using those two component in an ensemble learning manner can further improve the classification accuracy.

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our SDL model achieves relatively accurate classification on every major category and most minor categories.

Table 3 gives the classification accuracy of our proposed SDL model, ResNet-50 model, Kumar’s ensemble method and the accuracy of six best-performed solutions listed in the ImageCLEF2016 Subfigure Classification Challenge leader board. Obviously, handcraft feature engineering underperforms deep learning-based methods, and deeper network, such as ResNet-152, performs better than ResNet-50. However, our SDL model achieves the so far best classification accuracy in this challenge. Please note that our SDL model is capable of adapting any DCNN structures, which means it can benefit from much deeper models, such as ResNet-152.

IV. CONCLUSIONS

In this paper, we propose a synergic deep learning (SDL) model that contains a dual collaborative deep convolutional neural network and an additional synergic signal system to classify medical images and illustrations in the biomedical literature. To strength the collaborative learning of a dual nets, the synergic signal is used to verify whether an input pair belongs to a same category or not. It promotes that our SDL model has stronger representation ability to distinguish those easily confused inter-class samples and obvious diversity of intra-class samples. Experimental results on the ImageCLEF2016 Subfigure Classification Challenge dataset show that our proposed SDL model achieves the state-of-the-art performance in this medical image classification problem, with an accuracy higher than the first place on the Challenge leader board at the time of submission.

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