A Labeling-Free Approach to Supervising Deep Neural Networks for Retinal Blood Vessel Segmentation

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Abstract—Segmenting blood vessels in fundus imaging plays an important role in medical diagnosis. Many algorithms have been proposed. While deep Neural Networks have been attracting enormous attention from computer vision community recent years and several novel works have been done in terms of its application in retinal blood vessel segmentation, most of them are based on supervised learning which requires amount of labeled data, which is both scarce and expensive to obtain. We leverage the power of Deep Convolutional Neural Networks (DCNN) in feature learning, in this work, to achieve this ultimate goal. The highly efficient feature learning of DCNN inspires our novel approach that trains the networks with automatically-generated samples to achieve desirable performance on real-world fundus images. For this, we design a set of rules abstracted from the domain-specific prior knowledge to generate these samples. We argue that, with the high efficiency of DCNN in feature learning, one can achieve this goal by constructing the training dataset with prior knowledge, no manual labeling is needed. This approach allows us to take advantages of supervised learning without labeling. We also build a naive DCNN model to test it. The results on standard benchmarks of fundus imaging show it is competitive to the state-of-the-art methods which implies a potential way to leverage the power of DCNN in feature learning.

Index Terms—Deep neural networks, retinal blood vessel segmentation, labeling-free, prior knowledge, feature learning

I. INTRODUCTION

Retinal is a key component for our visual perception. It transforms incoming light to neural signal for further processing. Morphological features of retinal vessel can be used for various purposes such as monitoring the disease progression, treatment, and evaluation of various cardiovascular and ophthalmologic diseases [1].

While the pattern of retinal vessels delivers significant information for diagnosis [2], comprising arteries and lots of veins make manual segmentation both tedious and time-consuming [3]. Aimed to develop algorithms for vessel segmentation, it has been a main focus over years to exploit computer’s strong ability in computing to facilitate this work [4]. But complexities existing in retinal images such as nonuniform illumination, lower contrast [5], abrupt variation in branching patterns [6] makes it a nontrivial task to accomplish [5].

Although there has been a number of previous works related to this topic [7]. The Artificial Neural Networks, namely, Deep Learning [8], has been attracting more and more attention following the novel works by [9]. Inspired by the organization of the animal visual cortex [10]. Convolutional Neural Networks (CNN) has made a number of achievements in the field of computer visual [8]. It is composed of multiple processing layers, typically, filter bank layer, nonlinearity layer, feature pooling layer [11], to learn inherent characters of data with multiple levels of abstraction. It overcomes the previously existed drawbacks in processing natural data in their raw form and achieves competitive performance in pattern recognition [8].

In the scope of CNN, supervised learning strategy is commonly invoked in training stage [8], in which the learning system takes samples as input, and then measures the error between current output and its corresponding goal, known as label. Then gradient of the parameters (weight and bias) in the top layer which is nearest to the output is calculated. By exploiting back-propagation [12], configuration of each layer below the top will be rectified. CNN with deep structure (Deep Convolutional Neural
Networks, DCNN) have attracted much more attention since impressive results have been presented by [13]. It comes with much more layers [14], more powerful processor (graphics processing unit), and larger dataset [15] and is to achieve unprecedented performance ([13] et al.).

As mentioned above, labels are required in supervised learning for each input. As deep learning takes more advantages on large datasets [16], more labels are desired. However it is difficult to obtain massive samples together with the corresponding labels in terms of retinal vessel segmentation; further more, lack of labeled data becomes a major problem hampering us from utilizing its power for specific domain.

Our contributions are summarized as followings:

- we propose a novel approach to address the lack of labeled data by automatically generating samples and labels from domain-specific knowledge;
- we also provide a deep neural networks model to evaluate our approach.

II. RELATED WORKS

In previous works, [17] prepares the feature combining gray-level and statistical moment, then neural networks have been applied for pixel classification. This method falls in conventional supervised learning.

As for deep neural networks, [18] proposes a fully convolutional neural networks model for image segmentation, providing a framework for pixel-level segmentation using DCNN.

Inspired by this, recently, several methods have been proposed for retinal vessel segmentation in terms of deep learning. [6] formulates the segmentation task as a multi-label inference problem and exploits the dependencies among neighboring pixels to improve the performance. [3] utilizes a conditional random field to model the long-range interaction between pixels. [11] uses a Graphic Process Unit (GPU) implementation of deep neural networks to demonstrate its high effectiveness in segmentation. [5] conducts a comprehensive study in retinal vessel segmentation using deep neural networks under supervised learning. In their work, the system is fed with small patches cropped from a large one for training, before which the images have been preprocessed. A range of network architectures have also been evaluated in that work; among them, a fully connected layer is widely applied before the final output layer.

All these above are marked as supervised learning approaches, and, as mentioned in [7], they are likely to achieve better performance than their unsupervised counterparts. We also notice that manually labeled samples are required for all of them.

Still, there is a semi-supervised scheme in which multiple stacked denoised autoencoders (SDAE) have been trained to learn dictionary of visual kernels for segmentation [19], in which an additional layer is need to fuse each one’s output; However, as a paradigm of semi-supervised learning, labeled data is required in the final stage (fine-tuning).

III. PROPOSED METHOD

The proposed approach leverages the DCNN’s strong power in feature learning. We achieve this labeling-free approach via generating samples with prior knowledge and training the networks on the data set. The prior knowledge must be strong enough to guarantee desirable performance. This idea is inspired by the observation that blood vessels are clearly delineated in grayscale image, as Fig.1 illustrates, where we take an image from DRIVE data set [20] as an example.

Based on this observation, we assume that if a deep neural networks model can distinguish line segment from noise, it would be compatible with blood vessel. We hypothesize that with the great power of DCNN in feature learning, one can segment these vessels in grayscale images by training the nets on artificial data set automatically generated from prior knowledge. That is, no labeling is needed. To illustrate our idea, we use simple line segments to construct the samples, which is followed by a post-processing aimed to provide more prior knowledge; and then a naive DCNN model is built and trained to test our approach.

Generating samples functions as a key component, in our approach, since the images in our training data set are artificial (they are generated by computing). We work out this stage with two steps. First is to generate raw images, and then further processing is invoked to approximate real-world images more closely. In this section, we demonstrate the processes of generating raw images and improving the data set, respectively.
Fig. 1: A comparison between color image (left) and its grayscale version (right). Although information missing there is, it is possible to recover these vessels from the grayscale image. We also notice that the vessel share key features with line segment.

A. Raw Image Generation

In this phase, we construct images with simple line segments on empty background, based on the following rules we developed.

Rule 1-1: Most of the line segments’ nodes should be connected one after another. In real-world images, as we observe, the graph of the vessels is likely to contain many cliques. And we consider it one of the features the system needs to learn. That is, they are not being simply imposed, but of nontrivial structures.

Rule 1-2: The gray level of each line segment is expected to differ from others. This provides an alternative way to simulate the variation of illumination. While the intensity of the pixels, apparently, may vary locally in real-world images, it gets complicated to make a pixel-wise assignment. We simplify this process by using line-wise assignment instead, regarding to our hypothesis.

Rule 1-3: Line segment’s length should be able to vary in a predefined range. This rule is based on the observation that the blood vessels are not strictly straight, but zigzag in local. We make it a key component to bridge the gap between the simulation and the reality-based image, together with the direction variation (will be addressed in Rule 1-4).

Rule 1-4: The structure is encouraged to spread over the image while keep sparse. This rule focuses on the layout of the blood vessels. We notice that the vessels tend to cover the whole image and each vessel is distinct as they are clearly separated from each other. Let $\alpha$ denote the angle between a new branch (line segment) and its stem’s direction, to take account of this prior information, we set a predefined pair of angles (i.e. $\pm \alpha_m$) as candidate means for $\alpha$, as illustrated in Fig. 2, where normal distribution has been used to generate a sample of $\alpha$ (i.e. $\alpha \sim N(\pm \alpha_m, \sigma_\alpha)$).

To facilitate the construction, more details should be specified. In rule 1, we limit the number of the nodes (points where new branches begin, see Fig. 2), which incorporates with rule 1-4 in terms of keeping sparse. In rule 1-2, a random value is assigned to a line segment as its gray level. In rule 1-3, we define the mean of the length to facilitate the generation process. Besides that, we keep the line segments in a specified circular region; when a new branch tends to break out, we reject it and draw a new one. This trick tends to encourage the diversity of the structures, which approximates the zigzag feature more precisely.

With these rules, we developed Algorithm 1, simply, we use uniform distribution and normal distribution in the algorithm. Two of the generated images are shown in Fig. 3, and we notice that the labels are automatically obtained.
Fig. 3: Generated raw images based on our rules. They are constructed with only simple lines, but come with distinct features abstracted from the real-world objects, which makes it possible to use them as training samples. See rule 1-1~1-4 and Algorithm [1] for more details.

Algorithm 1: Raw Image Generation

```plaintext
//construct image with simple lines
Parameters: α_m, N, σ_L, L_m, max_chd, σ_α
img ←− 0
while node number < N do
    while chd[nodeIdx] < max_chd do
        length ∼ N(L_m, σ_L)
        α ∼ N(±α_m, σ_α)
        (x, y) ←− genPoint(P[nodeIdx], α, len)
        if (x, y) is out if the circle then
            continue
        end
        grayscale ∼ uniform distribution
draw line from P[nodeIdx] to (x, y) in
        img
        record (x, y) in P
        update variables
    end
end
return img
```

B. Improvement of the Samples

Typically, the process of training on large data set is to combat the noise existing in the data set. And, in this work, our samples come with two kinds of noise; the first comes from the approximation of the vessels’ structure; the other, similar to the real images, arises from the background.

Actually, in real-world images, noise in background comes as a major problem hampering the segmentation. That is, if the background of Fig.[1] was as clear as that of Fig[3], we would segment these vessels in straightforward ways.

In this stage, we tend to add artificial noise to the background for providing sufficient prior information. We construct the noise by combining two types of artificial noise, namely, global noise and local noise. We also make rules to develop our algorithm for improving our samples, with respect to the two types of noise.

**Rule 2-1:** There is global background noise in sample. The global background noise is designed to fully utilize the whole pixels to avoid trivial solution. In our implementation, we first add one random value to the image at each pixel; and then generate Gaussian noise for each pixel using identical parameter sets.

**Rule 2-2:** Local noise is necessary. Apparently, uniform Gaussian noise is insufficient to deliver our observation-based prior knowledge. To accomplish that, we consider introducing specific noise to the randomly selected patches (with fixed size). The noise should be capable of varying smoothly, which is to capture the feature of illumination variation. Under this goal, we use sine wave to generate these noise. For the reason of sample’s diversity and convergence of training process, we randomly draw a value as the phase while keep both amplitude and frequency fixed. The frequency’s setting is adapted to the patch’s size to guarantee sufficient intensity variation.

The philosophy behind pouring noise, to the raw images is to avoid trivial solution (over-fitting), similar to the novel work in [21]. We expect the nets to preserve and enhance the structures which share
key features (e.g. being thin and continuous) with the vessels in real-world images, while suppress the noise. From this perspective, in the proposed approach, the networks works as a filter which boosts the SNR in the output.

We derive Algorithm 2 to improve our samples based on rule 2-1 and rule 2-2. Some finally generated samples are shown in Fig.4.

Algorithm 2: Sample Generation

\[
\begin{align*}
&\text{// add background noise to a sample} \\
&\text{Parameters: } m_{\text{noise}}, \sigma_{\text{noise}}, N_{\text{max}}, \omega, A \\
&\text{// im}g \text{ is initially generated by Algorithm 1} \\
&\text{// global noise} \\
&b \sim \text{Uniform distribution} \\
&n_g \sim \mathcal{N}(m_{\text{noise}}, \sigma_{\text{noise}}^2) \text{i.i.d., same size as } img \text{'s} \\
&\text{select } n(n < N_{\text{max}}) \text{ patches // no overlap} \\
&\text{// local noise} \\
&\text{for each patch } P \text{ do} \\
&\quad \text{for each pixel } (x, y) \text{ in } P \text{ do} \\
&\quad\quad \alpha \sim \text{Uniform distribution} \\
&\quad\quad img_{[x,y]} \leftarrow img_{[x,y]} + A \sin(\omega f(x, y) + \alpha) \\
&\quad\quad \text{// } f(\cdot, \cdot) \text{ is a distance function} \\
&\text{end} \\
&\text{end} \\
&\text{return } img
\end{align*}
\]

IV. EXPERIMENTS

To test our hypothesis, in this section, we build a naive deep neural networks model and trained it on the data set, generated by the algorithms, and then tested it on DRIVE [20] and STARE [22] data set. To explore the importance of prior knowledge, we used two types of samples to train the model respectively.

A. Datasets

We evaluated our approach on two benchmark databases: DRIVE, and STARE databases.

1) DRIVE Database: The DRIVE [20] (Digital Retinal Images for Vessel Extraction) database has been established to enable comparative studies on segmentation of blood vessels in retinal images. The images were acquired using a Canon CR5 non-mydriatic 3CCD camera with a 45 degree field of view (FOV). Each image was captured using 8 bits per color plane at 768 by 584 pixels. The FOV of each image is circular with a diameter of approximately 540 pixels. For this database, the images have been cropped around the FOV. For each image, a mask image is provided that delineates the FOV.

The set of 40 images has been divided into a training and a test set, both containing 20 images. For the training images, a single manual segmentation of the vasculature is available. For the test cases, two manual segmentations are available; one is used as gold standard, the other one can be used to compare computer generated segmentations with those of an independent human observer. All human observers that manually segmented the vasculature were instructed and trained by an experienced ophthalmologist. They were asked to mark all pixels for which they were at least 70% certain that they were vessels. We used the first observer’s outputs as the ground truth. We only used the test set since our approach only took artificial images for training.

2) STARE Database: The STARE [22] (Structured Analysis of the Retina) database contains 20 images for blood vessel segmentation.

The slides are obtained by TopCon TRV-50 fundus camera at 35deg field of view. Each slide was digitized to produce a 605 x 700 pixel image, 24 bits per pixel (standard RGB). Ten of the images are of patients with no pathology (normals). Ten of the images contain pathology that obscures or confuses the blood vessel appearance in varying portions of the image (abnormals). The database contains two sets of manual segmentations prepared by two observers, and the former one is considered as the ground truth [5].

B. Experiments Settings

1) Deep Neural Networks Model: The networks (see Fig 5) are built without fully connected layer, which makes it portable to images of different sizes. This allows us to use smaller images as training samples to accelerate our training process. And the loss layer is a pixel-wise softmax layer (used for pixel-wise classification). We build a concatenation layer to follow the philosophy that high-level perception guides the work in lower levels. In the concatenation layer and the softmax layer, cropping has been used to handle the differences in size of the inputs. The implementation is based on
Fig. 5: Our networks model used for segmentation. We use this model to test our hypothesis. See Experiments for more details.

TABLE I: Performance metrics for retinal vessel segmentation

| Performance measures     | Description                                      |
|--------------------------|--------------------------------------------------|
| Sensitivity (Sn)         | TP/(TP+FN)                                       |
| Specificity (Sp)         | TN/(TN+FP)                                       |
| Accuracy (Acc)           | (TP+TN)/(TP+FP+TN+FN)                            |
| True positive rate (TPR) | TP/(TP+FN)                                       |
| False positive rate (FPR)| FP/(FP+TN)                                       |
| AUC                      | Area under the ROC curve                        |

MXNet \[23\] The experiments were conducted on hardware configuration: Intel Core i3-530 CPU with single NVIDIA GTX 760 graphics card, software configuration: Ubuntu 14.04, Python 2.7.

The networks have been trained with default hyperparameter settings, and Batch Normalization \[24\] has been applied.

2) Training Datasets: We built two types of training datasets to explore the differences caused by different prior knowledge. Images (e.g. Fig. 8b) in dataset\#1 are constructed with wider and more distinctive lines, while images (e.g. Fig. 8c) in dataset\#2 only contain lines of single type, and the noise in background makes them difficult to detect.

C. Performance Measurements

In this work, we treat the segmentation as a binary classification task. That is, each pixel will be either classified as blood vessel or background. For this reason, we evaluated our networks’ performance in terms of AUC, Sensitivity, Specificity and Acc (accuracy). Their definitions are described in TABLE I, where TP (true positive) means the number of pixels correctly classified into vessels, FP (false positive) is the number of pixels misclassified into vessels, TN (true negative) is the number of pixels correctly classified into background, and FN (false negative) is the number of pixels misclassified into background. ROC (receiver operation characteristic) curve is obtained by plotting the TPR against the FPR at various threshold settings. In our experiments, scikit-learn\[2\] has been utilized to calculate AUC and Acc.

D. Evaluations

In this subsection, we evaluate our nets, and explore the effects caused by different training datasets. The results show that:

- our networks achieve competitive performance among the state-of-the-art methods;
- prior knowledge is essential for our proposed approach.

We used some of the samples to test our nets. The results are shown in Fig. 6. As the result shows, the model has been able to distinguish line segments from the noise.

1http://mxnet.io

2http://scikit-learn.org
Fig. 6: Prediction map (right) on sample (left). Structures with desired features are preserved. Because of the convolution operations, they have different sizes. The nets are trained on dataset#2.

Fig. 7: Best result (according to AUC) of the trained networks on DRIVE test data set (using dataset#1). (a) Image from DRIVE test data set (b) Grayscale version (c) Our prediction map (d) Ground truth.

Then, we evaluated the networks on DRIVE and STARE data sets. For a given image (e.g. Fig 7a), we used its grayscale version (Fig 7b) to feed the networks, before that, an image inversion was required because of the difference between the training sample and the real image (see Fig 4 and Fig 1). The results are shown in Fig 7 and TABLEII.

The results of Fig 6 and Fig 7 imply the mechanism of the neural networks. That is, the deep neural networks give strong responses to line-like structures, while ignore others. This is the feature we are working for; and, as the results show, it yields a system compatible with vessel’s structure.

In Fig 8, we used the two training datasets (dataset#1, dataset#2) to train the networks respectively and tested the systems for same image. Intuitively, based on the constructions of the datasets, we thought dataset#2 (Fig 8c) would yield a more precise segmentation and the system would be more sensitive for line-like patterns; however, since it only contains thin lines the outputs would suffer from discontinuity. The results follow our assumption (refer to Fig 8).

It is also worth noting that, in this work, we do not focus on tricks in training deep neural networks, just a naive structure and a short iterating (within 200,000 iterations, 2 samples for each) with default settings, however, the system has achieved competitive performance (see TABLEII). Also, we give a comprehensive view of the nets’ performance on DRIVE dataset (TABLEIII).

V. CONCLUSIONS

In this work, we focused on using prior knowledge to leverage the great power of deep neural networks in feature learning for retinal blood vessel segmentation. The study is based on the fact that although the deep neural networks has been proved to be a powerful tool, the high cost of labeling hampers its applications in vast areas. We argue that, with strong domain-specific prior knowledge, we are able to drive the deep neural networks to an alternative direction where a desirable performance is available.

Based on this assumption, we propose a novel approach to supervising deep neural networks for blood vessel segmentation in fundus images which is free from manual labeling. In our approach, we pour our prior knowledge into the dataset to generate artificial training samples and labels which are used to train the deep neural networks. To illustrate our approach, we constructed the training samples with line segments; and then, we built a naive deep neural networks model and trained it on the artificial images in a straightforward way.

The results have shown that our approach achieved competitive performance on benchmark datasets, and provide considerable evidence for our
Fig. 8: Result comparison between different two datasets. (a) Image from DRIVE test data set (b) Sample from dataset#1 (c) Sample from dataset#2 (d) Ground truth (e) Result by dataset#1 (f) Result by dataset#2
hypothesis. As deep learning is still an ongoing study which is, currently, mainly based on intuition and engineering, we cannot strictly prove this hypothesis with this one application; but this work implies a potential way to leverage deep neural networks without manual labeling.

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