Retinal Vessel Detection Based on Deep Learning

F Febshia[1], C Rekha[2], T Agnes Ramena[3]
[1, 2, 3] Dept of ECE
[1, 2, 3] PET Engineering College

Abstract- *While recent advances in deep learning have significantly advanced the state of the art for vessel detection in color fundus (CF) images, the success for detecting vessels in fluorescein angiography (FA) has been stymied due to the lack of labeled ground truth datasets. Deep learning based image processing algorithms have shown compelling improvement in the analysis of color fundus (CF) images. Propose a novel pipeline to detect retinal vessels in FA images using deep neural networks (DNNs). The input FA image is decomposed into a two scale Gaussian image pyramid: one at the original image resolution and the other down sampled by a factor of 2. The images in each scale are processed independently. The resulting vessel maps in the lower resolution are upsampled to the original size using Gaussian pyramid expansion. Pixels where vessel is detected at any scale collectively comprise the estimated vessel map. The approach significantly reduces manual labeling effort while increasing engagement.*

Keywords- Fluorescein angiography, generative adversarial networks, vessel detection, retinal image analysis, deep learning.

I. INTRODUCTION

Recently deep learning based image processing algorithms have shown compelling improvement in the analysis of color fundus (CF) images. The CF images are color images of the retina captured under white light illumination using a fundus camera that consists of a specialized microscope equipped with a camera. The images mimic what physicians see with ophthalmoscopy and are the predominant form of retinal images. A DNN can detect retinal vessels in CF imagery with high accuracy and robustness and achieve performance close to human experts. Manually labeled ground truth datasets are a key ingredient in the success of these techniques. Three commonly used datasets that provide CF images and corresponding manually labeled pixel-wise binary vessel maps include DRIVE (forty 584 × 565 pixel images), STARE (twenty 605 × 700 pixel images), and the high resolution HRF (forty-five 504×2336 images) datasets.

The detection of retinal vessels is also of interest for alternative imaging modalities that are of independent diagnostic utility in the clinic. For instance, fluorescein angiography (FA) and optical coherence tomography angiography (OCT-A) are used for assessing retinal non-perfusion. FA provides a larger field of imaging beyond the macula, while commercially available OCT-A provides more detailed imaging of the macular micro-vasculature. FA images are captured after intravenous injection of sodium fluorescein dye. Blue illumination, over the wavelength range from 465 to 490 nm, causes the dye to fluoresce and emit photons in the 520-530 nm green-yellow wavelength band. The spatial pattern of fluorescence intensity is captured as an FA image, in which, the vessels with blood flowing through them appear brighter because of the fluorescent dye in the blood. Although, conceptually, one could redeploy the DNN architectures that are successful in CF imagery to these alternative modalities, the fundamental differences between the modalities require fresh training and the lack of ground truth labeled data becomes a key obstacle to such reuse. Specifically, for FA images, only one dataset is available: VAMPIRE which provides eight ultra-wide field FA (UWFFA) images (3072 × 3900 pixels, each) along with limited accuracy ground truth binary vessel maps. Manually annotating vessel maps for training a DNN is not a trivial task. Specifically, UWFFA images have high resolution and exhibit variations in contrast between the background and the vasculature, which pose a significant challenge for manual annotation. Fig. 1 shows sample FA images and highlights the particular challenge of contrast variations. The patch labeled in cyan in the middle UWFFA image is shown in an enlarged view on the right, as captured and with contrast enhanced. From the contrast enhanced view, one can appreciate that the region corresponding to the patch contains a large number of fine vessels that are rather difficult to see without contrast enhancement. In particular, ophthalmologists normally have difficulty in identifying fine vessels in the peripheral region without image enhancement because of the low contrast and brightness. High-quality annotation requires carefully adjusting image contrast for the entire FA image and labeling both major and minor vessels, making it a tedious, time-consuming, and labor-intensive process.

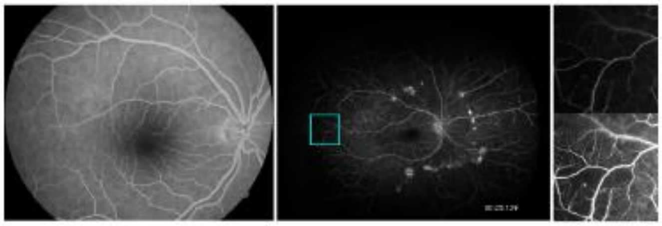


Fig. 1. Sample fluorescein angiography (FA) images. left: fundus FA. Middle: ultra-widefield FA. Right: enlarged view of the cyan rectangle (top and bottom: the original and the contrast-enhanced views, respectively). For a larger version of this figure see Fig. 1H in the Supplementary Material.

II. LITERATURE SURVEY

Presents a method for automated vessel segmentation in retinal images. For each pixel in the field of view of the image, a 41-D feature vector is constructed, encoding information on the local intensity structure, spatial properties, and geometry at multiple scales. An AdaBoost classifier is trained on 789 914 gold standard examples of vessel and nonvessel pixels, then used for classifying previously unseen images. The algorithm was tested on the public digital retinal images for vessel extraction (DRIVE) set, frequently used in the literature and consisting of 40 manually labeled images with gold standard. Results were compared experimentally with those of eight algorithms as well as the additional manual segmentation provided by DRIVE. Training was conducted confined to the dedicated training set from the DRIVE database, and feature-based AdaBoost classifier (FABC) was tested on the 20 images from the test set. FABC achieved an area under the receiver operating characteristic (ROC) curve of 0.9561, in line with state-of-the-art approaches, but outperforming their accuracy (0.9597 versus 0.9473 for the nearest performer).

Automatic segmentation of retinal blood vessels has become a necessary diagnostic procedure in ophthalmology. The blood vessels consist of two types of vessels, i.e., thin vessels and wide vessels. Therefore, a segmentation method may require two different processes to treat different vessels. However, traditional segmentation algorithms hardly draw a distinction between thin and wide vessels, but deal with them together. The major problems of these methods are as follows: (1) If more emphasis is placed on the extraction of thin vessels, the wide vessels tend to be over detected; and more artificial vessels are generated, too. (2) If more attention is paid on the wide vessels, the thin and low contrast vessels are likely to be missing. To overcome these problems, a novel scheme of extracting the retinal vessels based on the radial projection and semi-supervised method is presented in this paper. The radial projection method is used to locate the vessel centerlines which include the low-contrast and narrow vessels. Further, we modify the steerable complex wavelet to provide better capability of enhancing vessels under different scales, and construct the vector feature to represent the vessel pixel by line strength. Then, semi-supervised self-training is used for extraction of the major structures of vessels. The final segmentation is obtained by the union of the two types of vessels. Our approach is tested on two publicly available databases. Experiment results show that the method can achieve improved detection of thin vessels and decrease false detection of vessels in pathological regions compared to rival solutions.

Retinal images can be used in several applications, such as ocular fundus operations as well as human recognition. Also, they play important roles in detection of some diseases in early stages, such as diabetes, which can be performed by comparison of the states of retinal blood vessels. Intrinsic characteristics of retinal images make the blood vessel detection process difficult. Here, we proposed a new algorithm to detect the retinal blood vessels effectively. Due to the high ability of the curvelet transform in representing the edges, modification of curvelet transform coefficients to enhance the retinal image edges better prepares the image for the segmentation part. The directionality feature of the multistructure elements method makes it an effective tool in edge detection. Hence, morphology operators using multistructure elements are applied to the enhanced image in order to find the retinal image ridges. Afterward, morphological operators by reconstruction eliminate the ridges not belonging to the vessel tree while trying to preserve the thin vessels unchanged. In order to increase the efficiency of the morphological operators by reconstruction, they were applied using multistructure elements. A simple thresholding method along with connected components analysis (CCA) indicates the remained ridges belonging to vessels.

Detecting blood vessels in retinal images with the presence of bright and dark lesions is a challenging unsolved problem. In this paper, a novel multiconcavity modeling approach is proposed to handle both healthy and unhealthy retinas simultaneously. The differentiable concavity measure is proposed to handle bright lesions in a perceptive space. The line-shape concavity measure is proposed to remove dark lesions which have an intensity structure different from the line-shaped vessels in a retina. The locally normalized concavity measure is designed to deal with unevenly distributed noise due to the spherical intensity variation in a retinal image. These concavity measures are combined together according to their statistical distributions to detect vessels in general retinal images. Very encouraging experimental results demonstrate that the proposed method consistently yields the best performance over existing state-of-the-art methods on the abnormal retinas and its accuracy outperforms the human observer, which has not been achieved by any of the state-of-the-art benchmark methods. Most importantly, unlike existing methods, the proposed method shows very attractive performances not only on healthy retinas but also on a mixture of healthy and pathological retinas.

III. PROPOSED SYSTEM

The input FA image is decomposed into a two scale Gaussian image pyramid: one at the original image resolution and the other down sampled by a factor of 2. The images in each scale are processed independently. The resulting vessel maps in the lower resolution are upsampled to the original size using Gaussian pyramid expansion. Pixels where vessel is detected at any scale collectively comprise the estimated vessel map. To extract bright and curvilinear vessel structures in each scale, we apply the modified top-hat operation with nine line structuring elements, chosen to nominally be spaced 20 degree apart in angle, with lengths of 6/3 for the original/down-sampled scale.

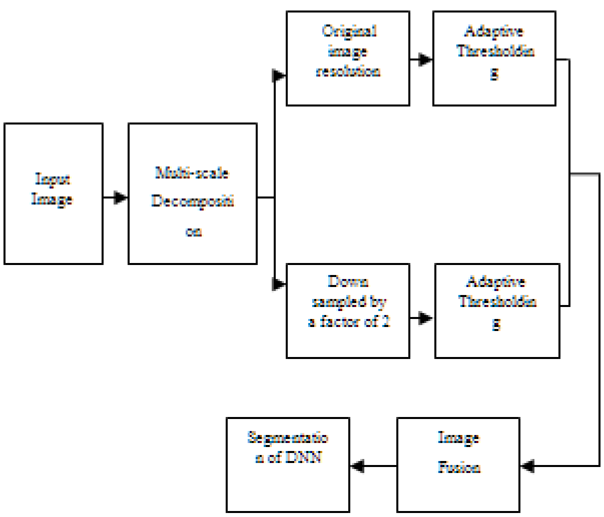


Fig 2 Block Diagram

Each top hat filtering yields a response image, where vessel pixel locations with a matching orientation are invariably high and other locations for background are usually low. The maximum value of 9 responses across different orientations at each pixel location is selected in the overall response map in which high and low values are likely for vessel and background pixels, respectively. The obtained soft vessel map is converted into a binary segmentation by locally adaptive thresholding. The threshold value for each pixel is based on the local mean intensity in the neighborhood of the pixel. As a post-processing step, we remove small incoherent random segments that have fewer than 100 pixels from the binary vessel maps.

The cross-modality transfer exploits the availability of near concurrently captured CF and FA images in combination with existing deep learning methods for detection of vessels in CF imagery, for which, multiple ground truth annotated datasets are available. A DNN is trained on existing labeled CF images to extract vessel maps from unlabeled CF images. The detected vessel maps are geometrically aligned with and transferred to FA images via robust chamfer alignment to a preliminary FA vessel map obtained with morphological analysis. The co-aligned pairs of FA and transformed vessel map are used as initial labeled data to train a DNN for vessel detection in FA images.

The human-in-the-loop learning approach is motivated by the synergistic relationship between deep learning and labeling. A well-trained DNN model can accurately detect vessel maps from FA images. Manually refinement of the predicted vessel map is much less time-consuming than labeling the entire image from scratch. The model performance improves with an enlarged training dataset. Thus, the training and the labeling make each other more effective. We initialize the approach with a DNN trained on the (approximate ground truth) labeled data generated from the cross-modality transfer. A human annotator then manually refines one or more of the predicted vessel maps to generate improved vessel map labels, which, in the next iteration, are incorporated in the training data to improve the DNN performance.

Repeat this human in-the-loop iterative process till the network performance improves significantly and the manual labeling introduces few changes. The end result is a trained DNN and a set of accurately labeled vessel maps. Both the cross-modality transfer and the iterative learning approach reduce the burden of manual labeling significantly and engage the annotators more effectively. Instead of requiring a large number of images to be annotated before improvements are realized, in the proposed iterative approach, the annotator sees improvements in the DNN performance from iteration to iteration as an immediate reward them for their effort. A by product of this engagement and reduction of tedium is that the images are labeled much more accurately than other studies that annotated the images from scratch.

In this project propose a novel pipeline that enables accurate vessel detection in FA images using DNNs by significantly reducing manual annotation effort. The proposed pipeline integrates the following novel elements: an unsupervised method for preliminary retinal vessel detection that is based on multiple scales and orientations morphological analysis, a cross-modality approach that transfers vessel maps from CF to FA images using robust chamfer alignment in an Expectation-Maximization (EM) framework, and an efficient and effective human-in-the-loop iterative deep learning process for detection of retinal vessels in FA imagery that significantly reduces the tedium of generating labeled data. Demonstrate the utility of the proposed pipeline by developing the first set of DNNs for detection of retinal vessels in FA images and evaluating the performance on alternative network architectures. The best performing method provides remarkably accurate results and offers very significant improvements over the prior methods. Results demonstrate that the approach adapts particularly well to the contrast variations that are typical in FA imagery. To facilitate further development of vessel

Detection in FA images, also release a new dataset of UWFFA images from the RECOVERY trial along with ground truth labeled vessels from our pipeline. In addition to the innovative pipeline for the generation of training data, demonstration of the first deep learning approaches, evaluation of alternative architectures, and the new ground truth labeled datasets are also contributions of the present work. The proposed pipeline is also significant from a clinical perspective. FA is a well-established method that provides a useful imaging modality for visualizing, assessing and understanding the impact of diseases on the vascular system. Retinal vasculature changes accessed via FA imagery play a key role in the clinical assessment of vasculature changes caused by multiple common diseases, including diabetes, hypertension, and atherosclerosis, and also for eye-specific diseases, such as retinal venous occlusive diseases and retinal vasculitis.

In current clinical practice, ophthalmologists manually review FA images to access disease conditions in retinal vasculature. These examinations are typically qualitative and subjective due to the limited time available during the clinical visits. Quantitative analysis of FA images, although highly desirable, requires inordinate time and patience to be performed manually and thus is not feasible in clinical settings. The proposed pipeline for detecting vessels in FA images offers an automated approach to examine retinal vasculature, which is a key component of computer-assisted retinal image analysis and diagnosis systems. Details of fine vessels are of particular diagnostic significance as changes are often fist observed in the fine vessels; a key strength of the method developed is the ability to reliably detect fine vessels, which are often not seen with non-FA modalities and, even for the FA modality, require significant iterative contrast manipulations for visual detection. Using the proposed pipeline, the results of retinal vessel detection achieve a level of accuracy that enables reliable computation of “digital biomarkers” from FA imagery that unlock the potential for improving clinical care, speeding up clinical trials, defining new endpoints of clinical relevance, and characterizing inter-individual variations.

CROSS-MODALITY GROUND TRUTH TRANSFER

Vessel Detection in CF Images

To detect vessels in CF images, we adopt an existing DNN proposed in that exploits adversarial learning. The model is trained on DRIVE dataset which scores an Area Under the Receiver Operating Characteristic Curve(AUC ROC) of 0.9803, an Area Under the Precision-Recall curve (AUC PR) of 0.915, and a Dice coefficient of 0.829. The pretrained network is applied to overlapping patches of CF images in the DRIsfahanCFnFA dataset. The final CF binary vessel map is obtained by thresholding the probability map obtained from the generator using Otsu thresholding.

Preliminary Vessel Detection in FA Images for Anchoring

A preliminary detection of vessels in FA imagery is obtained using an unsupervised method based on multiple scales and orientations morphological analysis that is attuned to the variations in directions and widths of retinal vessel structure. The preliminary detection need not be particularly precise; as noted in the next section, a low false positive rate is preferable even at the cost of a higher rate of missed detections. An overview of the approach is included here and additional detail, including specific parameter settings used, are provided in Section S.IV of the Supplementary Material. The input FA image is decomposed into multiple resolutions represented by an image pyramid. Images at each scale are processed independently and the resulting vessel maps at different scales are then combined together to generate a binary vessel map. A Gaussian pyramid expansion is used to resize vessel maps from each scale to the size of input FA image. Pixels where vessels are detected at any scale collectively comprise the estimated vessel map.

The key component in the preliminary vessel detection are morphological operators that extract locally linear patterns in terms of which the curvilinear network of interconnected vessels can be approximated. To detect vessel pixels at each scale, we choose a set of linear structuring elements $S\alpha$ with the same length but oriented along different angles α, ranging from 0° to 180°. We apply the top-hat operator to the FA images using the structuring elements $S\alpha$. The conventional top-hat operator which is defined as the difference between original and the corresponding morphological opening image, is sensitive to noise. Therefore, we adopt a modified top-hat filtering to improve the robustness of vessel detection. The modified top-hat operator $\odot$is defined as

$$X \odot S\_\alpha = X - \min((X.S\_\alpha)^{\circ} S\_\alpha, X)$$

Where X is the input image, and•and◦indicate the morphological operators of image closing and opening, respectively. Each top hat filtering operation yields a response image in which pixel locations for vessels with a matching orientation are invariably high and those for other locations are usually low. The results of the top-hat filters across different orientations are combined by taking the maximum, resulting in an overall map where high and low values are likely for vessel and background pixels, respectively. This soft vessel segmentation is converted into a binary vasculature map by locally adaptive thresholding. Typically, binary vessel maps obtained by this process have a few disconnected components. As a post-processing step, therefore perform an area opening operation to remove all small segments from the vessel map.

HUMAN-IN THE LOOP ITERATIVE LEARNING /LABELING

Although the cross-modality transfer allows generation of a reasonable labeled dataset for training DNNs for detecting vessels in FA images, the accuracy of the labeling is limited by the differences between the modalities and the performance limitations of the CF vessel detection. The network performance can be significantly improved by providing additional better labeled ground truth data. As indicated in Section I, manually annotating a highresolution UWFFA image is particularly tedious and time-consuming. In this section, we present the human-in the-loop learning approach that aims to further refine the DNN by incorporating more training data and to facilitate and expedite the manual annotation process.

Contrasts the conventional approach to annotation of training data against the proposed human-in-the-loop approach. For conventional approach, the annotation and the training are carried out in separate sequential phases, meaning that all images in the dataset are first annotated and then used for the training stage. The human-in-the-loop approach, however, is an iterative process that exploits the synergistic relationship between deep learning and labeling. The process is initialized with a trained DNN trained to detect vessels in FA images using the training data obtained by the cross-modality transfer approach. Estimated binary vessel maps that indicate the pixels corresponding to vessels are obtained for a small subset of images from an unlabeled (FA-only) dataset and used as the as the starting point for manual annotation. Specifically, the human annotator corrects the estimated binary vessel map by removing false positive detections and adding in false negative detections. The new labeled images are incorporated into the training dataset to refine the DNN in the next iteration. This process is repeated until all images are labeled. The proposed human-in-the-loop approach radically reduces the effort required for annotating images. In addition to reducing the time and tedium for annotation, the approach also benefits from a psychological advantage that it provides. The annotators see the improvements in the trained network from iteration to iteration and feel immediately rewarded for their effort instead of having to label many images before seeing any machine generated annotations. This engages annotators much better than denovolabeling approaches, analogous to how gamification of learning and education generates better engagement. Our results indicate that the approach generates significantly better labeled data than the traditional de novo labeling approach.

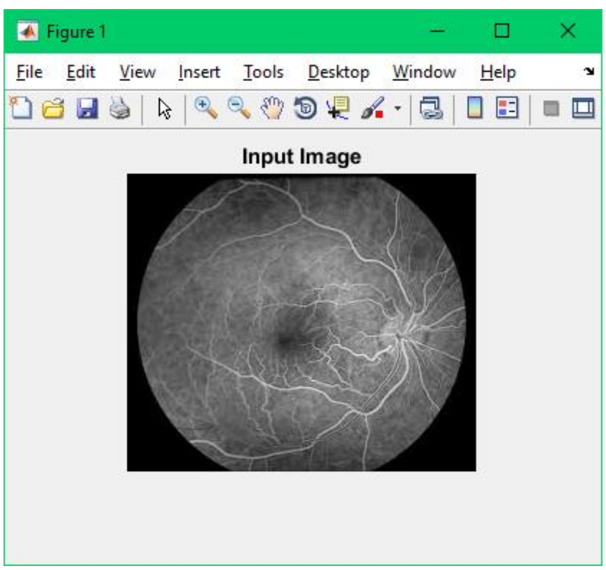
Network Architecture

We trained and evaluated a number of alternative DNN architectures for vessel detection in FA images. In this section, we describe the best performing approach that exploits the recent concept of generative adversarial network (GAN) , which was also the architecture used for the human-in-the loop labeling iterations. Detailed architectures for other neural networks are provided in the Supplementary Material. To apply GAN to vessel detection, we formulate the problem as an image-to-image translation. In this context, the network consists of a generator G, which is trained to learn a mapping from the FA image X to the vessel map V and a discriminator D, which aims to distinguish between real pairs (X,V) and generated pairs (X,G (X)) of FA images and vessel maps, where G(X) is the vessel probability map estimated from the generator and V is the binary ground truth vessel map. The idea is to jointly train G and D to achieve the min max operating point where the vessel maps generated by G minimize the maximum error for the discriminator D in distinguishing between real and generated pairs. The network architecture is visualized. For the generator, we adopt the UNet architecture, which comprises a down sampling path and an upsampling path. The key component in the UNet is the skip-connection that concatenates each upsampled feature map with the corresponding one in the down sampling path that has the same spatial resolution. The skip-connection is designed for detecting fine vessel structures. The discriminator receives either an image pair (X,V) (the blue and green bars) or (X,G (X)) (the blue and yellow bars).

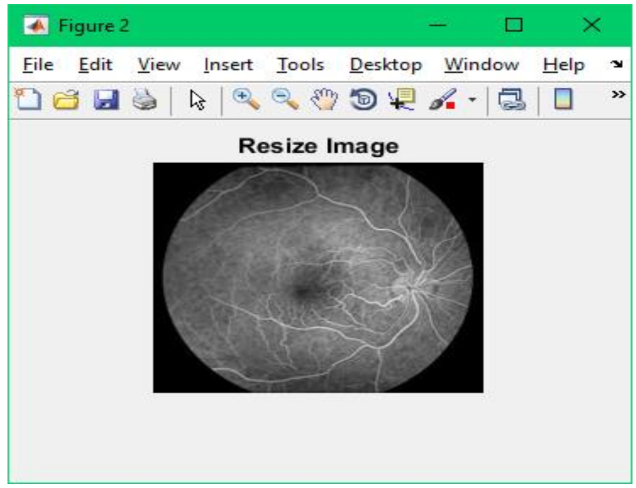
Training Protocol

Feed the network 256×256 patches extracted from the FA training data with a fixed stride length 128. Patches that contains less than 1% vessel pixels are excluded. To prevent neural networks from over-fitting, further enlarge the training set by performing on-the-fly data augmentation, i.e., randomly applying a list of transformations with different probabilities to each image before feeding into neural network as training data. Specifically, we consider following transformations: (1) rotating the image by an angle from −90◦ to 90◦, (2) horizontally and vertically flipping the image, (3) scaling the image by a factor of 2, (4) blurring the image using Gaussian filter, and (5) adjusting the brightness and contrast of the image. The network parameters are optimized using Adam optimizer on a NVidia Tesla V100 GPU. The learning rate is fixed as 0.001. The coefficients used for computing running averages of gradient and its square are 0.9 and 0.999, respectively. The batch size is 16 and the training dataset is shuffled between epochs. We split the data into a training set (80%) and a validation set (20%) and use the model that has the best performance on the validation set. The lambda in (11) is set to 1.

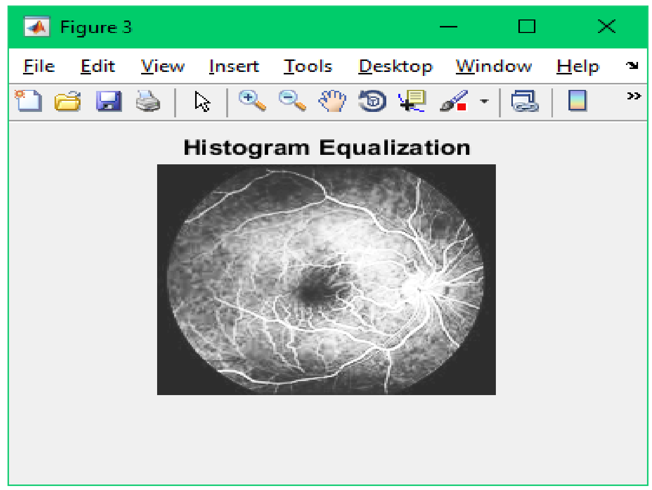
IV. SCREEN SHOTS



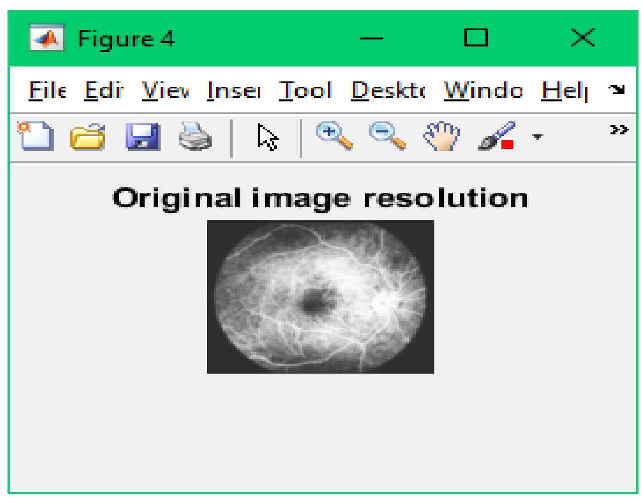
Input Image



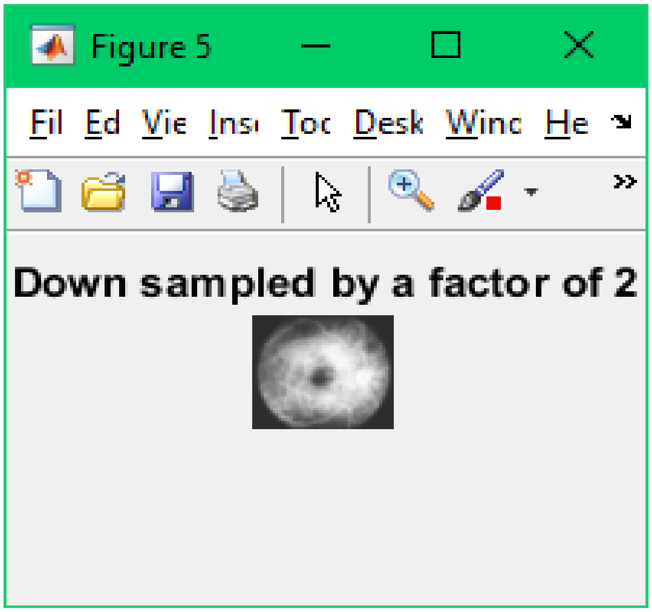
Resize Image



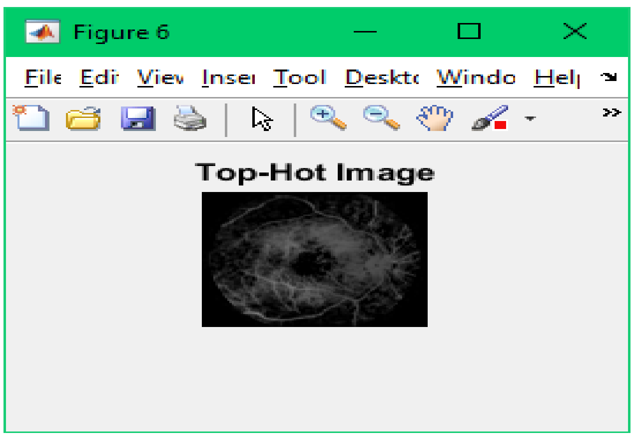
Histogram Equalization



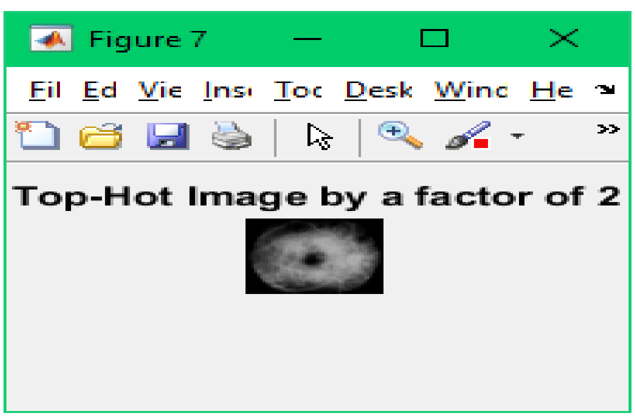
Original Image resolution



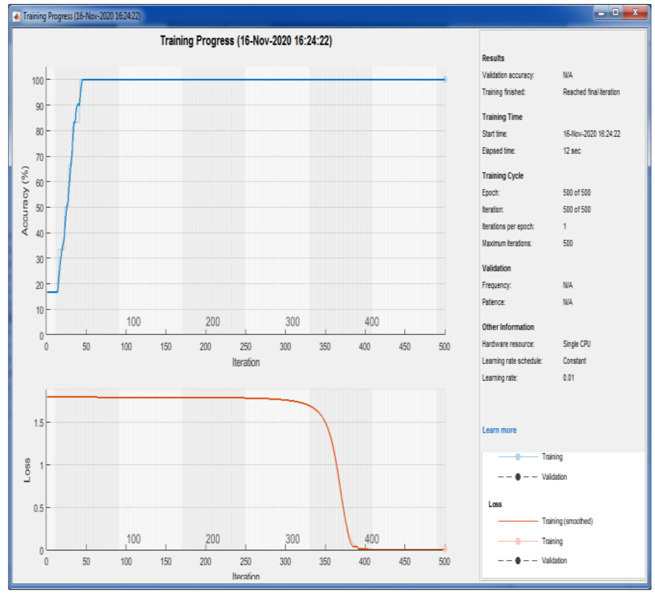
Down Sampled By A Factor 2



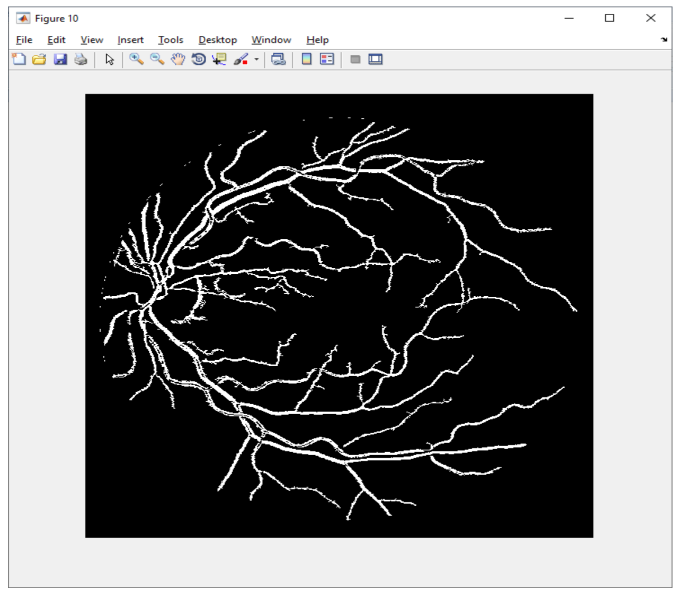
Top-Hot Image



Top-Hot Image by a factor 2



DNN Training Process



Segmentation Output

V. CONCLUSION

Proposed a novel deep learning pipeline for detecting retinal vessels in FA images. Using a cross-modality approach and a human-in-the-loop approach, our pipeline significantly reduces the effort required for generating labeled ground truth images. The proposed pipeline provided a particularly useful methodology for generating labeled ground truth data. While our focus here was on labeling vessels in FA retinal images, the key underlying ideas could be applied in other situations. The idea of cross-modality transfer by registering observations of the same object captured with different modalities is potentially useful in speeding up other ground truth labeling tasks. Used in combination with the human-in-the-loop approach, such methods can significantly reduce tedium and improving engagement, and improve availability of datasets with accurately labeled ground truth.

REFERENCES

[1] Al-Diri B., Hunter A and Steel D., "An Active Contour Model for Segmenting and Measuring Retinal Vessels," IEEE Transactions on Medical Imaging, vol. 28, pp. 1488-1497, Sep 2009.

[2] Fang B., Hsu W., Lee M.U., (2003): On the Detection of Retinal Vessels in Fundus Images.

[3] Fathi A., Naghsh-Nilchi A.R. (2012): Automatic wavelet-based retinal blood vessels segmentation and vessel diameter estimation. Biomedical Signal Processing and Control, vol.8(1), pp.71-80.

[4] Human eye anatomy: http://www.allaboutvision.com/resources/anatomy.htm (02.05.2016)

[5] Human eye: http://www.nkcf.org/how-the-human-eye-works/ (02.05.2016)

[6] Jiang X. Y and Mojon D., "Adaptive local thresholding by verification-based multithreshold probing with application to vessel detection in retinal images," IEEE Transactions on Pattern Analysis and Machine Intelligence, vol. 25, pp. 131-137, Jan 2003.

[7] Lam B. S. Y., Gao Y. S. and Liew A. W. C., "General Retinal Vessel Segmentation Using Regularization-Based Multiconcavity Modeling," IEEE Transactions on Medical Imaging, vol. 29, pp. 1369-1381, Jul 2010.

[8] Lupascu C. A., Tegolo D and Trucco E., "FABC: Retinal Vessel Segmentation Using AdaBoost," IEEE Transactions on Information Technology in Biomedicine, vol. 14, pp. 1267-1274, Sep 2010.

[9] Macula background: http://patient.info/doctor/macular-disorders (03.05.2016)

[10] Mendonca A. M and Campilho A., "Segmentation of retinal blood vessels by combining the detection of centerlines and morphological reconstruction," IEEE Transactions on Medical Imaging, vol. 25, pp. 1200-1213, Sep 2006.

[11] Miri M. S. and Mahloojifar A., "Retinal Image Analysis Using Curvelet Transform and Multistructure Elements Morphology by Reconstruction," IEEE Transactions on Biomedical Engineering, vol. 58, pp. 1183-1192, May 2011.

[12] Montgomery T.: Macula. http://www.tedmontgomery.com/the_eye/macula.html (03.05.2016)

[13] Nguyen U.T., Bhuiyan A., Park L.A., Ramamohanarao K., (2013): An effective retinal blood vessel segmentation method using multi-scale line detection. Pattern Recognition, vol.46, pp.703-715.

[14] Pattern recognition. http://global.britannica.com/technology/pattern-recognitioncomputer-science (07.04.2016)

[15] Pattern recognition. http://www.mathworks.com/patternrecognition.html (07.04.2016)

[16] Research Section, Digital Image for Vessel Extraction (DRIVE) Database. Utrecht, The Netherlands, Univ. Med. Center Utrecht, Image Sci. Inst. http://www.isi.uu.nl/Research/Databases/DRIVE/, (05.01.2016)

[17] Ricci E. and Perfetti R., "Retinal blood vessel segmentation using line operators and support vector classification," IEEE Transactions on Medical Imaging, vol. 26, pp. 1357-1365, Oct 2007.

[18] Soares J.V., Leandro J.J., Cesar R.M., Jelinek H.F., Cree M.J., (2006): Retinal vessel segmentation using the 2-D Gabor wavelet and supervised classification. IEEE Transaction of Medical Imaging, vol.25, pp.1214–1222.

[19] Staal J., Abramoff M. D., Niemeijer M., Viergever M. A and van Ginneken B., "Ridge-based vessel segmentation in color images of the retina," IEEE Transactions on Medical Imaging, vol. 23, pp. 501-509, Apr 2004.

[20] STARE Project Website. Clemson, SC, Clemson University.

[21] Sussman E.J., Tsiaras W.G., Soper K.A., (1982): Diagnosis of diabetic eye disease. The Journal of the American Medical Association, vol.247(23), pp.3231-3234.

[22] Wasan B., Cerutti A., Ford S., Marsh R., (1995): Vascular network changes in the retina with age and hypertension. Journal of Hypertension, vol.13(12), pp.1724-1728.

[23] You X., Peng Q., Yuan Y., Cheung Y., Lei J. (2011): Segmentation of retinal blood vessels using the radial projection and semi-supervised approach. Pattern Recognition, vol.44, pp.2314-2324.

[24] Zana F. and Klein J. C., "Segmentation of vessel-like patterns using mathematical morphology and curvature evaluation," IEEE Transactions on Image Processing, vol. 10, pp. 1010-1019, Jul 2001.

[25] Zana F. and Klein J. C., "Segmentation of vessel-like patterns using mathematical morphology and curvature evaluation," IEEE Transactions on Image Processing, vol. 10, pp. 1010-1019, Jul 2001.