Faculty of Engineering

Retinal Microvascular Feature Extraction Using Faster Region-based Convolutional Neural Network

Mohammed Enamul Hoque

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Mohammed Enamul Hoque

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DECLARATION

I declare that the work in this thesis was carried out in accordance with the regulations of Universiti Malaysia Sarawak. Except where due acknowledgements have been made, the work is that of the author alone. The thesis has not been accepted for any degree and is not concurrently submitted in candidature of any other degree.

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Signature

Name: Mohammed Enamul Hoque

Matric No.: 19020036

Faculty of Engineering

Universiti Malaysia Sarawak

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ABSTRACT

Artificial Intelligence (AI) more specifically Deep Learning (DL) incorporating with image processing is being employed widely to solve different refractory problems by academia and industry from the ophthalmology discipline. The microvascular structure of the human retina shows remarkable abnormalities responding to different kinds of hazardous ophthalmic and cardiovascular diseases. The high dimensionality and complex hierarchical microvascular structure of the human retina, and random retinal image accumulation create enormous size data. This scenario is offering the challenge of understanding and managing retinal image data. The original input data need to be projected into output data which has a smaller number of features whilst as much as possible preserve its native information. This process is known as feature extraction. A recently introduced DL approach, Convolutional Neural Network (CNN), is dedicated to extract and quantify the complex hierarchical image features with more abstraction. The supervised CNN methods employ different algorithms that iteratively learn from data for analyzing data and predicting outcomes. The implementation of CNN methods has proved their efficiency in the identification, localization, and quantification of interesting retinal image features such as exudates, microaneurysms. These features are considered remarkable signs for detecting Diabetic Retinopathy (DR), Hypertensive Retinopathy (HR), and stroke. The quantitative features such as vessel widening and deviation in bifurcation angle are also relative to these diseases. The recently reported DL-based retinal image feature extraction methods are not dedicated to extracting retinal vessel segments from multiple locations of the retinal image. Extracting retinal vessel segments from the retinal image is important for vessel diameter and bifurcation angle quantification. Moreover, employing inappropriate image processing techniques at the pre-processing level can lead to poor system performance. This work is dedicated to developing an image processing-based AI method for retinal vessel extraction from retinal images. This thesis includes a brief explanation of the proposed method, Faster Region-based Convolutional Neural Network (Faster RCNN) for retinal image feature extraction. At the initial stage of this proposed method, fundamental image processing was used for retinal image pre-processing. The retinal images were taken from the different public databases to train, test, and validate the performance of this proposed method. This proposed method obtained 91.82% Mean Average Precision (mAP), 92.81% sensitivity, and 63.34% Positive Predictive Value (PPV). According to the performance analysis, it can be expected to integrate this proposed method into the ophthalmic diagnostic tools after further development, evaluation, and validation.

Keywords: Retinal imaging, cardiovascular diseases, feature extraction, artificial intelligence, deep learning

Pengekstrakan Ciri Mikovaskular Retina Menggunakan Rangkaian Neural Konvolusional Yang Lebih Cepat di Wilayah

ABSTRAK

Kecerdasan Buatan (AI) lebih khusus Deep Learning (DL) yang digabungkan dengan pemprosesan imej digunakan secara meluas untuk menyelesaikan masalah refraktori yang berbeza oleh akademisi dan industri dari disiplin oftalmologi. Struktur mikrovaskular retina manusia menunjukkan kelainan yang luar biasa yang bertindak balas terhadap pelbagai jenis penyakit oftalmik dan kardiovaskular yang berbahaya. Struktur mikrovaskular hierarki dimensi tinggi dan kompleks retina manusia, pengumpulan gambar retina rawak menghasilkan data ukuran yang sangat besar. Senario ini memberikan cabaran untuk memahami dan mengurus data gambar retina. Data input asal perlu diproyeksikan ke dalam data output yang memiliki jumlah fitur yang lebih kecil sementara sebanyak mungkin menyimpan maklumat asalnya. Proses ini dikenali sebagai pengekstrakan ciri. Pendekatan DL yang baru diperkenalkan, Convolutional Neural Network (CNN), telah diperkenalkan yang didedikasikan untuk mengekstrak dan mengukur ciri-ciri gambar hierarki yang kompleks dengan lebih banyak abstraksi. Kaedah CNN yang diselia menggunakan algoritma yang berbeza yang secara berulang-ulang belajar dari data untuk memperbaiki dan menggambarkan data dan meramalkan hasil. Pelaksanaan kaedah CNN telah membuktikan kecekapan mereka dalam pengenalpastian, penyetempatan, dan pengukuran ciri-ciri gambar retina yang menarik seperti lesi, eksudat, mikroaneurisma. Ciri-ciri ini dianggap sebagai tanda luar biasa untuk mengesan penyakit kardiovaskular seperti Diabetic Retinopathy (DR), Hypertensive Retinopathy (HR), dan strok. Ciri-ciri kuantitatif seperti pelebaran kapal dan penyimpangan dalam sudut bifurkasi juga relatif terhadap penyakit ini. Kaedah pengekstrakan ciri retina berasaskan DL yang baru dilaporkan tidak dikhususkan *untuk mengekstrak segmen kapal retina dari beberapa lokasi gambar retina. Mengekstrak segmen kapal retina dari imej retina adalah penting untuk pengukuran diameter kapal dan sudut bifurkasi. Lebih-lebih lagi, menggunakan teknik pemprosesan gambar yang tidak sesuai pada tahap pra-pemprosesan boleh menyebabkan prestasi sistem yang buruk. Karya ini didedikasikan untuk mengembangkan kaedah AI berasaskan pemprosesan gambar untuk pengambilan kapal retina dari gambar retina. Tesis ini merangkumi penjelasan ringkas mengenai kaedah yang dikembangkan yang telah dilakukan untuk merancang pendekatan DL untuk pengekstrakan fitur gambar retina yang memanfaatkan RCNN yang Lebih Cepat. Pada tahap awal metode yang dicadangkan ini, pemrosesan gambar mendasar telah digunakan untuk pra-pemprosesan gambar retina. Gambar retina telah diambil dari pangkalan data awam yang berlainan untuk melatih, menguji, dan menilai prestasi kaedah yang dicadangkan ini. Kaedah DL, CNN yang dicadangkan ini memperoleh Ketepatan Purata Purata (mAP) 91.82%, kepekaan 92.81%, dan Nilai Ramalan Positif (PPV) 63.34%. Menurut analisis prestasi, diharapkan dapat menyatukan kaedah yang dicadangkan ini ke dalam alat diagnostik oftalmik setelah pengembangan, penilaian, dan pengesahan lebih lanjut.*

Kata kunci: *Pengimejan retina, penyakit kardiovaskular, pengekstrakan ciri, kecerdasan buatan, pembelajaran dalam*

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AI	Artificial Intelligence
ANN	Artificial Neural Network
AGE	Advanced Glycation End products
AP	Average Precision
AVR	Artery Venous Ratio
ARIC	Atherosclerosis Risk in Communities
AVRDB	Arteriovenous Ratio Data Base
AUC	Area Under Characteristics Curve
BDES	Beaver Dam Eye Study
CNN	Convolutional Neural Network
CWS	Cotton Wool Spot
CLRIS	Central Light Reflex Image Set
CMB	Cerebral Microbleeds
CAD	Computer-aided Detection
CRV	Central Retinal Vein
CRAO	Central Retinal Artery Occlusion
CRF	Conditional Random Field
CLAHE	Contrast Limited Adaptive Histogram Equalization

DR	Diabetic Retinopathy
DL	Deep Learning
DWI	Diffusion-Weighted Imaging
DRIVE	Digital Retinal Images for Vessel Extraction
DNN	Deep Neural Network
DS	Deep Supervision
DSC	Dice Similarity Coefficient
DAE	Denoising Auto-Encoders
DLT	Deep Learning Toolbox™
ELM	Extreme Learning Machine
FCNN	Fully Convolutional Neural Network
GPGPU	General-purpose Graphical Processing Units
GPU	Graphical Processing Unit
HR	Hypertensive Retinopathy
HRFID	High-Resolution Fundus Image Database
HRIS	High-Resolution Image Set
ILSVRC	ImageNet Large Scale Visual Recognition Challenge
ICR	Intraretinal Cystoid Fluid
IDRiD	Indian Diabetic Retinopathy Image Dataset
IPT	Image Processing Toolbox

IoU	Intersection over Union
KPIS	Kick Point Image
KNN	K-Nearest Neighbor
LSTM	Long Short Term Memory
ML	Machine Learning
MUSCLE Net	Multi-scale Convolutional Label Evaluation Net
MLP	Multi-Layer Perceptron
MV	Majority Voting
mAP	Mean Average Precision
NLP	Natural Language Processing
NSeSCNN	Non-Selective Sampling CNN
OCR	Optical Character Recognition
PCA	Principal Component Analysis
PPV	Positive Predictive Value
RNN	Recurrent Neural Network
RPN	Region-based Proposal Network
RCNN	Region-based Convolutional Neural Network
REVIEW	Retinal Vessel Image set for Estimation of Width
RVO	Retinal Vein Occlusion
ROC	Retinopathy Online Challenge

RF	Random Forest
ReLU	Rectified Linear Units
RBF	Radial Basis Function
RU-Net	Recurrent CNN based U-Net
R2U-Net	Recurrent Residual CNN based on U-Net
ROI	Region Of Interest
ResNet-50	Residual Network-50
RMSE	Root Mean Squared Error
SWT	Stationary Wavelet Transform
SVM	Support Vector Machine
SeSCNN	Selective Sampling CNN
STARE	Structured analysis of the Retina
VDIS	Vascular Disease Image

CHAPTER 1

INTRODUCTION

1.1 Study Background

Image Processing is a method where mathematical operations are implemented for signal processing systems by feeding image or video as input and getting either image or its related features or parameters in a group as the output (Gonzalez & Woods, 2008; Kipli et al., 2018). It is being utilized in image enhancement, data compression, machine vision, and manages problems from edge detection to pattern recognition and reconstruction (Adelson & Anderson, 1984; Knutsson, 1984). In the field of biomedical engineering, the application of digital image processing is dedicated to researches and diagnosis of diseases. This technology is also used in planning and supervising treatment for that diseases, and simultaneously monitoring the disease's state (Hill et al., 2001). In the medical sector, the importance of digital image processing is immense as it helps to diminish unexpected errors and obtain higher precision (Suckling et al., 1994).

For securing the expected results and creating automated applications in the medical sector, researchers are contributing to the advancements of image processing technology. Analysis of fundus retinal images is one of the most important sub-fields of biomedical engineering. Diabetic Retinopathy (DR) and Hypertensive Retinopathy (HR) are related to the changes in the microvasculature of retinal blood vessels, because of the simple and non-invasive visualization of the microvascular structure of retinal blood vessels (Abbasi-sureshjani et al., 2016; James, 2000; Witt et al., 2006). For this reason, analysis of the human fundus eye images has become the key point of diagnosing life-threatening cardiovascular diseases.

Several changes in the microvascular structure of the human retina are found to be associated as the pre-indicator of a subsequent vascular event such as hypertension, diabetes, and ischemic stroke (De Silva et al., 2011). Different research showed that acute stroke and ocular funduscopic abnormalities are related even though various vascular risk factors and blood pressure are optimally controlled (Henderson et al., 2011). The destruction of retinal arterioles and venules is found to be consistent with HR which can lead to blindness. Different methods of classification had been drawn up to simplify the early prediction of HR (Grosso, 2005). According to the population-based study of Y et al., (2013), there is a close association between HR and the risk of stroke. Some of the population-based studies revealed that the retinal image features such as hard exudates, microaneurysm, Cotton Wool Spot (CWS) are related to diabetes, hypertension, and stroke. Their research also showed that the changes in vessel diameter and bifurcation angle were associated with cardiovascular diseases and stroke mortality even the people were free from other stroke risk factors (Baker et al., 2008; Wang et al., 2011). Figure 1.1 shows the normal retina and retina with abnormalities.

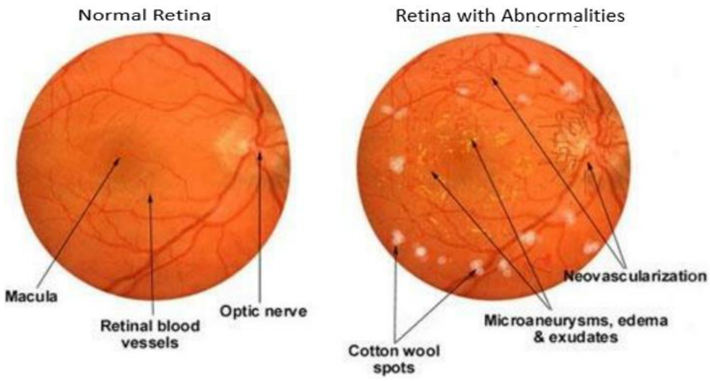

Figure 1.1: Normal retina and retina with abnormalities (Namrata & Arora, 2015)

The fundus retinal images are directly captured from a human eye with some other landmarks like the microcirculation system of the retina, fovea, optic disc, macula, microaneurysm, and exudates (Huang et al., 2018). This practical, basic image acquisition system can be utilized in large-scale screening programs. This imaging system can also be used in retinal image examination creating numerical and computational strategies. It is helpful to introduce the doctors to some of the symptoms like the hard exudates, microaneurysm, hemorrhages, and CWS. The development of the image analysis technique is significant to quantify the vessel width, vessel tortuosity, bifurcation angels, and vessel caliber. These techniques can be used for early detection of HR and DR, macular degeneration, acute stroke, glaucoma, and some other cardiovascular disease (Abbasi-sureshjani et al., 2016; Bonaldi et al., 2016; Cheng et al., 2016; Rasmussen et al., 2017; Seidelmann et al., 1954; Wigdahl et al., 2016; Witt et al., 2006).

Artificial Intelligence (AI) is being used vastly in Image Processing (IP) for solving different kinds of intractable problems by academia and industry. Image recognition and understanding are considered a remarkable subfield of AI. In biomedical engineering especially in ophthalmology, AI more precisely ML and DL methods are being applied to develop intelligent systems for diagnosing the diseases, planning and supervising treatment for that diseases (Kipli et al., 2018).

In practice, retinal images data have high dimensionality, this led to enormous size data. To overcome this problem, ML and DL can be used. Here, the original input data need to be projected into output data which has a smaller number of features whilst as much as possible preserve its native information. This is known as feature extraction. These task-driven ML and DL techniques, use a variety of algorithms that iteratively learn from data to improve, describe data, and predict outcomes. In a way, this efficaciously contributes to the modern ophthalmological diagnostic digital image processing systems.

Understanding and overseeing retinal images have become more intricate because of the random accumulation of images (Ziad Obermeyer, 2017). The new technologies for diagnostic, therapeutic, and clinical information management require intelligent tools to oversee them securely, and proficiently. Radiology, pathology, and dermatology have a striking similarity to ophthalmology as they are profoundly dependent on diagnostic imaging. In recent times, the most efficient applications of AI-based analyses are being used in diagnostic imaging (Jiang et al., 2017). Figure 1.2 shows the statistical representation of the implementation of AI-based applications in medical technology

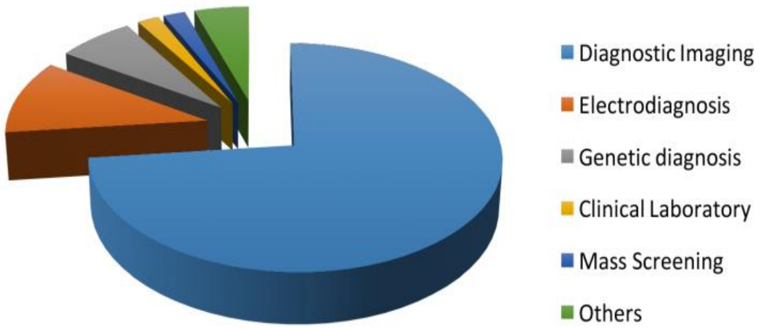

Figure 1.2: AI-based application in medical technology (Jiang et al., 2017)

The benefit of AI in medicine is highly impressive. Artificial Intelligence is especially reasonable for dealing with the multifaceted nature of 21st-century ophthalmology. Artificial Intelligence can help ophthalmologists to utilize effective algorithms for detecting features from enormous volumes of image data. Employing AI can potentially decrease diagnostic and therapeutic mistakes, and encourage customized medicine (Schmidt-Erfurth et al., 2018). Moreover, AI can perceive specific patterns of the disease and relate novel features to gain creative scientific understanding. If ophthalmologist wishes to retain control of their expert in future, they should grasp wise algorithms and instruct themselves in applying AI in a useful way (Schmidt-Erfurth et al., 2018).

To help the physicians with the early detection of the lethal condition, researchers from biomedical engineering disciplines are being involved more enthusiastically. The field of AI and digital image processing have a variety of concerns of numerous applications in ophthalmology. The used pre-processing techniques of recently reported AI-based retinal feature extraction methods are not efficient to process noisy retinal images that contain pathology. Moreover, existing AI-based retinal image feature extraction techniques are solely dedicated to extracting the blood lesion such as exudates, haemorrhages (Hoque & Kipli, 2021). Extracting the entire vessel structure or significant vessel segments is crucial to quantify vessel diameter and bifurcation angle. This study aims at developing an algorithm for retinal image vessel extraction employing DL and image processing techniques.

1.2 Problem Statement

Analyzing the fundus retinal image, the possibility of this risky cardiovascular disease such as DR, HR can be predicted. But most of the existing methods for the extraction of retinal image vessels are based on image processing. Image processing-based methods are not fully automated. The existing AI-based methods are still in the development phase as these methods provide less accuracy in comparison with the manual measurement (City et al., 2011). The existing image processing-based methods need the involvement of a good number of observers that make the diagnosing systems lengthier. The bulkiness of the observers also leads the diagnosing system to provide an inaccurate result. To overcome these limitations an AI-based fully automated disease-diagnosing system can play an important role in ophthalmology for detecting DR, HR.

Pre-processing of the retinal image is challenging due to the highly varied microvascular structure of the human retina. An inefficient pre-processing strategy can