HYBRIDIZATION OF OPTIMIZED SUPPORT VECTOR MACHINE AND ARTIFICIAL NEURAL NETWORK FOR THE DIABETIC RETINOPATHY CLASSIFICATION PROBLEM

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by

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"In the name of Allah, most Gracious, most Compassionate"

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LIST OF ABBREVIATIONS

ANN	Artificial Neural Network
CART	Classification and Regression Tree
CDSS	Clinical Decision Support System
CM	Confusion Matrix
CV	Cross Validation
CWS	Cotton-Wool-Spot
DM	Diabetes Mellitus
DR	Diabetes Retinopathy
DRIVE	Digital Retinal Images for Vessel Extraction
DT	Decision Tree
EX	Exudate
HbA1C	Glycated Hemoglobin
HM	Haemorrhage
HGB	Haemoglobin
IBK	Instance-Bases learning with parameter k
k-NN	k-Nearest Neighbour
LR	Logistic Regression
LDA	Linear Discriminant Analysis
MA	Microaneurysm
ML	Machine Learning
NP	Nondeterministic Polynomial

NPDR	Non-Proliferative Diabetic Retinopathy
PNN	Probabilistic Neural Network
PDR	Proliferative Diabetic Retinopathy
RVT	Retinal Vascular Tortuosity
RFI	Retinal Fundus Image
SIVA	Singapore I Vessel Assessment
STARE	Structured Analysis of the Retina
SVM	Support Vector Machine

PENGGABUNGAN ANTARA MESIN GABUNGAN VEKTOR OPTIMUM DAN RANGKAIAN NEURAL BUATAN UNTUK MASALAH KLASIFIKASI DIABETIK RETINOPATI

ABSTRAK

Retinopati diabetes (DR) adalah salah satu penyakit paling mengancam yang menyebabkan buta kepada pesakit diabetes. Dengan peningkatan jumlah kes DR pada hari ini, pemeriksaan mata telah menjadi tugas yang mencabar bagi pakar mata kerana mereka perlu menangani sejumlah besar imej retina untuk didiagnosis setiap hari. Pemeriksaan dan pengesanan awal DR memainkan peranan penting untuk membantu mengurangkan kejadian morbiditi visual dan kehilangan penglihatan. Tugas pemeriksaan dilakukan secara manual di kebanyakan negara yang menggunakan skala kualitatif untuk mengesan kelainan pada retina. Walaupun pendekatan ini berguna, pengesanan tidak tepat. Penyelidik sebelum ini telah mencuba beberapa percubaan untuk klasifikasi DR secara automatik, namun ia perlu diperbaiki terutamanya dari segi ketepatan. Sekumpulan literat menunjukkan bahawa klasifikasi DR boleh dilakukan menggunakan ciri-ciri klinikal yang terhasil daripada ujian darah seperti hemoglobin, trigliserida, creatine dan nilai glukosa. Malah subjek ini telah dikaji sebelum ini, tetapi masih menjadi subjek penyelidikan yang berterusan. Oleh itu, penyelidikan ini bertujuan untuk mendapatkan nilai prestasi optimum atau hampir optimum dalam kajian klasifikasi diabetes menggunakan pembelajaran mesin yang diawasi. Terdapat banyak algoritma yang tersedia untuk tujuan pengelasan seperti K-Jiran Terdekat, k-Means, Mesin Vektor Sokongan, Pokok Keputusan, Rangkaian Neural Buatan dan Analisis Diskriminasi Linear. Oleh kerana banyak masalah klasifikasi telah diselesaikan dengan hasil yang baik, algoritma K-Jiran Terdekat, Rangkaian Neural Buatan, dan Algoritma Vektor Sokongan digunakan dalam kajian ini. Daripada ketiga-tiga algoritma ini, salah satu daripada algoritma yang mempunyai ketepatan algoritma tertinggi dipilih untuk ditingkatkan pada peringkat

seterusnya. Daripada hasil kajian, Mesin Vektor Sokongan menunjukkan ketepatan tertinggi iaitu pada 76.62%. Oleh kerana hasilnya mempunyai ruang penambahbaikan, ia telah diperbaiki dengan menggunakan dua kaedah yang merupakan pengoptimuman pembolehubah dan teknik gabungan. Teknik pengoptimuman pembolehubah yang digunakan adalah untuk memastikan bahawa Mesin Vektor Sokongan dijalankan dengan pembolehubah terbaik manakala teknik gabungan digunakan untuk memasukkan unsur Rangkaian Neural Buatan ke dalam Mesin Vektor Sokongan. Hasilnya, prestasi ketepatan Mesin Vektor Sokongan telah meningkat kepada 85.45% apabila menggunakan pengoptimuman pembolehubah dan 94.55% apabila menggunakan teknik gabungan. Kekuatan Mesin Vektor Sokongan adalah keupayaan untuk mengendalikan kerumitan dengan bantuan kernel manakala kekuatan Rangkaian Neural Buatan terletak pada keupayaan pembelajarannya dengan kehadiran lapisan tersembunyi. Gabungan kekuatan daripada kedua-dua algoritma membolehkannya menghasilkan penyelesaian yang lebih baik dalam masalah klasifikasi DR.

HYBRIDIZATION OF OPTIMIZED SUPPORT VECTOR MACHINE AND ARTIFICIAL NEURAL NETWORK FOR THE DIABETIC RETINOPATHY CLASSIFICATION PROBLEM

ABSTRACT

Diabetic Retinopathy (DR) is one of the most threatening disease which caused blindness for diabetic patient. With the increasing number of DR cases nowadays, diabetic eye screening has become a challenging task for ophthalmologist as they need to deal with a large number of retinal image to be diagnosed every day. Screening and early detection of DR play a vital role to help reducing the incidence of visual morbidity and vision loss. The screening task is done manually in most countries using qualitative scale to detect abnormalities on the retina. Although this approach is useful, the detection is not accurate. Previous researchers have tried a few attempts to propose an automatic DR classification, however it needs to be improvised especially in terms of accuracy. A group of literates showed that DR classification can be performed using the clinical features resulted from the blood test such as glycated haemoglobin, triglyceride, creatine and glucose value. Even this subject have been studied previously, but it remains the subject of on-going research. Hence, this research aims to obtain optimal or near-optimal performance value in the study of diabetic classification using supervised machine learning. There are many algorithms available for classification purpose such as k-Nearest Neighbour, k-Means, Support Vector Machine, Decision Tree, Artificial Neural Network and Linear Discriminant Analysis. Due to the success of many classification problems been proposed with good result, k-Nearest Neighbour, Artificial Neural Network, and Support Vector Machine algorithms are used in this research. From these three algorithms, one of the algorithms with the highest algorithm accuracy is selected to be improved in the next stage. From the result, Support Vector Machine showed the highest accuracy which was at 76.62%. Since the result has a room of improvement, it has been

improved using two methods which were hyperparameter optimization and hybrid technique. The hyperparameter optimization technique used to ensure that Support Vector Machine run with the best hyperparameters while hybrid technique used to incorporated the element of Artificial Neural Network into the Support Vector Machine. From the result, the performance of accuracy of Support Vector Machine had improved to 85.45% when using hyperparameter optimization and 94.55% when using hybrid technique. The strength of Support Vector Machine is on the ability to handle complexity with the help of kernel trick while the strength of Artificial Neural Network lies on its learning capability with the presence of hidden layer. The combination of strengths from two algorithms enabled it to offer a better result in solving DR classification problem.

CHAPTER 1

INTRODUCTION

1.1 Background

Diabetes mellitus (DM) can be defined as a metabolic disorder of carbohydrate, fat and protein which is mainly caused by abnormal insulin secretion and/or action (Organization, 1999). It affects on the body's ability to process and consume glucose for energy. Untreated, diabetes can cause many problems include diabetic ketoacidosis and non-ketotic hyperosmolar coma. Serious long-term complications include heart disease, kidney failure, and damages to the eyes. The eye is the most common organ affected by diabetes leading to Diabetic retinopathy (DR) which can cause permanent loss of vision to diabetic patients. DR is a part of microvascular complication of DM and it affects 1 in 3 person with DM (François, 1981).

The number of DR prevalence is increasing year on year. This increasing trend raises concern among all the people around the world. With the increasing number of cases nowadays, abnormal retinal classification becomes a challenging task for ophthalmologists as they need to deal with a large number of retinal images to be diagnosed every day. Screening and early detection of DR are playing an important role to help reduce the incidence of visual morbidity and vision loss. The screening tasks are done manually in most countries (Zaki *et al.*, 2016).

Usually, ophthalmologist identifies relative characteristics such as to differentiate between normal healthy vessels and abnormal vessels based on their experience which can lead to inconsistency during grader process (Abdalla *et al.*, 2015). This issue creates a need for a tool that can help the experts to categorize, classify and stage the severity of DR in order to establish adequate therapy. Among the solutions that have been proposed by previous researchers is to come out with a DR classification that can help the ophthalmologist in the grading process. There are various methods have been done for DR classification (Selvathi *et al.*, 2012).

Retinal imaging, which is a classification technique performed based on the abnormalities found on retinal fundus image such as exudates, microaneurysm, hemorrhages and also blood vessels, have been used by a few researchers. Although the retinal imaging technique facilitates early detection of DR, they required additional equipments which were quite cost-prohibitive or sometimes unavailable especially in rural area.

On the other hand, a new method of classification has been proposed by the researchers which is using the clinical features. Clinical features can be defined as a biological indicators for process that are involved in developing a disease. The clinical features such as glycated haemoglobin, triglyceride, creatine and glucose are the lab results from the blood test. It can be the input to the algorithm of DR which is built using machine learning. Several studies have been conducted to develop a good algorithm as listed in (Piri *et al.*, 2017). However, there is still some room for improvement especially in the accuracy of the algorithm.

Therefore, this study was proposed to classify DR with the objective of finding DR algorithm through clinical features with optimal or near-optimal performance matrices. In the beginning, three machine learning algorithms were considered which were k-Nearest Neighbour, Artificial Neural Network and Support Vector Machine. The selected algorithm was then improved using hyperparameter optimization and hybrid technique.

There are several advantages of this study. First and foremost, the blood tests used as the clinical variables in this study were selected by doctors, thus the validity of the features used are unquestionable. Equally important, this dataset encompasses three classes of diabetic patients which are patients that do not have DR (NODR), patients with non-proliferative DR (NPDR) and patients with proliferative DR (PDR). Previously, DR classification focus only on two classes which were to classify whether a person being diagnosed with DR or not. The classification developed in this study can assist the doctors to perform an optimum decision-making regarding the type and medication to be prescribed. Figure 1.1 shows the scenario of this research.

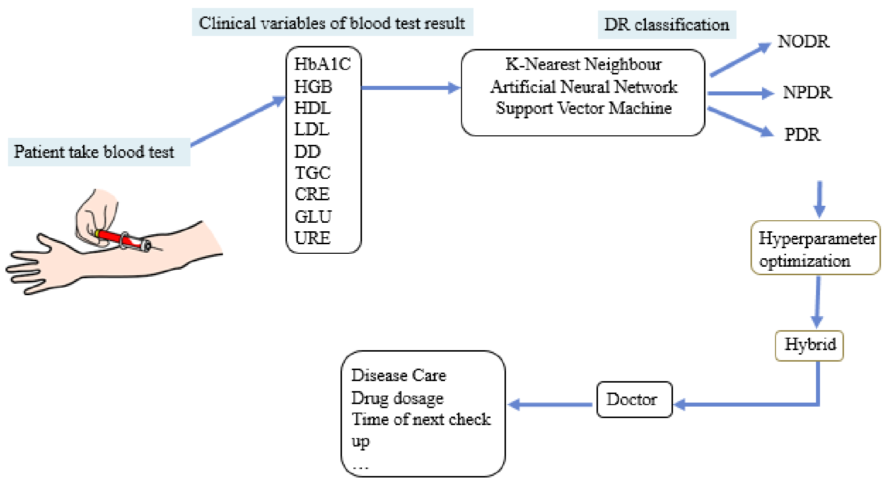

Figure 1.1: Research Scenario

1.2 Motivation

According to WHO Global report, the number of adults living with diabetes has almost quadrupled since 108 million in 1980 to 422 million adults in 2016. This dramatic rise is largely due to the rise in type 2 diabetes and factors driving it include overweight and obesity (Zimmet *et al.*, 2016). One of complication arise from DM is DR. According to American Academy of Ophthalmology, currently DR prevalence rate has been estimated at 28 million people. The numbers is estimated to be increase if prompt action is not taken.

With the high prevalence of the disease drawing attention from all parties to step up prevention and treatment of the disease including people in the field of technology. Possibility of collaboration between experts from different area can be achieved with the sophisticated technology nowadays (Sanchez *et al.*, 2014). Currently, the application of computational technique have had a huge impact in health sector. Computational technique such as machine learning is popularly used to predict the presence and absence of a disease (Ramani *et al.*, 2012). These methods play a vital role in improving the way for detection, diagnosis and treatment of the disease.

The choice of clinical features as indicators of the assessments in machine learning is because it is not cost prohibitive compared to the other automated assessment that have been proposed before, such as portable smart-phone based Clinical Decision Support System (CDSS) (Prasanna *et al.*, 2013) and smart-phone algorithm integrated with microscopic lenses (Bourouis *et al.*, 2014).

The automated system can help the experts in improving decision making and become a standard guideline for the diagnosis. With the health care industry continually looking to improve efficiency and throughput, this research potentially can be an important part of a strategy to improve performance especially in department of ophthalmology. In addition, the task of categorizing, classifying and staging the severity of DR is extremely important in order to establish adequate therapy. It could be very significant for preventing eye disease from progressing to the point of no return. With proper management, the case of blindness and visual loss can be prevented (Wu *et al.*, 2013).

Besides, it also can be diagnosed and treated effectively if the analysis of symptoms at their beginning could be performed (Mustafa *et al.*, 2016). Thus, this research seems to be a satisfactory solution that can provide fast result and timely manage of diabetic retinopathy diagnosis. In conclusion, this research is expected to give significant impacts to community and would become one of the keys for optimizing the health sector service in the future.

1.3 Research Problem

Currently, ophthalmologist identify relative characteristics such as to differentiate between normal healthy vessels and abnormal vessels through naked eyes inspection (Abdalla *et al.*, 2015). These inspections are carried out using an ophthalmoscope to directly inspect the fundus of the eye. The pupil will dilate before it is examine (Garg and Davis, 2009). Usually, the experts identify relative characteristics such as to differentiate between normal and abnormal retina based on their experience (Kalitzeos *et al.*, 2013).

The retinal mostly evaluated using qualitative scale such as "mild", "moderate", "severe" and "extreme". Occasionally, it is useful however, it is not that effective especially when comes to early detection of diabetic retinopathy, and hence early diagnosis treatment. Issue of variability in grading arise from this manual grading as the boundaries between the grades may differ between observers (Mapayi *et al.*, 2016), prone to error (Wu *et al.*, 2017) and there is uncertainties in decision making (Bajestani *et al.*, 2018).

Therefore, a new method which is using an automated assessment such as DR classification model using the clinical features. Automated assessment or system means the diagnosis of DR with the assistance of machine learning model. The function is to assist the ophthalmologist and facilitate clinical procedures has been proposed. Many attempts by previous researchers to produce high accuracy classification model have been developed. However, there is some space for improvement for a more accurate model (Zaki *et al.*, 2016). The accuracy of the current model is still low and may be increased (Mowda, 2016; Mustafa *et al.*, 2016; Amin *et al.*, 2016). In order to produce a model with the highest accuracy, the chosen of the best and efficient algorithm is playing a significant role. To make the system automated needs to know the algorithm most suitable for the dataset (Katore and Umale, 2015).

In a machine learning model, the value of hyperparameters used could affect the result produced. Thus, it is important to find the best set of hyperparameters in order to ensure that the model produced high accuracy value. The prosess of finding the best hyperparameters should be done automatically using hyperparameter optimization as the searching space for the best hyperparameters is limited in manual approach (Thornton *et al.*, 2013).

Besides, in the area of machine learning, hybrid technique is known to be one of the methods that can be used to improve the accuracy of the algorithm (Miškovic, 2014). This technique has been widely applied to various domains of study such as education, agriculture and security. However, in the study of DR, it has not been widely implemented. Therefore, it is good to conduct a study to test how the hybrid technique could improve the DR classification model.

Thus, the questions that arise in this research include:

What is the most efficient algorithm for DR classification among k-NN, ANN and SVM?

Does the selected algorithm be improved using hyperparameter optimization?

Does the optimized algorithm be improved using a hybrid technique?

The summary of the problem statement and research questions is shown in Figure 1.2.

1.4 Objectives of the Research

The main objectives of the research is to obtain optimal or near-optimal performance in the study of diabetic retinopathy classification through clinical features. The aim of this research

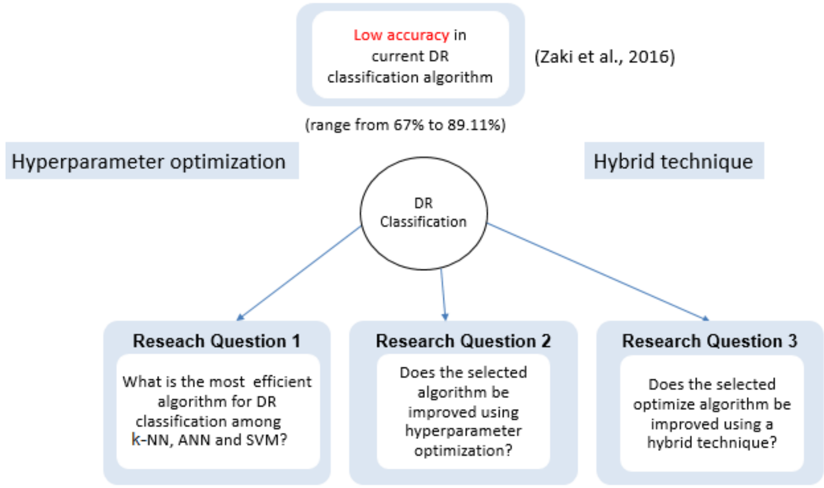

Figure 1.2: Summary of the problem statement and research question

is supported by three specific objectives:

(i) To evaluate the performance of selected supervised machine learning algorithms for DR classification

(ii) To improve performance of the selected machine learning algorithm using hyperparameter optimization

(ii) To further improve the optimized machine learning algorithm using hybrid technique

The main problem focus in this research is based on the accuracy of classification algorithms. In the first objective, initial investigation is needed to find the best algorithm with the accuracy performance. The second objective is proposed to improve performance of the selected algorithm by optimizing hyperparameters. Since the performance is still low, the third objective is proposed to further improve the optimized algorithm by adopting the other improvement method which is hybrid technique.

1.5 Assumptions and Constraints

For this research, a few constraints are considered:

(i) DR is assessed based on clinical variables and not retinal imaging

(ii) Clinical variable values are based on quantitative values

(iii) Each data item represents information on one person

(iv) Training data set must be a clean data

1.6 Scope of Research

Research in the health sector study involves a large scope study area and also involves some degree of flexibilities. Therefore, some scopes and limitations have to be made in order to make the study manageable. A clear scope and a right limitation make the study more understandable.

DR classification can involve any variables from clinical examination. However, this study only focused on nine features which were Glycated Hemoglobin (HbA1C), Hemoglobin (HGB), High-Density Lipoprotein (HDL), Low Density Lipoprotein (LDL), Diabetes Duration, Triglyceride, Creatinine, Glucose, URE). These features are selected by the doctors (Evirgen and Çerkezi, 2014).

In the computational part, the focus was on using machine learning techniques. Machine learning can be categorized according to the task it performs, either classification and prediction or association rules and clustering. Classification and prediction is a predictive model while clustering and association rules is a descriptive model (Verma *et al.*, 2016). This research only focused on classification and not considering the other task of data mining.

1.7 Outline of Thesis

This proposal is organized into seven chapters. The structure of thesis is shown in Figure 1.3. Brief descriptions of the content of each chapter are given as follows:

(i) Chapter 1 begins with discussions on some background, motivation, research problem, objectives, assumptions and constraints of this research.

(ii) Chapter 2 provides some insight of the background and related works in the problem domains regarding various techniques introduced, that would help in the understanding of the overall context of the thesis.

(iii) Chapter 3 describes the research methodology employed in this research including the research framework, data sources, instrumentation, performance measure, and experimentation and analysis used.

(iv) Chapter 4 discusses on how the supervised machine learning algorithms was adopted to the study of DR classification problem.

(v) Chapter 5 proposes a solution to improve the performance of Support Vector Machine by introducing hyperparameter optimization. Three different kernels with their respective parameters were tested.

(v) Chapter 6 proposes second method of improving SVM which is a hybrid of optimized support vector machine and artificial neural network (SVM-NN). The element of ANN were chosen to be incorporated into the optimized SVM since it can overcome the limitation in the optimized SVM.

(vi) Lastly, Chapter 7 concludes the findings and contributions and discusses the potential future work that might be employed in this research.

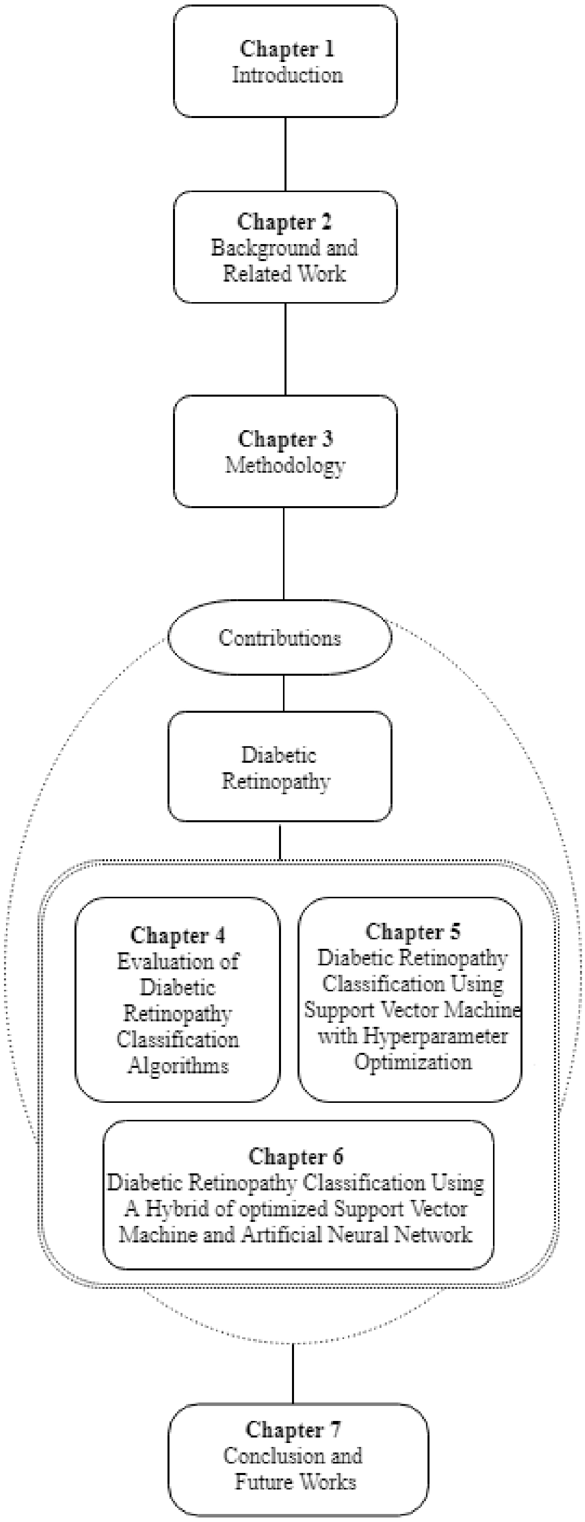

Figure 1.3: Structure of thesis

CHAPTER 2

LITERATURE REVIEWS

2.1 Introduction

This chapter will outline the background study regarding the concept and theories of diabetic retinopathy. First and foremost, the discussion start by introducing the underlying disease which is diabetic retinopathy (DR), the causes and complications in Section 2.2. Following with the Section 2.3 that discusses on the abnormalities found on the retinal affected by DR and also clinical variables that always being used in the diagnosis of DR. Then, it is continues with the discussion on the current approaches in classification of DR. The details on machine learning techniques is discusses in Section 2.4 and Section 2.5. Through these studies, the transparent overview of the domain problems is elaborated in details. The trends and directions of this study is discusses in Section 2.6. The last section of this chapter presents conclusion for this chapter. Figure 2.1 shows the content structure for Chapter 2.

2.2 Diabetic Retinopathy

Diabetic retinopathy is one of the complications arised from diabetes mellitus. The name is given regarding changes in the retina, that occur over a period of time in diabetics. It occurs when the small blood vessels in the retina contain high level of glucose (Habashy, 2013). Almost all the 30 or more cell types in retina are thought to be affected by diabetes. A person with diabetes Type 1 and Type 2 is at risk of developing DR (Patel *et al.*, 2016).

The complications of the DM are characterized by hyperglycemia. Hyperglycemia is defined by increased glucose production (Inzucchi *et al.*, 2015). One of injuries arising from hyperglycemia is injury to vasculature. This injury can be classified as small vascular injury

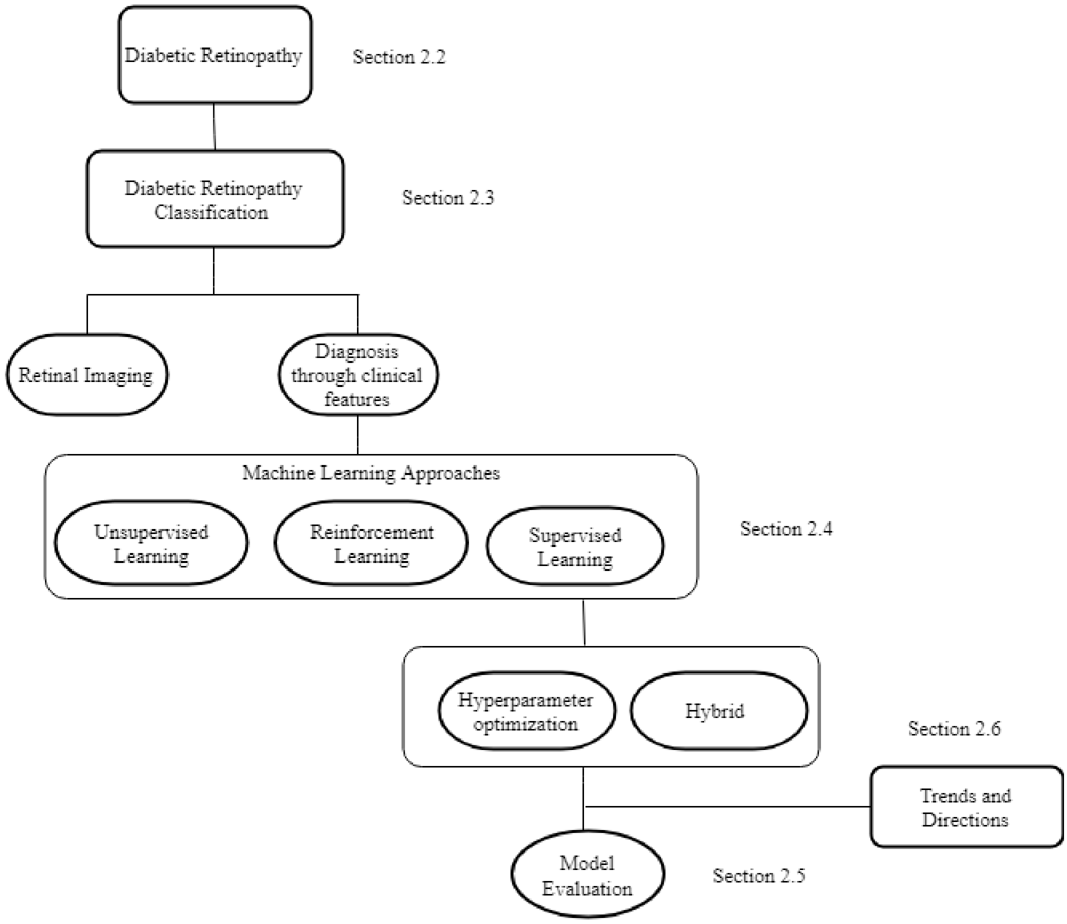

Figure 2.1: Content structure for Chapter 2

(microvascular disease) or injury to the large blood vessels of the body (macrovascular disease). There are three types of microvascular disease which are diabetic nephropathy, diabetic retinopathy and diabetic neuropathy. According to Shingade and Kasetwar (2014), DR is a frequent microvascular complication of diabetes and the highest cause of blindness and vision loss especially among working out population of the world.

Before vision loss occur to the patient, there are several signs of abnormalities in arise on the retinal. The experts make a diagnosis based on these abnormalities. Small blood vessels in the back of eye called as retinal blood vessels. In the beginning, sugar level in blood retina increase and causes blood vessel to become weak. The vessel then leaks the blood and lipoproteins fluid.

Among the abnormalities arise is microaneurysm (MA). It is small red dots on the surface of retina. The presence of balloon like swelling in the retina's blood and blood vessels are blocked then it can be microaneurysm. This is happened due to occlusion of vessel capillary and frequent leaks of fluid (Sreejini and Govindan, 2015). MA appears in the earlier stage of DR and remains in the development of the disease (Antal and Hajdu, 2012).

The size of MA usually range from 10 micrometer to 100 micrometer in diameter, and is smaller than tthe diameter of major optic veins (Pereira *et al.*, 2014). There are some objects on the retinal image which are quite similar to MA in size and shape, thus making it difficult for the experts to differentiate MA from them (Wu *et al.*, 2017). MA is a major symptoms of non-proliferative diabetic retinopathy (NPDR).

Another abnormality that may arise is the presence of exudates (EXs). EXs are yellow or white structures in the retina. Thess lesions arise due to the damage of blood vessels of retina when there are leaking of lipid out of the blood vessels. This lipid present in the form of yellow structure called hard exudates whilst white structure are called soft exudate (Sreejini and Govindan, 2015). They are appears depending on their presence or occurrence in vision.

Hard exudates have boundaries while soft exudates have no boundaries and are also known as cotton wool spots (Bhaisare *et al.*, 2016). However, if exudates are found within one disc diameter of the fovea, they are called exudative maculopathy (Rahim *et al.*, 2016).

Next, the other abnormalities arise is haemorrhage (HM). According to Watkins (2003), HM may exist within the middle layers of the retina and as "dots" or "blots". It is occur due to bleeding and it appear as small dot. Dot haemorrhages are an indication of diabetic retinopathy (Bhaisare *et al.*, 2016). In other rare case, HM occurs in the superficial nerve fibre layer and appears as flamed shaped (Watkins, 2003).

Yet another abnormality involved is tortuosity of the retinal blood vessel. According to Oxford Dictionary, the word "tortuos" can be defined as: "full of turns and twists". Tortuosity can be defined as the abnormal curvy, loopy or kinky shapes of vessels extending from the optic disc to the peripheral without bifurcation or between two major (Abdalla *et al.*, 2015). According to Mustafa *et al.* (2016) the causes of tortuosity come from several causes such as blood vessel congestion, high blood flow and angiogenesis (Turior *et al.*, 2013; Dougherty *et al.*, 2010).

An increase in the vessel tortuosity has an association with severity of the disease. A few studies conducted by (Iorga and Dougherty, 2011; Sasongko *et al.*, 2012, 2011; Zaki *et al.*, 2016) found early evidence on the association between tortuosity and development of DR and the beginning of microvascular damage in diabetic patients (Zaki *et al.*, 2013; Mustafa *et al.*, 2016). Table 2.1 summarizes the characteristics of DR lesions depicted from Patel *et al.* (2016).

Diabetic retinopathy can be classified into two stages which are non-proliferative diabetic

Table 2.1: Characteristics of diabetic retinopathy lesions

Lesion	Color	Size	Shape	Edge	Class
MA	Dark Red	Small	Round	Clear	Dark
HM	Dark Red	Small-Large	Dot-Flame Shaped	Clear-Blur	Dark
EX	Yellowish	Small-Large	Irregular	Sharp	Bright
CWS	Whitish	Small-Medium	Oval Shaped	Blur	Bright

retinopathy (NPDR) and advanced, proliferative diabetic retinopathy (PDR). It is classify based on the level of microvascular degeneration and related ischemic change. NPDR can be categorized into sub-classified (Gudla *et al.*, 2018):

- mild
- moderate
- severe
- very severe

The progression of DR is observed based on abnormalities of the vasculature using screening process (Stitt *et al.*, 2016). The screening process is conducted by ophthalmologist by detecting abnormalities on retina. The abnormalities on the retina is identified based on qualitative scale (Zaki *et al.*, 2016).

Automatic detection of DR involves detection and segmentation of any abnormalities from the image of retina (Patel *et al.*, 2016). Images of retina are taken by a device called fundus camera. This images are called retinal fundus images (RFI). Images of the internal surface of retina, macula, optic disc, posterior pole, and blood vessels tortuosity are taken by this camera (Amin *et al.*, 2016).

RFI is then assessed quantitatively by a semi-automated computer program (Singapore I Vessel Assessment [SIVA], version 2.0, National University of Singapore. The output from

SIVA will produce quantitative measurement of tortuosity and the other retinal vascular parameters (vascular caliber, fractal dimension and branching angles) (Tan *et al.*, 2015).

2.3 Diabetic Retinopathy Classification

The process of classifying DR patients are usually conducted through eye screening. Screening and early detection of DR are playing an important role to help reduce the incidence of visual morbidity and vision loss. The screening tasks are done manually in most countries (Zaki *et al.*, 2016). This inspection is carried out using an ophthalmoscope to directly inspect the fundus of the eye. The pupil is dilated before it is examined.

Usually, the experts identify relative characteristics such as to differentiate between normal and abnormal retina based on their experience. The retinal is mostly evaluated using qualitative scale such as mild, moderate, severe and extreme. However, the issue of variability in grading arise from this manual grading as the boundaries between the grades may differ between observers and also this kind of evaluation prone to error (Wu *et al.*, 2017).

As an alternative to the manual grading, the researchers proposed methods that can be used for DR diagnosis. Different approaches have been adopted by previous researchers. Among the approaches that usually used are classification through retinal imaging and diagnosis through clinical features. Both of these approaches will be elaborate in Section 2.3.1 and Section 2.3.2 respectively.

2.3.1 Retinal Imaging

In the area of DR classification, many researchers have studied DR with different intelligent methods and aims. Most of the existing DR classification or detection has mainly focused on the computational analysis of the eye fundus using image processing algorithms (Saleh *et al.*, 2017). Currently, research in image processing are focuses on how to extract signs of DR from the fundus image (Nayak *et al.*, 2008; Shahin *et al.*, 2012; García *et al.*, 2013; Sharma *et al.*, 2014a; Maher *et al.*, 2015; Navarro *et al.*, 2016).

Usually, computer vision technique is used to build models for the detection of the signs. These algorithms facilitate early detection of DR, thus retinal image is required. Therefore, they unable to address the evident barrier of patients' access to the specialist eventhough they might ease their burden to assess the image (Piri *et al.*, 2017). Besides, there have been also studies performed to build clinical decision support system (CDSS) that matches with lenses or an ophthalmoscope that can be used on smartphone (Piri *et al.*, 2017). A smartphone-based algorithm integrated with microscopic lenses was proposed by Bourouis *et al.* (2014) to capture retinal images. A neural network model has been used in their study to analyze images and provide the results.

In the another study, a portable smartphone-based classify diabetic retinopathy using image analysis and machine learning was proposed by (Prasanna *et al.*, 2013). This portable smartphone can be used for initial screening by attaching an ophthalmoscope to capture fundus image. The algorithm that was install in the smartphone will play role to process the captured image.

Despite all the sophisticated and benefits of algorithms presented in these studies, they are cost prohibitive as additional equipment is required. Therefore, the researchers are moving to a new technique which is a diagnosis through clinical features.

2.3.2 Diagnosis through clinical features

With the limited capacity of health care systems to screen and treat DR, there is need to reliably identify and triage people with DR. The clinical features may given a better understanding of DR, and contribute to the development of novel treatments and new strategies to prevent vision loss in people with diabetes (Jenkins *et al.*, 2015).

The concept of clinical features is important for a good diagnosis. Clinical features can be defined as biological indicators for processes that are involved in developing a disease that may or may not be causal (Paul and Rifai, 2006; Vasan, 2006). It has been proposed that, for clinical features to be useful for the clinicians treating, it should meet at least two criteria:

1) Evidence from prospective studies in a broad range of populations demonstrating independent prediction of vascular events with significant reclassification of risk.

2) Therapies that modify these clinical features need to be available that would otherwise not be used in the at-risk individual.

Standardization of the measure, high reproducibility, low variability, biological plausibility are also significant (Ridker *et al.*, 2004; Hlatky *et al.*, 2009). Therefore, a clinical feature cannot be considered if it is not predictive or causal to a disease, but it can still shed light on the process involved in the development of a disease, in measuring outcomes and designing therapies (Balagopal *et al.*, 2011).

In DR, among the clinical features that are consistently being identified as important are duration of diabetes (Buse, 1998; Tapp *et al.*, 2003; Control and Group, 1993; Khaw *et al.*, 2001; Fong *et al.*, 2004), insulin treatment (Group, 1998b; Khaw *et al.*, 2001; Matz, 2000), glycemic control (Evans *et al.*, 1999; Little, 2000; Matz, 2000), hypertension (Control and Group, 1993; Group, 1998a). Besides, the other features that also have been documented are type of diabetes, age, level of serum cholesterol or triglycerides, obesity, gender, physical activity and age at diabetes onset (Özmen *et al.*, 2007).

These clinical features are used to diagnosed whether a person fall into category of no diabetic retinopathy (NODR), non-proliferative diabetic retinopathy (NPDR) or proliferative diabetic retinopathy (PDR) through machine learning approaches such as in Bajestani *et al.* (2018).

2.4 Machine Learning Approaches

Machine learning can be defined as the process of machine learn from experience in the scientific field. The term “machine learning” is identical to “artificial intelligence” according to many scientist and some of them agree that machine learning is part of artificial intelligence (Al-Paydin, 2009). An intelligent system should have the ability to learn. Machine learning purpose is to developing computer systems that can learn and adapt from their experience (Kavakiotis *et al.*, 2017).

A computer program is said to learn from experience, with respect to some tasks given and the performance measure. Its performance at the task given can be improved throughout the experience (Wilson and Keil, 2001). Machine learning are typically classified into three categories which are reinforcement learning, supervised learning and unsupervised learning. Each class can serve the different purposes of machine learning such as classification, prediction, clustering and association. The purpose of can be satisfy by developing machine learning model. Its can help people to find solutions to many problems such as in speech recognition, robotic and financial services.

The machine learning models are developed mostly using algorithms based on its category. This section briefly explains the definition and algorithm involved for each category of machine learning, which are unsupervised, reinforcement and supervised learning.

2.4.1 Unsupervised Learning

Unsupervised learning is about finding human-interpretable patterns, associations or correlations describing the data (Velickov and Solomatine, 2000). It also called as pattern discovery. Discovery methods in machine learning are those that automatically identify patterns in the data. The knowledge extracted from the pattern discovery are very useful to prediction model (Rejove et al., 2000). This approach can also help provide understanding of the data (Maimon and Rokach, 2009). It produces new, nontrivial information based on the available data set. On the supervised modeling, the aim is to gain an understanding of the analyzed system by uncovering patterns and relationship in large datasets (Kantardzic, 2011). Thus, two main tasks involve in unsupervised learning are clustering and association rules.

Clustering can be defined as a process of grouping similar data into a cluster and dissimilar data into different clusters. It also can be defined as the process of organizing objects into groups whose members are similar in some ways. It is almost similar to classification. But, the difference is clustering can be considered as unsupervised learning which is contrast to the classification task. Clustering algorithm categorizes a data set into several groups such that the similarity within a group is larger than among groups (Verma *et al.*, 2012).

Association rule-based function in a way to find the relationships or correlation between items in a dataset. It is used in many recommender system. It assumes that each item has the same level of significance. However, in real practice some items might be more important than others. Therefore, decision makers have to reflect this importance level to the item based a weight assigned. The weightage is assigned considering the significance of the criteria defined by the decision makers. Among the problems that can be solved using association rule is market basket analysis problem (Altuntas and Selim, 2012). It is useful to obtain an idea of what concept structure exist in the data and for model creation (Zhang *et al.*, 2008).

2.4.2 Reinforcement Learning

Reinforcement learning can be understand as a framework for learning control policies that are commonly used by the agent, through interacting with its environment (Feng *et al.*, 2017). It is learn by interactive in dynamic environment. In reinforcement learning, while the system learn through direct interaction with the environment, its receive reward (or penalty) for its action in trying to solve the problem (Al-Paydin, 2009).

There are two significant strategies in solving reinforcement learning problems. First, to search in the space of behaviors with the purpose of finding the one that performs best in the environment. This approach has usually been adopted in the algorithm such as genetic algorithm and genetic programming as well as some other novel search techniques (Schmidhuber, 1996). Second, to use statistical technique and dynamic programming method to estimate the significance of taking actions in the states of the environment (Kaelbling *et al.*, 1996).

In other to maximize the performance while learning, it has to be concern on how an agent ought to take actions in the environment. Instead of being set up the desired actions in advance, the agent imitates the learning behaviors of human beings and usually perform trial and error process to find a suit action to obtain the most reward (Wang *et al.*, 2016). The concept of reward and punishment in reinforcement learning is used in various issues of machine learning (Harandi and Derhami (2016)) such as learning algorithm (Zang *et al.* (2013)), feature selection (Dulac-Arnold *et al.* (2012)) and web pages ranking algorithm (Derhami *et al.* (2013)).

2.4.3 Supervised Learning

Supervised learning tends to allow the user to submit records with unknown field values and product outcome of interest. The system will guess the unknown values based on previous patterns discovered from database (Verma *et al.*, 2016; Taranu, 2016). According to Velickov and Solomatine (2000), supervised learning is constructing one or more sets of data models (such as rule set, neural nets, support vectors, Decision Tree), performing inference on the available set of data, and attempting to predict the behaviour of new data sets. Thus, the two main tasks involved in supervised learning are classification and regression.

Classification is the most common action in supervised machine learning. It can be defined as a process of assigning labels or classes to different objects or group. It involved two step; model construction and model usage. Model construction is used to analyze training dataset of a database. The training set contain a set of attributes and the respective outcome, usually name as goal or prediction attribute. The algorithm construct in the training set tries to discover relationship between the attributes that would make it possible to predict the outcome. Next, model usage used the constructed model for classification. The algorithm is given a data set not seen before, called testing set.

The test set contains same set of attributes and the constructed algorithm analyses the input and produces a prediction. Prediction task involves the development and use of a model to assess the class of an unlabeled object or to assess the value or value ranges which a given object is likely to have (Verma *et al.*, 2016). The accuracy of the classification is assessed based on the percentage of test samples or test dataset that are correctly classified (Nagarajan and Chandrasekaran, 2015). In a medical database the training set would have relevant patient information recorded previously, where testing set is determine the class for each patient information. Figure 2.2 shows the general approach for building classification model. In the begining, the dataset is divided into training set and testing set. The model that has been developed will learn the training set. After completed the iteration in training phase, the model will be apply to testing set.

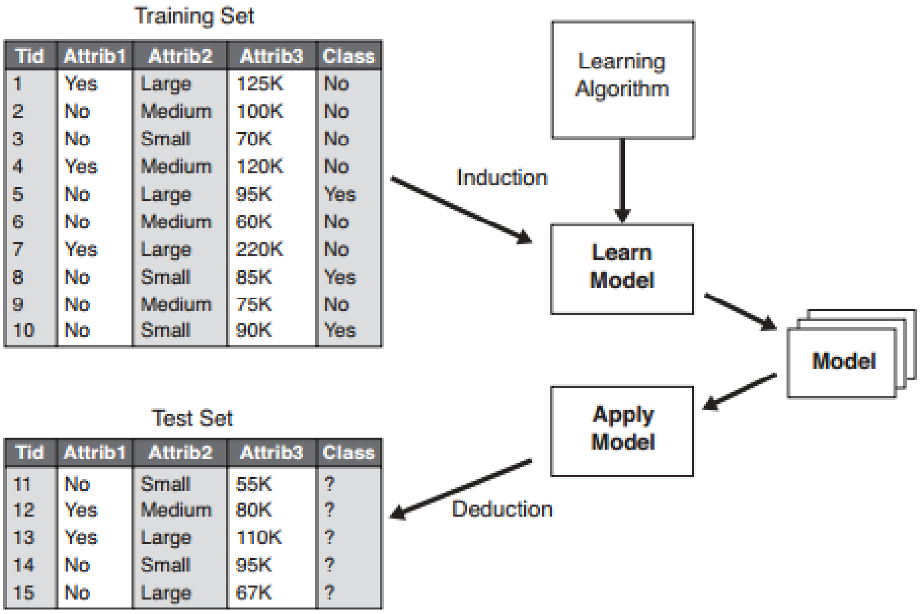

Figure 2.2: General approach for building classification model

For regression, the technique is almost similar to the problem of classification. The different is because it usually described as a process of induction of the data model of the system (using some machine learning algorithm) that able to predicting response of the system that have yet to be observed. Besides, the other difference is that regression usually output a real value as a response, which is in contrast to the classification that output the class label. Example of a problem that is usually solved using the regression model is time series prediction, where measurements/observables are taken over time for the same features (Velickov and Solomatine, 2000).

There are many algorithms in the area of machine learning that have potential to solve the problem of DR classification. However, there are three criteria that have been decided as guidelines to choose algorithm for this study. First, the algorithm must be a supervised machine learning as the data used for this study is labelled data. Next, the algorithm must have ability to handle numerical as the variables in the dataset are numerical variables. Thirdly, the algorithm is known to have the success of many classification problems been proposed with good result. Based on the highlighted criteria, five algorithms are chosen to be studied namely Naive Bayes,