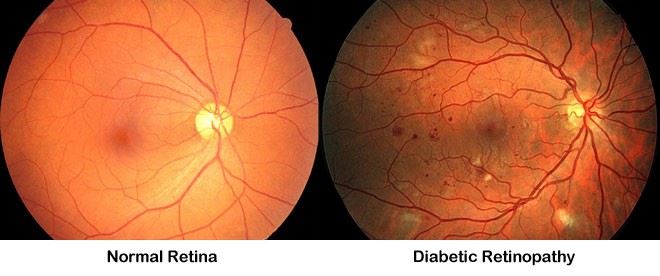
Applying Artificial Intelligence to fundus photography for early detection of diabetic retinopathy.

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# Abstract

Diabetic retinopathy (DR) is the leading cause of vision loss among working age populations globally. [1] Medically underserved populations are often unaware they have diabetic retinopathy until it reaches stage 4 Proliferative retinopathy. This is the stage where vision loss occurs, and the disease can no longer be treated or prevented; only arrested. The advances in artificial intelligence (AI) make the diagnoses of DR, and more importantly, the classification of DR levels a quicker and more accurate process than sending hundreds of fundus photographic images to a doctor for review. Additionally, by training a well-written AI model, field technicians can be deployed to remote areas with a smartphone, minimal tools and training to collect fundus images for DR screenings and classification. While the AI model is not an attempt to replace doctors, significant populations can be screened at cheaper and faster rate than current processes.

## Introduction

Diabetic Retinopathy (DR) is a disease which affects 4.1 million Americans over age 40 and according to the Centers for Disease Control (CDC), 900,000 Americans have ‘vision threatening diabetic retinopathy.’ [2] The National Institutes of Health (NIH) claim that Native Americans are twice as likely as non-Hispanic whites to suffer from diabetic retinopathy [3]. The state of South Dakota currently home to more than 80,000 Native Americans and many are unaware they have DR until they begin losing vision.

Early detection is key to the treatment of DR. Using recent advances in smartphone technology, downloadable photographic imaging software, over-the-counter Mydriatic eye drops and minimal training: a field technician can deploy to underserved communities and return collected fundus images for analysis through an AI model. The application of AI methodologies to optical fundus images can serve both the healthcare system and the global community by making the screening process for DR highly mobile, more affordable, and more accurate than the current systems in use today.

This paper examines the traditional approach to DR screenings, accuracy of human interpretations of fundus imagery, and the comparison to AI interpretations. The methodologies’ employed will be convolutional neural networks (CNNs), Oxford’s Visual Geometry Group 19 algorithm (VGG19), Inception V3 model and an ensemble model. The predictions will be generated by CNNs using Keras and Tensorflow libraries in a deep learning system. Data sets will include publicly available DR sets with both labelled and unlabeled images.

The methodologies employed will include recently published scientific papers as well as our own results with our employment and modifications of the aforementioned Inception V3 and VGG19 CNN models. While our results may not raise to the same level of the Phd scientific teams who spent years on research, our AI models do demonstrate that a graduate student with a basic knowledge of AI and programming skills can successfully employ these AI methodologies to achieve results on par with medical doctors.

Motivation

Optometrists are somewhat siloed from endocrinologists, cardiologists and even general practitioners. Most optometrists are set up in a practice located away from a hospital and usually set apart for routine eye exams, glasses and contact lens fittings and sales. Ophthalmologists, on the other hand, who perform the surgical treatments for optical issues, are usually located within a hospital or surgical clinic and have more sophisticated imaging tools at their disposal.

The eyes are often referred to as ‘the window to the soul,’ recent studies are proving fundus imagery can reveal a great deal about the overall health of the body. [4] The images taken during a routine annual eye exam can provide an endocrinologist with the data not only necessary to diagnose DR, but often to enable an accurate categorization of the DR from class 0 (no diabetic retinopathy) to class 4 (proliferate diabetic retinopathy). Cardiologists are also able use this fundus imagery to predict blood flow anomalies including cardiovascular disease, stroke, and even predict heart attacks. [5] General practitioners can also screen these images for a myriad of anomalies and heretofore unknown to the patient conditions.

The current methods for diagnosing diabetic retinopathy are fluorescein angiography (FA) and optical coherence tomography (OCT). FA involves injecting a special fluorescein dye into a patient’s veins, waiting for an hour and then taking fundus photographs. This is both invasive and time-consuming. There have also been numerous cited cases where patients had allergic reactions to the fluorescein dye. OCT uses light waves to take cross-sectional pictures of the eye and retina with thickness measurements. These machines are fixed, very large and cost approximately $100,000. The fundus images captured through OCT can cost from $600 per image to over $39,000 for a full set of images.

The costs, invasiveness and lack of portability in the current systems led us to research a more portable and affordable ways to screen underserved populations for DR. Our research concluded that with mydriatic eye drops (sold over the counter for $8-$40), a 20D convex camera lens, and a smartphone with lighted camera app, one can take fundus imagery for use in AI models testing for DR. This low-cost and highly portable method demonstrates that underserved populations can indeed get quality screening for DR and possibly even CVDs. This paper will largely focus its research on the DR application but discuss CVD in future research options.

## Related Work

Summary of AI applications in renal analysis using *standard fundus*:

***study authors & year algorithms data set performance (sensitivity/specificity)***

***[6]Gulshan et al. 2019 Inception V4 EyePAC Sens:97-98% Spec:89-92%***

***[7]Abramoff et al. 2018 VGG19 Messidor2 Sens:87% Spec:91%***

***[8]Bellemo et al. 2019 ResNet SiDRP Sens:92% Spec:89%***

Summary of AI applications in renal analysis using *smartphone fundus*:

***study authors & year algorithms data set performance (sensitivity/specificity)***

***[9]Rajalakshmi et al. 2018 Eye Art (private) Sens:96% Spec:80%***

***[10]Natarajan et al. 2019 Remidio EyePAC Sens:96-100% Spec:79-88%***

***[11]Rogers et al. 2019 Pegasus (private) Sens:89-99% Spec:82-94%***

The published research results above not only show the AI algorithms are identifying and classifying DR at a rate equal to or higher than current doctors, but also yield surprising results when moving away from the $100,000 OCT and invasive FA systems and instead relying on smartphone technology for fundus imagery.

## Methodology

CNNs seemed most appropriate for our research. Specifically, we applied VGG19 and Inception V3 using Keras, Tensorflow and Sci-Kit libraries to a labeled dataset of 3671 fundus images. We trained (80%) and validated (20%) under the labeled data set and then tested again with unlabeled images. The labelled data sets were broken into the standard medical classifications:

Class 0: No DR detected

Class 1: Mild DR

Class 2: Moderate DR

Class 3: Severe DR

Class 4: Proliferative DR

Classes 0-3 are not only treatable but also reversable when caught at this stage. Unfortunately, by Class 4 vision loss is already occurring and while the DR can often be arrested at Class 4, the disease can neither be cured nor reversed and lost vision cannot be restored.

Our models used a public data set of 3,671 labelled fundus images, which classified as:

***Class 0: 1806 | Class 1: 371 | Class 2: 1000 | Class 3: 194 | Class 4: 300***

We ran 50 epochs each of VGG19 and Inception V3 using a batch size of 32, 90 steps per epoch and 20 validation steps. Our training data was 80% with validation at 20%.

## Results

Our CNNs demonstrated the following overall results:

Inception V3

VGG19

Chart

Description automatically generatedChart, histogram

Description automatically generated

## Graphical user interface, text, application, email Description automatically generated

VGG19

## Graphical user interface, text, application, email Description automatically generated

Inception V3

The VGG19 results show and accuracy of 79.4% with Precision at 74.8%.

The Inception V3 results show and accuracy of 77.9% with Precision at 74.6%

## Conclusion/Future work

While artificial intelligence does not look to replace medical doctors, its application to medical imaging can be immediately beneficial. The ability to collect image data from underserved populations in medically remote areas can bring about the vast reduction in vision loss. Early detection is the key for successful treatment of both diabetic retinopathy and cardiovascular diseases. While this paper demonstrates the effectiveness of artificial intelligence model application to fundus imagery, the scope of our further research includes this application of AI to a binary classification for cardiovascular diseases(CVDs) and finally the development of a smartphone application TEHI (the eyes have it). TEHI is not designed to give a medical diagnosis, but rather a reasonable screening for one to get more professional medical diagnostics as needed.

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