DEEP LEARNING MODEL FOR DIAGNOSING DIABETIC RETINOPATHY

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1 INTRODUCTION

It's estimated that 537 million people have diabetes globally, of which 27% of people develop a preventable blindness-causing disease called diabetic retinopathy (DR) (Federation) (Zegeye et al. (2023)). DR is a disease that is the result of damage to the blood vessels in the retina, a direct complication of diabetes (Staff). Adequate DR screening for diabetics in the early stages of this disease can help to identify early changes in the retina before any vision impairment kicks in (World Health Organization). However, with many countries lacking the infrastructure needed to carry out screening, a shortage of ophthalmologists, and many DR patients not even aware they have the disease, the importance of early DR screening can not be stressed enough (Gargeya & Leng (2017)) (Google (b)).

In recent years, advancements in deep learning have opened the door for use in identifying diseases such as DR (Alyoubi et al. (2020)). Thus, this project aims to develop a system that is capable of detecting the stages of DR using deep learning techniques. The goal of this project is to use pictures of the retina (fundus images) taken during DR screening and develop a model that is capable of detecting the severity of the diseases based on the stages of DR with an associated probabilistic percentage. Such a system will allow for assisted, faster, early diagnosis of DR, and initiate early treatment, leading to slowing down the onset of vision impairment.

Given the severity of DR is based on small changes in the retina, many ophthalmologists may not give the correct diagnosis of the severity of DR. With recent advancements in deep learning, it is a promising method for the classification of retinal fundus images due to its ability to learn complex data and recognize important patterns within a single image. Where the demand for DR screening is increasing yet a shortage of infrastructure and prone to human error, deep learning is the solution that can assist doctors in more confident early diagnosis of DR in more patients and thus, increase accessibility of DR screening for more people.

2 BACKGROUND AND RELATED WORK

The following below are five prior works that were taken into consideration for the development of this project. Most papers explored are a variation of some of the works done below. Some utilize a grading based approach of the 5 stages of DR (Hsu (2024)):

1. No Diabetic Retinopathy
2. Mild Nonproliferative Diabetic Retinopathy (Mild NPDR)
3. Moderate Nonproliferative Diabetic Retinopathy (Moderate NPDR)
4. Severe Nonproliferative Diabetic Retinopathy (Severe NPDR)
5. Proliferative Diabetic Retinopathy (PDR)

The others are only concerned with detection based classification of DR vs. no DR.

2.1 DEVELOPMENT AND VALIDATION OF A DEEP LEARNING ALGORITHM FOR DETECTION OF DIABETIC RETINOPATHY IN RETINAL FUNDUS PHOTOGRAPHS

Researchers at Google utilized transfer-learning using the Inception-v3 architecture proposed by Christian Szegedy et al. for classification between referable and non-referable Diabetic Retinopathy. This neural network was then trained on 128,175 retinal fundus images obtained from EyePACS and 3 local eye hospitals in India using 80% of the development data for training and 20% for tuning hyperparameters (Szegedy et al. (2015)). They used ReLU for the activation function, Stochastic Gradient Descent as the optimizer, cross-entropy loss function, and batch normalization. The model was tested on the 9,963 image EyePACS-1 and the 1,748 image Messidor-1 datasets (Gulshan et al. (2016)).

The metric used for testing was Area Under the Curve (AUC), which is used to evaluate the performance of a classification model. It is scored from 0 to 1, models closer to 1 have a near perfect identification model (Google (a)).

Key results from Google's research demonstrate high performance achieving a 0.991 AUC score and 0.990 AUC score respectively with a high sensitivity and specificity rate on both datasets, proving that deep learning techniques are highly effective in this application (Gulshan et al. (2016)).

2.2 Automated Identification of Diabetic Retinopathy Using Deep Learning

A custom convolutional neural network was developed by Rishab Gargeya and Theodore Leng classifying retinal images as having or not having diabetic retinopathy (DR) and an associated probability percentage of the presence of DR using a softmax activation function. This model was trained on 75,137 images obtained from EyePACS using a 5-fold stratified cross-validation approach. They used ReLU activation function, cross-entropy loss function, residual shortcuts, and batch normalization. In addition, a global average pooling layer was used for classification of results through a gradient-boosting classifier and visualizing a heat map of regions of interest that aided in the model's prediction. Tested on the Messidor-2 and E-Ophtha datasets, key results show their model achieved a 0.94 AUC score and 0.95 AUC score respectively with specificity and sensitivity scores in the low 90s (Gargeya & Leng (2017)).

2.3 Using a Deep Learning Algorithm and Integrated Gradients Explanation to Assist Grading for Diabetic Retinopathy

The Inception-v4 architecture proposed by Christian Szegedy et al was used by researchers at Google for the classification of the 5 stages of Diabetic Retinopathy with an associated probability distribution over the 5 stages of DR using a softmax function (Szegedy et al. (2016)). The model was trained on 1.6 million images from EyePACS and 3 indian eye hospitals with 2000 images used for validation and tuning and 1796 images for testing from EyePACS. Integrated gradients were also used to generate a heatmap visualization of ROIs that aided in the model's prediction. Key results show the model had an overall accuracy of 88.4% but a 57.9% accuracy of mild to worse cases of DR and a 96% accuracy for no DR cases. The paper also showed that assistance from the model helped Opthamologists be more accurate in their diagnosis of worse cases than without (Sayres et al. (2019)).

2.4 Deep convolutional neural networks for diabetic retinopathy detection by image classification

In this paper, Shaohua Wan, Yan Liang, and Yin Zhang used the publicly available 35,126 image Kaggle DR dataset to classify the 5 stages of diabetic retinopathy using the ResNet, VGG, GoogleNet, and AlexNet architectures. Considering the imbalance in the dataset, various data augmentation techniques such as noise reduction, flipping, stretching, and rotations were used to balance the class distributions and increase the data set to 20 times its size. In addition, stochastic gradient descent was used as the optimizer. Key results show that amongst the models tested, VggNet-s performed the best with a 5-class overall accuracy of 95.68% (Wan et al. (2018)).

2.5 Deep Learning for the Detection and Classification of Diabetic Retinopathy with an Improved Activation Function

Usharani Bhimavarapu and Gopi Battineni proposed a new activation function $f(x) = \frac{x}{\cos(x)}$ that has been seen to outperform other commonly used activation functions including ReLU for diabetic retinopathy classification. Using transfer learning, they trained Inception-v3, VGG-19, ResNet-50, AlexNet, GoogleNet, SqueezeNet, and ResNet-152 models using the proposed activation function and a variant of the adam optimizer - Nadam optimizer. These models were trained on the Kaggle, CHASE, DRIVE, and DIARETDB0 datasets for a total of 88,904 images. Results showed that when testing the following models using the proposed activation function against other activation functions, the ResNet-152 model using the proposed function performed the best with a 99.41% accuracy (Bhimavarapu & Battineni (2022)).

3 Data Processing

We plan to use the publicly available 35,126 image Kaggle DR, 3662 image APTOS 2019 datasets for training and validation while the 1748 image Messidor-1 and 1058 image Messidor-2 will be used for testing (Karthik (2019)) (Guillaume PATRY) (Krause et al. (2018)) (Patry (n.d.)) (Emma Dugas (2015)). All of the aforementioned datasets contain images for the 5 stages of diabetic retinopathy.

However, in all of these datasets, there is a significant imbalance in the distribution of data across the 5 stages with most images under the no DR class. Therefore, the following data augmentation techniques will be performed:

- Image resizing: All images are to be resized to a dimension of 256x256 to ensure consistent image size and reduce the effect of black border in each retinal fundus image.
- Image rotations and mirroring: Images are to be rotated 90, 120, 180, and 270 degrees and be mirrored to artificially increase class imbalance between No DR and the other 4 stages of DR.
- Data Normalization: All image pixel intensities are to be normalized to a similar distribution, ideally between 0 to 1 to ensure consistent performance.
- Noise reduction: A Gaussian filter is to be used to reduce the noise in the image and introduce variability of image quality to the model replicating real-world conditions.
- Image Contrast: The contrast of all images is to be changed to make features more pronounced as done in. This is to be done on a uniform scale between [-0.2, 0.2] (Gargeya & Leng (2017)).

More of these techniques will be applied to cases of DR as there is significantly less data amongst these classes compared to the data for No DR across all used datasets. Doing these augmentation and processing techniques will ensure better generalization for the model (Alyoubi et al. (2020)).

4 Architecture

Based on the related projects, utilizing convolutional neural networks (CNNs) were the most effective methods for image classification and diagnosis of DR from retinal fundus images. In the same manner, a CNN model is to be developed through the course of this project that would be able to classify between the stages of DR. The feature learning encoder and the fully connected layers will be used in a complete neural network for classification of these DR stages.

The architecture for training the neural network is outlined in the following:

4.1 CNN

- The input, a $256 \times 256 \times 3$, fully colored image, initially will be sent through a series of convolutional layers with multiple sets of kernels (filters) working in parallel to extract different features. More kernels are to be created in parallel deeper into the network, as the initial convolutional layers are to capture the low level features within the image and the later convolutional layers are to capture the higher level features.
- In each set of these convolutional layers, the images are to be convolved across all three color channels and be processed further through a ReLU activation function.
- Max pooling is to be employed after each convolution layer to reduce the dimensions of the feature maps.
- To aid in mitigating the vanishing gradient problem, residual shortcuts will be exploited. The vanishing gradient problem is commonly faced among large neural networks, where the gradients become very small as back propagation repeatedly takes place through many layers (Rastogi). A relatively large neural network is to be designed to capture complex features. To be able to train the neural network and create more complex connections, more layers are to be created. However, to deal with the vanishing gradient problem, residual shortcut layer blocks are to exist throughout the image encoder. The idea is to create blocks of convolutional layers, where the input is to be directly added to the output. This is to ensure that the gradient does not vanish by allowing inputs to skip certain layer connections and improve the performance of our overall model.
- After passing the image through the convolutional layers, the image is to be flattened to be reduced to one dimension and passed through a set of fully connected layers for classification.

4.2 FCNN

- The fully connected classifier is to consist of hidden layers that are each combined with ReLU activation functions.

- The Adam optimizer is to be used with mini-batch training.
- For normalization, layer normalization will be used and the dropout technique will also be used to promote the learning of more distinct features through regularization.
- General cross entropy will be used to calculate the loss, as there are 5 different classes the model is to identify.
- Finally, to determine the probabilities of each class, we will connect the last layer to a SoftMax activation function.
- The last layer is to be connected to a SoftMax function to determine the probabilities of each class and determine the final output.

Finally, random searches are to be conducted using different configurations to find the optimal setting and best results of the model. Figure 1 shows a holistic view of the proposed architecture.

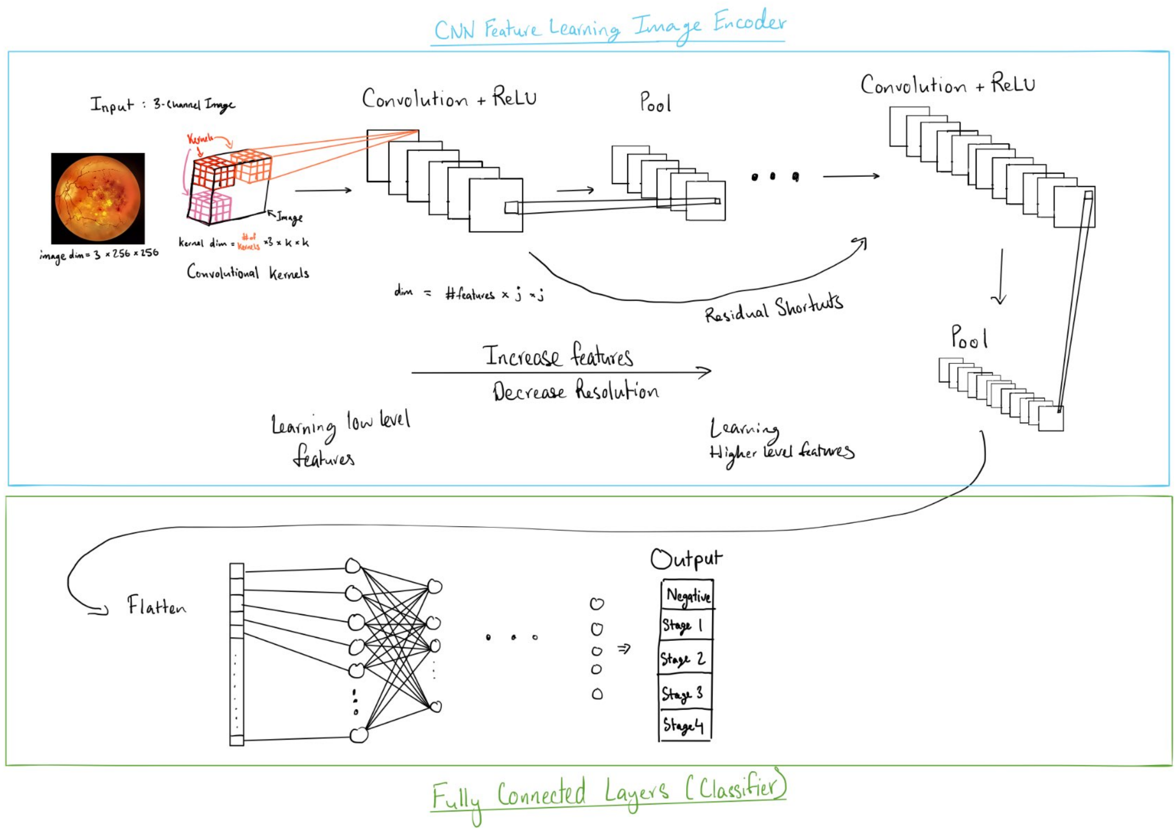

Figure 1: Illustration of CNN Architecture for DR Diagnosis Model.

5 Baseline Model

We will employ a Support Vector Machine (SVM) as our baseline model, to establish a performance benchmark for our neural network. The SVM has been used previously for diabetic retinopathy detection (Gargeya & Leng (2017)) and was chosen due to its ability to handle multi-class classification, which is necessary for identifying the various stages of diabetic retinopathy. SVMs determine a hyperplane that can effectively separate classes present in the data. This is done through the use of kernel functions, which transforms the input data into higher-dimensional spaces in order to manage non-linear classification tasks. Radial Basis Function (RBF) kernels are used for its ability to capture complex patterns in retinal images as research shows that SVMs with RBF kernels have performed well in diabetic retinopathy detection, achieving high accuracy (Tsao et al. (2018)). By establishing the performance of our SVM baseline, we aim to demonstrate the improvements achieved with our more complex neural network model.

6 Ethical Considerations

Amongst the ethical issues that are raised through our model, the most prominent being the bias and fairness of our model. Our data, consisting of Kaggle DR, APTOS, Messidor-1 and Messidor-2, will be sample select, and will thus may not be representative of the entire population that this set belongs to (Karthik (2019)) (Guillaume PATRY) (Krause et al. (2018)) (Patry (n.d.)) (Emma Dugas (2015)). Moreover, the small sample of data may perform well for certain groups of people but prove to be inefficient when testing on other groups. Depending on the age and ethnicity of the retina scans that we will be fed into the our model, our model may prove to not be so accommodating to a diverse range of individuals

Furthermore, the collection and use of medical data may be considered a breach of sensitive personal information, and thus would involve violating patient trust and confidentiality. Fortunately, the data we will be utilizing can be found publicly with patient consent taken into consideration. Taking into further considerations, developing a successful neural network which accomplishes the goal we established might result in an over reliance on automated diagnostic systems potentially leading to a reduction in healthcare providers diagnostic skills or oversight

Lastly, the dataset that we will be utilizing is imbalanced as the amount of cases pertaining to each class is different, some being significantly larger in quantity than others. More specifically, our collected data set contains more non DR cases compared to DR cases. This could potentially skew the result of our neural network towards diagnosing patients with having healthy eyes instead of eyes suffering from DR. This is due to the fact that our neural network learns from healthy retina images more so than retinas with DR. Ultimately this could hinder the usability of our model.

7 Project Plan

To work together, the team will meet after the labs and tutorials on Wednesdays around 8 p.m. EST. Our methods of communication will be through our WhatsApp group chat for messaging and Discord group chat to hold meetings. If a member is struggling with an issue that they are not able to resolve individually, then the matter should be brought to the team immediately to find a solution as a group. The team plans on collaborating on Github to maintain the codebase. In order to ensure no critical conflicts, members are to pull, test, merge, test again and push working code that is well commented along with specific git commit messages. Table 1 outlines the plan for the tasks delegated amongst the team along with the internal deadlines.

Assignments	**Tasks**	**Team Member**	**Internal Deadline**	**Due Date**
Project Proposal	Introduction	Abubaker	4/6/2024	6/6/2024
	Ethical Considerations	Abubaker	4/6/2024	6/6/2024
	Risk Register	Abubaker	4/6/2024	6/6/2024
	Illustration/ Figure	Abdullah	4/6/2024	6/6/2024
	Architecture	Abdullah	4/6/2024	6/6/2024
	Background & Related Work	Iftier	4/6/2024	6/6/2024
	Data Processing	Iftier	4/6/2024	6/6/2024
	Baseline Model	Sami	4/6/2024	6/6/2024
	Project Plan	Sami	4/6/2024	6/6/2024
	Link to Github or Colab Notebook	All Members	4/6/2024	6/6/2024
	References	All Members	4/6/2024	6/6/2024
	Structure, Grammar & Mechanics	All Members	4/6/2024	6/6/2024
Progress Report	Project Description	Abdullah	29/6/2024	4/7/2024
	Data Collection	All Members	25/6/2024	4/7/2024
	Pre-Processing of data	Abdullah	26/6/2024	4/7/2024
	Hyperparameter tuning	All Members	28/6/2024	4/7/2024
	Contribution and Responsibilities	All Members	29/6/2024	4/7/2024
	Data Preparation/ Processing	Sami	28/6/2024	4/7/2024
	Initial model training	Iftier	28/6/2024	4/7/2024
	Baseline Model	Abubaker	29/6/2024	4/7/2024
	Primary Model	Iftier	29/6/2024	4/7/2024

Table 1: Assignment and Task Schedule

8 Risk Register

8.1 A team member decides to drop the course

Solution: Discussions regarding potentially dropping out of the course must occur 2 weeks prior to the student decision to drop the course. The Student who is planning to drop the course must call an emergency meeting where it will be discussed with the group on how we will re-distribute the work that the team member was responsible for. An appointment with an instructor or TA will also be held in order to determine what the best possible course of action our team should take, and if we could potentially get another student to join our team.

8.2 Team discussion or argumentation with regards to making a decision is taking an excessive amount of time

Solution: A poll will be held amongst members of the team who will vote which idea or decision we will make, and the idea with the most votes will be enforced regardless of any team objections. If the team can not decide on a particular idea through a poll, the team's elected leader will be given the authority to make the final decision regardless of any protesting that exists as a result of the decision. If the team's argumentation or discussion escalates to an unacceptable level such as insulting and vulgarity, the team will make an appointment with a TA to resolve our internal conflict.

8.3 If a team member or numerous team members have not completed their own tasks that they were assigned with at the deadline that the team established

Solution: The team will implement a three strike system in which if a team member misses internal deadlines it will count as a strike, he will be given a warning, and a penalty of increased workload will be established for that team member. After the second strike, a penalty of even more increased workload coupled with having no say in the upcoming group decisions we make. After the third strike, a meeting will be held with an instructor or TA filing a complaint against this member and discussing what further course of action we should take.

8.4 Convolutional neural network failed to perform properly

Solution: Each team member will be responsible for a certain aspect of the neural network code in order to expiate the debugging process. One will be responsible for the logic flow of the syntax to ensure the network is doing what we want it to be doing. The rest of the team will be responsible for going through different hyperparameters and observing their structure. After our efforts, if we still have not mended the issue that was raised, we issue an emergency meeting to discuss what our next course of action should be.

9 Link to Github or Colab Notebook

https://github.com/UltimateForce21/DiabeticRetinopathyCNN

REFERENCES

Wejdan L. Alyoubi, Wafaa M. Shalash, and Maysoon F. Abulkhair. Diabetic retinopathy detection through deep learning techniques: A review. *Informatics in Medicine Unlocked*, 20:100377, 2020. ISSN 2352-9148. doi: https://doi.org/10.1016/j.imu.2020.100377. URL https://www.sciencedirect.com/science/article/pii/S2352914820302069.

Usharani Bhimavarapu and Gopi Battineni. Deep learning for the detection and classification of diabetic retinopathy with an improved activation function. *Healthcare (Basel, Switzerland)*, 11(1):97, 2022. doi: 10.3390/healthcare11010097. URL https://doi.org/10.3390/healthcare11010097.

Jorge Will Cukierski Emma Dugas, Jared. Diabetic retinopathy detection, 2015. URL https://kaggle.com/competitions/diabetic-retinopathy-detection.

Internation Diabetes Federation. IDF Diabetes Atlas 2021 – 10th edition. https://diabetesatlas.org/idfawp/resource-files/2021/07/IDF_Atlas_10th_Edition_2021.pdf. accessed Jun. 6, 2024.

Rishab Gargeya and Theodore Leng. Automated identification of diabetic retinopathy using deep learning. *Ophthalmology*, 124(7):962–969, 2017. ISSN 0161-6420. doi: https://doi.org/10.1016/j.ophtha.2017.02.008. URL https://www.sciencedirect.com/science/article/pii/S0161642016317742.

Google. Classification: Roc curve and auc — machine learning — google for developers. https://developers.google.com/machine-learning/crash-course/classification/roc-and-auc, a. accessed Jun. 6, 2024.

Google. Diagnosing preventing diabetic retinopathy with ai. https://about.google/stories/seeingpotential/, b. accessed Jun. 6, 2024.

G.G. Guillaume PATRY. Messidor. https://www.adcis.net/en/third-party/messidor/. accessed Jun. 6, 2024.

Varun Gulshan, Lily Peng, Marc Coram, Martin C. Stumpe, Derek Wu, Arunachalam Narayanaswamy, Subhashini Venugopalan, Kasumi Widner, Tom Madams, Jorge Cuadros, Ramasamy Kim, Rajiv Raman, Philip C. Nelson, Jessica L. Mega, and Dale R. Webster. Development and Validation of a Deep Learning Algorithm for Detection of Diabetic Retinopathy in Retinal Fundus Photographs. *JAMA*, 316(22):2402–2410, 12 2016. ISSN 0098-7484. doi: 10.1001/jama.2016.17216. URL https://doi.org/10.1001/jama.2016.17216.

Jason Hsu, MD. Diabetic retinopathy. *American Academy of Opthalmology*, 04 2024. URL https://eyewiki.aao.org/Diabetic_Retinopathy.

Sohier Dane Karthik, Maggie. Aptos 2019 blindness detection, 2019. URL https://kaggle.com/competitions/aptos2019-blindness-detection.

Jonathan Krause, Varun Gulshan, Ehsan Rahimy, Peter Karth, Kasumi Widner, Greg S. Corrado, Lily Peng, and Dale R. Webster. Grader variability and the importance of reference standards for evaluating machine learning models for diabetic retinopathy. *Ophthalmology*, 125(8):1264–1272, 2018. ISSN 0161-6420. doi: https://doi.org/10.1016/j.ophtha.2018.01.034. URL https://www.sciencedirect.com/science/article/pii/S0161642017326982.

Guillaume Patry. Messidor-2. ADCIS, n.d. URL https://www.adcis.net/en/third-party/messidor2/. Accessed: Jun. 6, 2024.

V. Rastogi. Residual networks (resnet). https://medium.com/@vaibhav1403/residual-networks-resnet-fb20330a7aed. accessed Jun. 6, 2024.

Rory Sayres, Ankur Taly, Ehsan Rahimy, and Kimberly Blumer. Using a deep learning algorithm and integrated gradients explanation to assist grading for diabetic retinopathy. *Ophthalmology*, 126(4):552–564, 2019. doi: 10.1016/j.ophtha.2018.11.016. URL https://doi.org/10.1016/j.ophtha.2018.11.016.

Mayo Clinic Staff. Diabetic retinopathy. https://www.mayoclinic.org/diseases-conditions/diabetic-retinopathy/symptoms-causes/syc-20371611. accessed Jun. 6, 2024.

Christian Szegedy, Vincent Vanhoucke, Sergey Ioffe, Jonathon Shlens, and Zbigniew Wojna. Rethinking the inception architecture for computer vision. *arXiv.org*, 2015. URL https://arxiv.org/abs/1512.00567v3. Accessed: Jun. 6, 2024.

Christian Szegedy, Sergey Ioffe, Vincent Vanhoucke, and Alex Alemi. Inception-v4, inception-resnet and the impact of residual connections on learning. *arXiv.org*, 2016. URL https://arxiv.org/abs/1602.07261. Accessed: Jun. 6, 2024.

Hsi-Yuan Tsao, Po-Yu Chan, and Eric C.-Y. Su. Predicting diabetic retinopathy and identifying interpretable biomedical features using machine learning algorithms. *BMC Bioinformatics*, 2018. URL https://bmcbioinformatics.biomedcentral.com/articles/10.1186/s12859-018-2277-0. Accessed: 06 June 2024.

Shaohua Wan, Yan Liang, and Yin Zhang. Deep convolutional neural networks for diabetic retinopathy detection by image classification. *Computers Electrical Engineering*, 72:274–282, 2018. ISSN 0045-7906. doi: https://doi.org/10.1016/j.compeleceng.2018.07.042. URL https://www.sciencedirect.com/science/article/pii/S0045790618302556.

World Health Organization. Diabetic retinopathy screening: A short guide. https://iris.who.int/bitstream/handle/10665/336660/9789289055321-eng.pdf. accessed Jun. 6, 2024.

Abayneh F. Zegeye, Yared Z. Temachu, and Chalie K. Mekonnen. Prevalence and factors associated with diabetes retinopathy among type 2 diabetic patients at northwest amhara comprehensive specialized hospitals, northwest ethiopia 2021. *BMC Ophthalmology*, 23(1):9, 2023. doi: 10.1186/s12886-022-02746-8. URL https://doi.org/10.1186/s12886-022-02746-8.