Statement of Purpose

There is a pressing need to close the gap between medicine and state of the art Artificial Intelligence (AI). To that end, **I am passionate about pushing the frontier of medicine forward with AI**. During my undergraduate, I applied machine learning for the diagnosis of Dry Eye Disease (DED)—over five percent of US adults suffer from DED, making it the most common ocular disease. This research statement describes the two projects I conducted for DED diagnosis and my future outlooks in medical AI.

Experience

For the past two years, I have studied machine learning applications for DED with **Berkeley Artificial Intelligence Research (BAIR)** and **Berkeley's Clinical Research Center (CRC)**, co-advised by **Professor Stella Yu** and **Professor Meng Lin**. Currently, DED diagnoses rely on clinicians' experience, training, and expertise resulting in highly imbalanced standards around the world. The goal of our work was to build objective machine learning tools to yield faster, more accurate diagnoses and improve our understanding of the complex, multifaceted dry eye condition.

Predicting Dry Eye-Related Signs, Symptoms and Diagnoses with Meibography Images My first project leveraged a dataset collected by our clinicians consisting of patient eye images, ocular signs, reported symptoms, demographic data, and diseases relating to DED. We began by running the patient eye images through a previously developed neural network from our lab [1] to yield quantitative values associated with the structure of the meibomian glands—they are located in the eyelids and produce oils that help protect and lubricate the eye. In other words, the output of the network served as a way to distill each image into a few important feature values.

We combined the image feature values with the signs, symptoms, and demographic data to study all the variables together. We started by analyzing the relation between all pairwise variables using Pearson correlation and mutual information. We found that many variable pairs were highly correlated. We further clustered the variables with hierarchical and spectral clustering to discover that many variables could be grouped together because of their high association with each other. In essence, we found that the dataset features had a lot of latent correlation.

With the existing redundancy in the dataset in mind, I suggested we use logistic regression to predict the disease. However, highly correlated features tend to cause linear models to have increased variance and decreased precision. I found that by pruning redundant variables, the accuracy of the prediction went up significantly. Ultimately, we ran a recursive pruning algorithm to pick only the essential features for prediction of the diseases. **Our model was able to predict diseases linked to DED with an accuracy ranging from 74% to 85%**. Not only did the model yield high accuracy predictions but we were also able to analyze the top predictive features based on the logistic regression model weights. While some of these top features reinforced prior clinical knowledge, other top features were previously undiscovered. Collectively, these top features will serve as an important tool for clinical prediction of various diseases linked to DED. **Professor Meng Lin gave a talk to present the findings of this research at the 2022 American Academy of Optometry (AAOPT) annual meeting. This work [2] will be submitted in January 2023 to Opthalmology, the journal of the American Academy of Ophthalmology, in which I am the first author** and also served as the first part of my undergraduate thesis.

Tracking the Dynamics of the Tear Film Lipid Layer The first project gave me perspective on the variables relating to DED. One variable that Professor Lin suggested we explore further was the tear

film lipid layer. When a blink occurs, the tear film spreads over the eye in order to protect and lubricate the ocular surface. Tear film instability is a known factor for DED, and is thought to be regulated by the thin lipid layer that covers and stabilizes the tear film. The spread of the tear lipid layer, following a blink, can be visualized and recorded with an interferometer.

Our initial task was to determine the relative average lipid layer thickness during the spread—the lipid layer thins as it covers the whole eye after a blink and we wanted to understand the rate at which it thins. [3] devised a way to compute the relative lipid layer thickness using the RGB color values from a recording of the ocular surface. Previously my lab was just using a software package to manually pick points on the lipid layer over the iris and have the software compute an average lipid layer thickness value for every frame. In order to automate this process, we needed a way to pick random points only over the iris and avoid the pupil, eyelashes, and sclera (the white region of the eye surrounding the iris). I built a segmentation algorithm which used clustering and active contours to find the region associated with the iris. With the segmentation model, I was able to automate the previously manual approach.

However, we quickly realized that our method lacked precision: we were computing the average thickness value, despite the thickness values varying vastly at different points on the tear film. **I made the key proposition that we should track discrete points on the spreading lipid layer** and compute thickness values for each point respectively. Thus, each discrete moving point on the lipid layer would have its own associated thickness reading for each frame. This effort started with visually enhancing the visibility of the lipid layer through sharpening, histogram equalization, frequency filtering, and average frame subtraction. With the enhanced video, we used both Lucas-Kanade and Farneback's optical flow algorithms to track distinct feature points on the spreading lipid layer. When we initially ran our tracking algorithm, we realized that it was subject to noise from eye movements in the recordings. In order to stabilize the video, we used [4]'s pupil tracking method to align all the frames with respect to the center of the pupil. We further refined the pupil tracking algorithm by implementing the Kalman Filter.

Prior to my approach, no techniques existed to automatically track the spread of the tear film lipid layer. This method makes significant progress towards automated analysis of the tear film. Most importantly, we showed that there is a positive correlation between the severity score of DED and spread time of the tear film lipid layer. Using my tracking algorithm, we will be conducting a large scale quantitative investigation on hundreds of subjects' tear films in February 2023. With the incoming data, we plan to train an unsupervised optical flow deep learning model for tear lipid layer tracking. **This work [5] was presented at the 2022 Medical Imaging Workshop in NeurIPS in which I am the first author** and also served as the second part of my undergraduate thesis. I also gave a talk to present this research to our potential collaborators at Alcon.

Future Outlook

My research experience in AI applications for DED diagnosis has not only prepared me for graduate studies, but has also inspired me to continue to work at the intersection of medicine and AI in hopes to make a lasting impact. However, more broadly, I am open to researching any applications of machine learning for human advancement.

References

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