Research Statement

Artificial intelligence (AI) has enjoyed a meteoric rise to fame in recent times. And while the potential applications of AI in medicine seem endless, medical AI continues to lag behind when compared to the rest of the field of AI. **There is a pressing need to close the gap between medicine and state of the art AI**. To that end, I am passionate about pushing the frontier of medicine forward with machine learning. This research statement outlines my research experience in AI applications for ophthalmology.

Experience

For the past two years, I have worked at the intersection of machine learning and ophthalmology. I have worked jointly at **Berkeley Artificial Intelligence Research (BAIR)** and **Berkeley's Clinical Research Center (CRC)** supervised by **Professor Stella Yu** and **Professor Meng Lin** respectively. I describe two research projects, both of which apply machine learning for diagnosis of Dry Eye Disease (DED)—over five percent of US adults suffer from DED, making it the most common ocular disease.

Machine Learning for Ocular Disease Diagnosis, Signs, and Symptoms My first project leveraged a dataset consisting of patient eye images, ocular signs, reported symptoms, and demographic data to help diagnose dry eye disease. Our first approach was to use computer vision on the patients' eye images to predict the diseases. We trained a separate ResNet binary predictor for each disease with the eye images as the input. However, using standard deep learning techniques, our results were no better than randomly guessing the disease based on the data distribution. We realized that deep learning was not going to be the solution to our problem.

Our focus shifted from the image data to the signs, symptoms, and demographic data. 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, we wanted to use logistic regression to predict the disease with high accuracy. However, highly correlated features tend to cause linear models to have increased variance and decreased precision. We 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. **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. **This work [1] will be submitted in December 2022 to the Ophthalmology Journal 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 a micro-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. Hwang et al. 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 the active contours to find the region associated with the iris. With the segmentation model, I was able to quickly 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 [2]'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.

With our robust tracking algorithm, we were able to confirm prior work that the displacement of the lipid layer, following a blink, can be characterized by an exponential decay curve. We also showed that the tear lipid layer thinning rate and displacement of the lipid layer are directly correlated. Most importantly, **we showed that there is a positive correlation between the Ocular Surface Disease Index (a score indicating the severity of dry eye disease) and spread time of the tear film lipid layer**. Using my tracking algorithm, we plan to do a large scale quantitative investigation on hundreds of subjects' tear films in Spring 2023. With the incoming data, we plan to train an unsupervised optical flow deep learning model for tear lipid layer tracking. **This work [3] 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.

References

[1] **Tejasvi Kothapalli***, Peter Wang*, Andrew D. Graham, Stella X. Yu, and Meng C. Lin. A proposed machine learning approach to ocular disease diagnosis, signs, and symptoms. *In Preperation for Proceedings to Ophthalmology.*

[2] Bartlomiej Kowalski, Xiaojing Huang, Samuel Steven, and Alfredo Dubra. Hybrid fpga-cpu pupil tracker. *Biomedical Optics Express*, 12(10):6496–6513, 2021.

[3] **Tejasvi Kothapalli**, Charlie Shou, Jennifer Ding, Jiayun Wang, Andrew D. Graham, Tatyana Svitova, Stella X. Yu, and Meng C. Lin. Tracking the dynamics of the tear film lipid layer. *NeurIPS Medical Imaging Workshop*, 2022.