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Pupillometry and Gaze Tracking for Early Detection of Diabetic Retinal Neuropathy(DRN)

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# 1. Problem Statement

Diabetic Retinal Neuropathy (DRN) is considered a precursor of one of the complications of diabetes mellitus and constitutes neural damage that tends to take place in the retina at an earlier stage, preceding a better-known condition of diabetic retinopathy, which is distinguishable by more conspicuous microvascular retinopathy. In Diabetic Retinal Neuropathy (DRN), early natural degeneration of photoreceptors and the ganglion cells, in addition to other changes and interruptions in the retina, has been noted, and therefore it has also been associated with later retinal vasculopathy. Early detection and introduction of clinically and medically supported preventive therapies and measures for this retinal vasculopathy could enable the prevention of resulting progressive and irreversible vision loss [1]. However, the focal point in many standard practices and screenings is usually related to microvascular lesions, for example in autonomic neuropathy resulting from diabetes, a slower pupillary light reflex (PLR) has been clinically observed even before retinopathy [2] and similarly chromatic pupillometry in an another other study found inner retinal impairments in diabetics even without any retinopathy [3]. These findings, therefore, tend to highlight the usefulness of early detection measures using such pupillometry and gaze tracking techniques, and the need for such measures to be extensively studied, clinically validated and made accessible.

# 2. State of the Art

Dynamic pupillometry techniques highlighted how maximum constriction velocity and amplitude were significantly lowered in patients with type 2 diabetes, regardless of the presence of retinopathy, in comparison to controls. Pupillary dilation in the same study was also found to be slower in diabetics [2]. It was observed that even in cases of an early stage of diabetic retinopathy, reduced constriction amplitude and velocity were evident. These two studies tend to be indicative that pupillary constriction amplitude, velocities and latency are affected by neural deficits in diabetes mellitus, especially as the disease progresses or even worsens [2] [4]. Another notable study indicates how even patients without retinopathy showcased reduced pupillary responses to blue and red light in comparison to diabetics with retinopathy using a handheld chromatic pupillometer [3]. These pupillary light reflex (PLR) metrics, such as relative reflex (amplitude), constriction velocity, latency and post-illumination pupil response (PIPR) [3], therefore, in summary, can serve as reliable and objective biomarkers of diabetic retinal neuropathy.

However, gaze and eye movement tracking is less studied, but still a promising field of research in applications of early detection. In a study, for example, participants followed a target on the screen in a proposed low-cost video eye tracking test. This allowed for modelling the eye trajectories and extraction of features of saccadic latency and precision, and this pilot study indicated that participants with diabetes and neuropathy had reduced accuracy of eye movements and longer saccade latencies than controls. These features, therefore, contributed to achieving 95% accuracy in classifying diabetic neuropathy in comparison to controls, indicating that even simple saccadic tests can be useful in determining subclinical neuropathy [5]. In some microperimetry studies, other gaze metrics such as fixation stability and drift during steady gaze have also been explored, reporting poor fixation stability for diabetic macular edema patients in comparison to other healthy controls [6].

# 3. Proposed Solution

We propose a solution which can be delivered by utilising accessible resources and observing the time sensitivity of the project. A camera-based non-invasive screening tool that proposes for early detection of the serious medical condition of diabetic retinopathy by capturing and analysing varied ocular biomarkers that tend to degenerate in earlier stages of the condition, as discussed in the state of the art section of this concept paper.

The following biomarkers will be monitored under the proposed solution:  
- Pupillary Light Reflex (PLR): Diabetic Retinal Neuropathy (DRN) is associated with delayed or reduced PLR because of the damage that occurs early on in the retinal ganglion cells and autonomic pathways. Reduced latency, reduced constriction velocity, and delayed redilation velocity in patients with diabetes, even before the emergence of any visible retinopathy [2,4], reinforce the utility of such biomarkers in the proposed solution.

- Baseline pupil diameter also serves as an important biomarker, as noted in that diabetics with DRN were noted to exhibit significantly smaller baseline pupil diameters and the tonic pupil size under ambient lighting showcases a measure of sympathetic-parasympathetic balance [1].   
  
- Fixation stability is adversely impacted in patients with DRN, as signal transmission in the retina is negatively affected, leading to diminished fixation stability during visual tasks. Bivariate and Contour Ellipse Area (BCEA) or even Standard Deviation (SD) of gaze position during a task requiring steady fixation can be used in measuring fixation stability of the involved participants [7].

- Saccade Metrics involving longer latency and reduced precision are also noted during saccades. This tends to happen in DRN due to disruption in oculomotor pathways. In diabetic populations, an increased variability in endpoint accuracy and delays in initiating gaze shifts have also been noted in endpoint accuracy [5].   
  
The overall system design under the proposed solution will involve delivering a visual stimulus (e.g., screen flash) and then recording the pupil response using a standard web camera in a laptop. Open source libraries (e.g., OpenCV, MediaPipe, Dlib) can be used for pupil segmentation, extracting eye landmarks and estimation of the gaze direction by processing the video feed in real time. Different PLR metrics, such as latency (time from stimulus to constriction of the pupil), redilation speed, constriction amplitude, and post-illumination pupil response (PIPR) for determining sustained constriction post stimulus, shall be measured as these metrics have shown association with neural dysfunction in diabetic retinal neuropathy [2-4]. Fixation stability (e.g., standard deviation of gaze coordinates) and saccadic response(e.g., time taken to shift gaze to a new stimulus) will also be determined as they have been noted to showcase a correlation with degradation in the ocular pathway in many diabetics [5,7]. The raw data can be logged in there for better visualisation and for longitudinal tracking, ensuring a non-invasive screening method for DRN.

# 3. Software Architecture

The proposed solution is based on a simple, modular and Python-based non-invasive software architecture methodology for screening of Diabetic Retinal Neuropathy (DRN). It is based on focusing on capturing and analysing the pupillary light reflex (PLR) and gaze behaviour of participants, making it lightweight and easily executable using minimal hardware and software requirements at this earlier stage of deployment of the proposed solution.

# 3.1 Stimulus Delivery Module

The proposed solution can be launched using a simple command-line terminal and therefore is able to present for the user different visual stimuli, such as-screen flash, allowing measurement for different ocular responses, including pupillary light reflex (PLR) evaluation.

# 3.2 Video Capture and Input Module

The component interfaces in the proposed solution’s software architecture using OpenCV (VideoCapture class) and the video streams are proposed to be captured in real-time and stored temporarily. Metadata generation, for example, the test identifiers or frame timestamps, is also expected, as they are essential in aligning ocular responses with stimulus onset.

# 3.3 Detection of the Eye Region and Pupil Tracking

MediaPipe’s Face Mesh solution can be used as it allows for tracking over 400 facial landmarks, including those surrounding the eye region [8]. For the proposed solution, the eye region is important and the region of interest (ROI), and using different parameters like grayscale conversion, adaptive thresholding and Gaussian blur for pupil detection. Boundaries of the pupil can also be identified, allowing for the extraction pupil center along with the radius in each frame using contour detection [2,3].

# 3.4 Ocular Biomarker Calculation Module

This layer of the proposed solution allows for the computation of certain physiological features that serve as biomarkers for Diabetic Retinal Neuropathy (DRN). All of these calculations can be implemented using NumPy for numerical operations.

These include different biomarkers such as the following:

**3.4.1** **Pupillary light reflex (PLR) latency:** It can essentially be described as the time that is taken at the onset of the light stimulus and the initiation of pupil constriction [2,3]. **Delay between flash and pupil reaction (neural response).** The current normative range for PLR latency was determined to be within 0.20-0.30 seconds [9].

**3.4.2 Post-illumination pupil response (PIPR):** It can be described as the degree of sustained constriction post light offset [3]. **Post-illumination reaction — autonomic recovery.** The current normative range for PIPR was determined to be greater than 0 so it should be a positive value within healthy test results [12].

**3.4.3. Constriction amplitude:** It can be described simply as the difference between the baseline and minimum pupil diameter after stimulus delivery [2]. **How much pupil shrinks — reflex strength.** The current normative range for constriction amplitude was determined approximately to be >1.2mm [10].

**3.4.4 Baseline pupil diameter (Baseline size):** It can be briefly described as the size of the resting pupil under ambient light conditions [2]. **Normal pupil size before flash.** The current normative range for Baseline pupil size was determined approximately to be in range of 2 – 6 mm [11].

**3.4.5 Fixation stability:** It can be described as the standard deviation (SD) or even the Bivariate and Contour Ellipse Area (BCEA) of gaze coordinates during the sustained fixation testing of the participant involved [7]. **Gaze SD (X/Y) - Gaze stability — precision of eye movement and BCEA - Elliptical gaze error area — attention focus measure.** The current normative range for Gaze Standard deviation (SD) was determined approximately to be <0.02 [13, 5] and for BCEA <1.5 [14, 6].

**3.4.6 Saccades (count) - Number of rapid eye shifts — cognitive response proxy.** The current normative range for saccades (count) was determined approximately to be <=100 [5].

# 3.5 Results and Visualisations

This layer of the proposed solution essentially allows for recording data from each session in an organised and structured format (e.g., CSV) and generates visualisations such as time-series plots of pupil diameter and gaze trajectories for better and enhanced understanding of the collected data. Each patient’s diagnostic classification is determined by evaluating core neuro-ophthalmic and oculomotor biomarkers against defined normative thresholds derived from academic literature. These include PLR latency (0.20–0.30 s), constriction amplitude (>1.2 mm), baseline pupil size (2–6 mm), post-illumination pupil response (PIPR > 0 mm), gaze stability (SD < 0.02 for both X and Y), BCEA (<1.5 deg²), and saccade count (≤100). Each parameter that falls outside its normative range is flagged. If four or more markers are flagged, the patient is classified as "High Risk of DRN" (highlighted in red); if two or three markers are abnormal, the status is "At Risk of DRN" (yellow); one or zero abnormal markers results in a "Normal" classification (green). This multivariate rule-based model enables preliminary screening by quantifying neuro-visual deviations and emphasising early dysfunction patterns.

The **Pupil Response Plot** illustrates the temporal change in pupil diameter following a light stimulus, capturing key phases such as baseline size, constriction onset, minimum diameter, and post-illumination recovery. This graph reflects the functional integrity of the pupillary light reflex pathway and allows visual assessment of latency, amplitude, and recovery dynamics.

The **Gaze Stability Plot** displays the patient’s eye movement fixation over time, showing spatial dispersion in the X and Y axes. A tightly clustered fixation pattern indicates stable gaze and attentional control, whereas scattered data suggest poor fixation stability, often associated with visual or cognitive impairments.

The **Download PDF Report** button generates a consolidated summary of the patient's visual biomarker assessment. The PDF includes individual metric values for pupillary and gaze-related biomarkers, clearly labelled with normative reference ranges. It also embeds diagnostic plots—namely the pupil response curve and gaze stability scatter plot—allowing visual inspection alongside numerical data. This facilitates portable, shareable documentation of each subject's screening outcome. The results interface incorporates interactive **tooltips** alongside each biomarker, offering concise clinical explanations to aid interpretability for non-expert users.

A **preliminary cautionary pop-up** appears upon results load, emphasising that the screening tool is in an early academic development phase and not yet intended for formal diagnosis. Additionally, a persistent **disclaimer box** reinforces that all thresholds and interpretations are based on published normative research, highlighting the need for further clinical validation.

# 3.6 App flow (With the Help of Screenshots)

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Figure 1: The app's flow – The clinician starts by logging in. http://www.127.0.0.1:5000

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Figure 2: The app's flow –The clinician is then directed to the dashboard page where they can overview the general information of the app, and from there they can click the “Begin new test” button, which directs them to the main test page.

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Figure 3: The app's flow – The clinician, after clicking on the begin test button, reaches the test page where they can add a new patient name, and then the test begins. It takes at least 2 minutes for the test to finish and patient ideally should be stable, looking directly at the camera and under proper lighting for better results and more accurate results. Once the test is completed for the particular patient the information appears to view the test results if the test was conducted successfully.

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Figure 4: The app's flow – The results table displays key pupillary and gaze biomarkers with values, normative ranges, and colour-coded interpretations. Tooltips explain each term, aiding quick understanding of clinical relevance and deviations.

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Figures 5 & 6: The app's flow – The two graphs represent:

1. **Pupil Diameter Over Time** – shows how the pupil size changes in response to a light stimulus, indicating reflex strength and latency.
2. **Gaze Stability Over Time** – tracks eye movement to assess focus steadiness and possible neurological irregularities.

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Figures 7 & 8: The app's flow – The **Download PDF** button lets clinicians save a summary report containing all biomarker results, interpretations, and visual plots of pupil response and gaze stability for offline review or sharing.

Link to our GitHub: https://github.com/Tanmaytc25/drn\_screening\_app-Group-07.git

# 3.7 Current Limitations and Future Improvements

The system's diagnostic accuracy is currently constrained by several factors. Biomarker thresholds are derived from published academic ranges and have not yet been clinically validated on large, diverse populations. Accurate measurement requires the patient to remain stable under controlled lighting while maintaining direct gaze at the camera for 2–3 minutes, conditions that may be challenging in real-world settings. Additionally, hardware limitations such as the use of older webcams (e.g., MacBook 2015) can affect image quality and tracking precision. Future enhancements will involve robust calibration procedures, expanding normative datasets across diverse demographics, and conducting large-scale clinical trials to refine diagnostic accuracy and usability across platforms, improved hardware compatibility, machine learning–based classification, and validation through clinical trials across varied demographics and settings.

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