Journal of Science and Technology
ISSN: 2456-5660 Volume 8, Issue 12 (Dec -2023)
www.jst.org.in *DOI:https://doi.org/10.46243/jst.2023.v8.i12.pp46 -60*

Ensemble Model-based Clinical Decision Support System for Inherited Retinal Diseases in Pediatric Age

K. Smita[1], G.Sanjana Reddy[2], J.Nikhila[2], N.Deekshitha[1]
[1]Assistant Professor,[2]UG Students, Department of Information Technology
[1,2]Malla Reddy Engineering College for Women, Maisammaguda, Dhulapally, Kompally, Secunderabad-500100, Telangana, India.

To Cite this Article

K. Smita , G.Sanjana Reddy, J.Nikhila, N.Deekshitha**, "Ensemble Model-based Clinical Decision Support System for Inherited Retinal Diseases in Pediatric Age "** *Journal of Science and Technology, Vol. 08, Issue 12,- Dec 2023, pp46-60*

Article Info

Received: 24-11-2023 Revised: 04-12-2023 Accepted: 14-12-2023 Published: 24-12-2023

ABSTRACT

In recent years, advancements in healthcare technology have paved the way for innovative approaches to clinical decision support systems (CDSS), especially in the context of inherited retinal diseases (IRD) affecting the pediatric population. IRD represent a group of genetically transmitted conditions that affect the structure and function of the retina, leading to visual impairment or blindness. The pediatric age group is particularly vulnerable to these diseases, necessitating early and accurate diagnosis for effective intervention and management. Traditional diagnostic systems for IRD often rely on a single approach, such as genetic testing, clinical examinations, or imaging techniques. While these methods have contributed significantly to our understanding of these diseases, their limitations in handling the complexity of genetic variations and the heterogeneity of disease manifestations underscore the need for a more sophisticated and integrated approach. Ensemble models offer a departure from the limitations of traditional systems by combining the strengths of various models, thereby improving diagnostic accuracy and reliability. Therefore, this research proposes an ensemble model based CDSS for inherited retinal diseases in the pediatric age group. By harnessing the power of diverse models, this approach can provide clinicians with a more comprehensive and accurate assessment of the underlying genetic factors and disease progression. Additionally, the proposed ensemble model based CDSS integrates diverse predictive models to enhance diagnostic accuracy and aid in the management of IRD in pediatric patients. Ultimately, the significance extends to improving patient outcomes, enabling earlier interventions, and contributing to the development of targeted therapies for IRD in the pediatric population.

Keywords: clinical decision**,** inherited retinal diseases, IRD, pediatric age, CDSS.

1. INTRODUCTION

Inherited Retinal Diseases (IRDs) represent a significant cause of severe visual deficits in children [1]. They frequently are cause of blindness in childhood in Established Market Economies (1/3000 individuals). IRDs can be divided into diseases of the outer retina, namely photoreceptor

degenerations (e.g., Leber Congenital Amaurosis, Retinitis Pigmentosa, Stargate disease, Cone Dystrophy, Achromatopsia, Chloridaemia, etc.), and diseases of the inner retina, mainly retinal ganglion cell degeneration (e.g., congenital glaucoma, dominant optic atrophy, Leber hereditary optic neuropathy). Both conditions are characterized by extremely high genetic heterogeneity with over 200 causative genes identified to date, which represent a remarkable obstacle to a rapid and effective diagnosis, also considering that the same gene could cause different and heterogeneous clinical phenotypes.The clinical evaluation of IRDs is routinely based on a complex pattern of clinical tests, including invasive ones, that are not always appropriate for infants or young children. For example, electrophysiological testing, that represents the most informative clinical investigation for the diagnosis of inner and outer retinal diseases, often requires sedation of the children. Sedation affects the retinal response and requires a complex healthcare environment (e.g., operating room, paediatric, anaesthesiologist, dedicated instrumentation, etc.) with high costs for the health system. Therefore, the clinical diagnosis is not easy and requires specialized centres. Consequently, it takes a long time for the young patients and their relatives to receive a correct and complete screening.Photoreceptor cells (rods and cones) exhibit fast temporal kinetics and cause a brisk pupillary constriction in response to light, whereas the inner retinal melanopsin containing intrinsic photosensitive Retinal Ganglion Cells (ipRGCs) exhibits slower temporal kinetics and elicits a sustained pupillary constriction to light stimuli, persisting after light cessation [2].

Figure. 1. DP-2000 binocular pupillometer.

The relative contributions of the three receptor types (rod, cone, and melanopsin photopigments) to the Pupillary Light Reflex (PLR) have been examined by manipulating the characteristics of large-field (90) flash stimuli and the adaptation conditions (light vs. dark adapted) [3].

2. LITERATURE SURVEY

Kawasaki, et al. [4] proposed the mutational spectrum and genotype-phenotype correlations of IRD. Methods: they developed a targeted panel of 164 known retinal disease genes, 88 candidate genes, and 32 retina-abundant microRNAs, used for exome sequencing. A total of 179 Chinese families with IRD were recruited. Results: In 99 unrelated patients, a total of 124 mutations in known retinal disease genes were identified, including 79 novel mutations (detection rate, 55.3%).

Iadanza, et al. [5] proposed automatic detection of genetic diseases in paediatric age using pupillometry. They are classified in outer and inner retina diseases, and often cause blindness in childhood. The diagnosis for this type of illness is challenging, given the wide range of clinical and genetic causes (with over 200 causative genes). It is routinely based on a complex pattern of clinical tests, including invasive ones, not always appropriate for infants or young children. A different

approach is thus needed, that exploits Chromatic Pupillometry, a technique increasingly used to assess outer and inner retina functions. This paper presents a novel Clinical Decision Support System (CDSS), based on Machine Learning using Chromatic Pupillometry in order to support diagnosis of Inherited retinal diseases in paediatric subjects.

Melillo, et al. [6] proposed a pilot study in order to evaluate clinical feasibility, reliability and utility of chromatic pupillometry. The study sample consists of sixty patients, affected by inherited ocular diseases. A pupillometric system, including definition of pupillometric protocols, have been set up. They present the comparison between the measurements obtained in one patient affected by Retinitis Pigmentosa and a healthy age-matched control in order to disclose differences in chromatic pupillometry parameters between case and control.

Iadanza, et al. [7] proposed the Electronic Medical Record, named ORÁO and specifically developed to collect ophthalmologic and pupillometric data. The platform is a cloud- based application, with a RESTful and three-tier architecture. These features make it available via web for the ophthalmologists involved in the project and working in two different University centres. The platform has been designed by the whole team and developed by the Department of Information Engineering of the University of Florence.

Iadanza, et al. [8] proposed ORÁO: RESTful cloud-based ophthalmologic medical record for chromatic pupillometry. The physicians involved in the project belong to two different University centres: the data they gather must be collected in an electronic medical record reachable via web. Therefore, a specified medical record has been designed. It has been realized as a .NET application with RESTful architecture. The user-interfaces have been built with the aim to reduce the risk of error and with particular attention to usability, according to standards.

Melillo, et al. [9] proposed Early diagnosis of Inherited Retinal Diseases, such as Retinitis Pigmentosa (RP). It is challenging in paediatric patients, because their diagnosis mainly relies on relatively invasive tests. They conducted a pilot study to evaluate the usefulness of chromatic pupillometry in RP. They recruited 20 RP cases and 20 healthy subjects based on the following inclusion criteria: age between 8 and 16 years; willingness to participate in this pilot study; a refraction error in absolute value < 5 dioptres; absence of any diseases or drugs that could influence the pupillary response; no corneal or lens opacity; no pupillary alteration. Controls should have no known ocular diseases.

Crippa Sylvain V, et al. [10] proposed Chromatic pupillometry in children. They aimed to evaluate the pupil responses to colored light stimuli in the paediatric population. Fifty-three children with normal vision and without any history of ocular disorders were tested with a portable pupillometer. Four test sequences were used: five dim blue (470 nm) stimuli presented in half log steps ranging from −3.15 to −1.15 log cd/m^2 after 3 min of dark adaptation, five red (622 nm) stimuli of −1.15, −0.7, −0.15, 0.3, and 0.85 log cd/m^2 after 1 min light adaptation, one bright blue stimulus of 2.2 log cd/m^2 and one bright red of 2 log cd/m^2.

Delfino, et al. [11] proposed the techniques and equipment for automated pupillometry. They investigated the accuracy of methodologies and equipment that use computerized pupillometry to identify pathologies or disorders, as well as the viability and usability of existing pupilometers. In this sense, creating a pupilometer capable of stimulating and varying wavelengths, providing an interface to preview the exam, and embedding the classification algorithms is a great challenge.

Najjar, et al. [12] proposed Handheld chromatic pupillometry can accurately and rapidly reveal functional loss in glaucoma. Pupillometric features were extracted from individual traces and

compared between groups. Features with the highest classification potential, selected using a gradient boosting machine technique, were incorporated into a generalised linear model for glaucoma classification. Receiver operating characteristic curve analyses (ROC) were used to compare the performance of HCP, optical coherence tomography (OCT) and Humphrey Visual Field (HVF). Finally, Pupillary light responses were altered in glaucoma compared with controls.

Sher, et al. [13] proposed the Chromatic pupilloperimetry measures correlate with visual acuity and visual field defects in retinitis pigmentosa patients. The pupil responses of 10 patients with RP (mean age, 41.3 ± 16.2 years) and 32 healthy age-similar controls (mean age, 50.7 ± 15.5 years) for 54 focal blue and red stimuli presented in a 24-2 VF were recorded. The pupilloperimetry measures were correlated with Humphrey VF mean deviation, best-corrected visual acuity, and ellipsoid zone area. The chromatic pupilloperimetry measures significantly correlated with retinal function and structure in patients with RP at various disease stages.

Rukmini, et al. [14] proposed Chromatic pupillometry methods for assessing photoreceptor health in retinal and optic nerve diseases. The pupillary light reflex is mediated by melanopsin-containing intrinsically-photosensitive retinal ganglion cells (ipRGCs), which also receive input from rods and cones. Melanopsin-dependent pupillary light responses are short-wavelength sensitive, have a higher threshold of activation, and are much slower to activate and de-activate compared with rod/cone-mediated responses. Given that rod/cone photoreceptors and melanopsin differ in their response properties, light stimuli can be designed to stimulate preferentially each of the different photoreceptor types, providing a read-out of their function.

Rajan, et al. [15] proposed the quantification of relative afferent pupillary defect by an automated pupillometer and its relationship with visual acuity and dimensions of macular lesions in age-related macular degeneration. The occurrence of relative afferent pupillary defect (RAPD) secondary to optic nerve diseases and widespread retinal disorders is well established. However, only very few reports of RAPD in macular disorders exist in the literature. In this study, they used automated pupillometer to evaluate RAPD in eyes with macular lesions. Best-corrected visual acuity was also found to have a significant correlation with lesion size on the OCT as well as the length of ellipsoid zone disruption in unilateral cases.

3.PROPOSED METHOD

3.1. Pupillometric Data

A first preliminary stage of the CDSS is devoted to the analysis of the raw files, produced by the binocular pupillometer after each measurement session, for the export of the following relevant data:

- Patient ID;
- Bilateral pupillary diameter signals related to each phase of the protocol;
- Diagnosis, i.e., ‘‘Pathologic’’ or ‘‘Healthy’’, as performed by a clinical specialist.

3.2. Feature extraction

After the pre-processing stage, the following 8-elements vector of features is extracted from each pupillometric signal:

- MAX: maximum pupil diameter at baseline;
- MIN: minimum diameter in correspondence with the peak constriction;
- DELTA: absolute difference between the above values;

- CH: percentage maximum constriction (with respect to the pupillary diameter at rest);
- LATENCY: delay between the light stimulus and the onset of the pupillary constriction;
- MCV: mean constriction velocity;
- MDV: mean dilation velocity;
- CVmax: maximum constriction velocity.

The above eight features, calculated on the filtered signal, were chosen in accordance to the literature about pupillometry in several pathologies and in biometric authentication. The same features are regularly used by the clinicians involved in this project and are also provided by the equipment itself in its output files. The time interval used to derive the above features was properly restricted so as to minimize the risk of inaccurate values: namely, MAX and LATENCY are computed in the first second whereas the others are obtained using a 5-s window.

Feature	Description	Expression
MAX	Maximum diameter at base line	$MAX(r(t))$
MIN	Minimum diameter corresponding to the peak constriction	$MIN(r(t))$
DELTA	Difference between Max and Min	$MAX - MIN$
CH	Percentage maximum constriction	$\frac{DELTA}{MAX}$
LATENCY	Delay between stimulus and onset of the pupillary constriction	Computed using custom script
MCV	Mean constriction velocity	$\frac{DELTA}{t_{min} - LATENCY}$
MDV	Mean dilation velocity	$\frac{r(t)\ 80\%}{t_{80\%} - t_{min}}$
CV_{max}	Maximum constriction velocity	$MIN\left(\frac{dr(t)}{dt}\right)$

The rationale behind the definition of the pupillary LATENCY is that the contraction starts a few milliseconds after the light stimulus is applied. In detail, this parameter is estimated as follows: the first derivative $dx\,(t)$of the pupillometric signal is computed; then, starting from its absolute minimum, the array of values is checked backwards and the time instant corresponding to $dx\,(t) = 0$ is identified. The detection of an inflection point is avoided since, despite the preliminary SG-smoothing, $dx\,(t)$ signals are characterized by significant noisy components and zero-crossings are less sensitive to flickering signals. Although this might seem the easiest strategy, it was chosen not to identify the inflection point because it is not possible to have a perfectly smoothed signal which determines a noisy derivative graph. Conversely, the zero-crossing detection is less influenced by flickering signals.

3.3. Features reduction

According to the adopted measurement protocol, previously detailed in the ‘‘Participants and experimental setup’’ section, a total of 288 features was extracted from the 36 pupil reactivity signals, available for each subject to be classified. Due to the relatively high number of features, feature

reduction represented a key preliminary operation which was applied to avoid overfitting of the training dataset. In ML applications, a general rule of thumb is to keep the dimension of the input feature space below one fifth of the total number of observations, i.e., the best subjects.

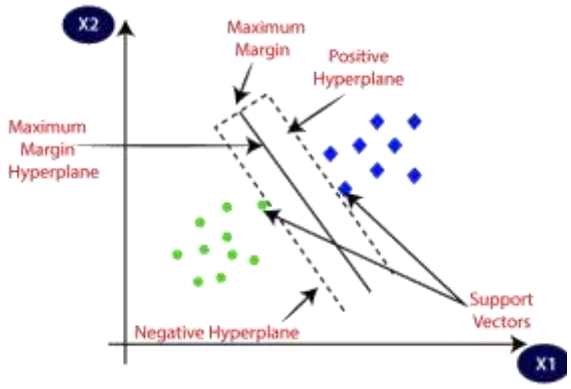


Figure. 2. Support Vector Machine.

In general, the system is designed (so as) to separately label the left and right eyes and, then, to classify the related subject by means of an OR logical operator, i.e., the subject is diagnosed with RP if at least one of the eyes is assigned with the ‘‘Pathologic’’ label (thus improving the global sensitivity of the CDSS). This choice is related to the fact that the artifacts might be not equally distributed between the two eyes. For example, a patient with a frequent blinking in his/her left eye would generate a cleaner signal for his/her contralateral eye. An SVM was selected as supervised (eye) classification algorithm because of its proven solidity and versatility for classification problems. Each SVM classifier was fed with the pupillometric feature vectors acquired from the left and right eyes of 30 of the enrolled subjects (see Participants and experimental setup). Linear and RBF kernels were alternatively used for both the left and right-eye classifiers, so as to explore and compare their performances.

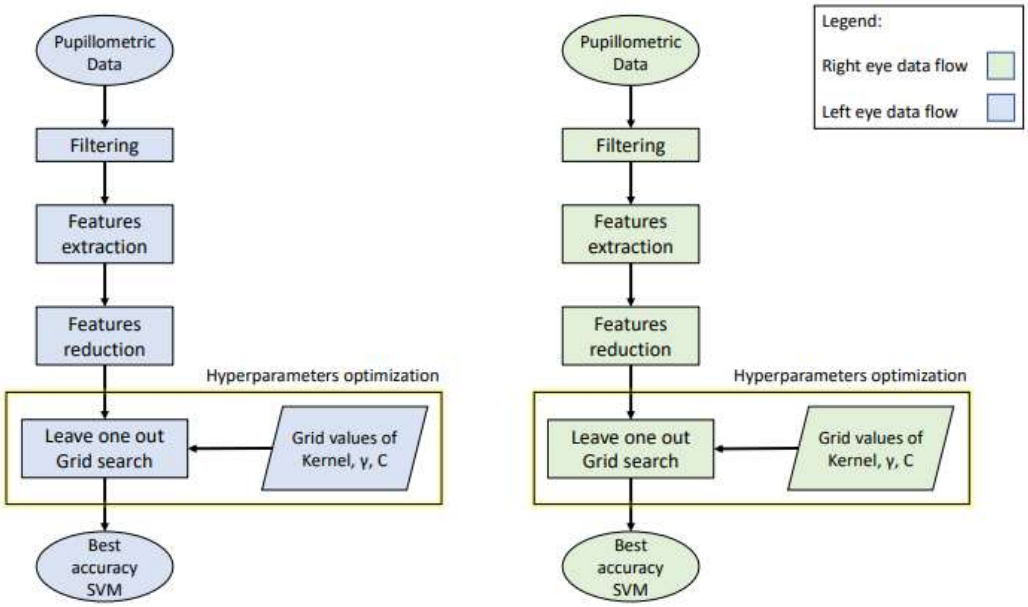


Figure. 3. Data analysis, selection of features and optimization of the SVM parameters.

The optimization of the hyper-parameters of the SVM, i.e., the boundary constant C and the scale λ of the non-linear RBF kernel, represents a fundamental step for the achievement of improved classification performances. The tuning process was carried out separately for each eye by means of a grid search and a leave-one-out cross-validation strategy. Support Vectors are simply the coordinates of individual observation. The SVM classifier is a frontier that best segregates the two classes (hyper-plane/ line). In the SVM classifier, it is easy to have a linear hyper-plane between these two classes. But another burning question which arises is, should need to add this feature manually to have a hyper-plane. No, the SVM algorithm has a technique called the kernel trick. The SVM kernel is a function that takes low dimensional input space and transforms it to a higher dimensional space i.e., it converts not separable problem to separable problem. It is mostly useful in non-linear separation problem. Simply put, it does some extremely complex data transformations, then finds out the process to separate the data based on the labels or outputs you've defined.

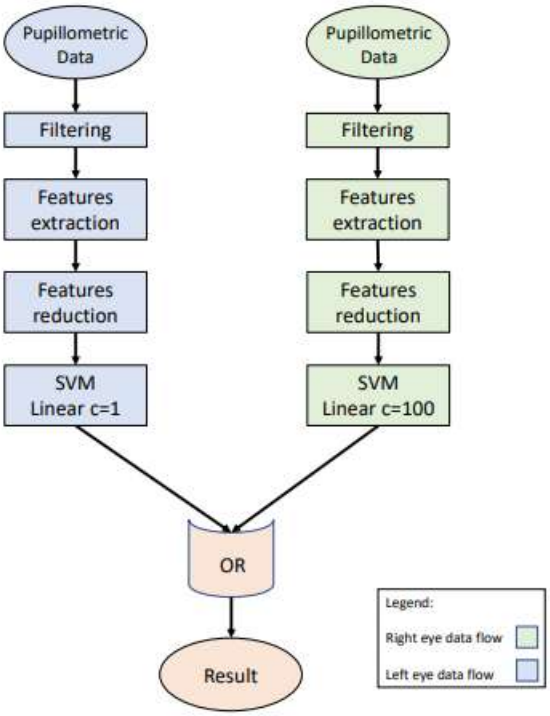


Figure. 4. Decision support process using existing SVM.

SVM can be of two types:

- *Linear SVM:* Linear SVM is used for linearly separable data, which means if a dataset can be classified into two classes by using a single straight line, then such data is termed as linearly separable data, and classifier is used called as Linear SVM classifier.
- *Non-linear SVM:* Non-Linear SVM is used for non-linearly separated data, which means if a dataset cannot be classified by using a straight line, then such data is termed as non-linear data and classifier used is called as Non-linear SVM classifier.

Some applications of SVM include:

- Text and hypertext classification
- Image classification
- Recognizing handwritten characters

- Biological sciences, including protein classification.

4. RESULTS AND DISCUSSION

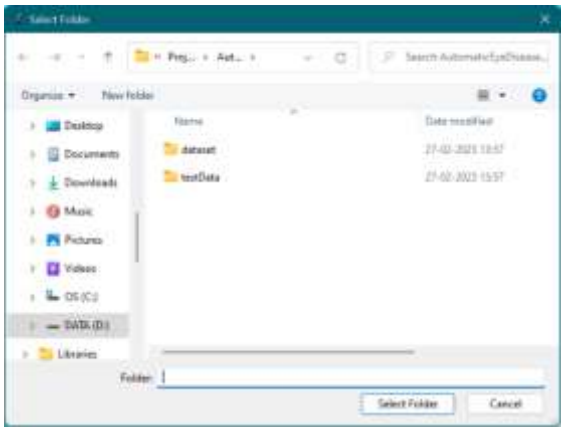
This project describes the concept to detect eyes pediatric age genetic diseases using Pupillometry device data as this device is very accurate and it's not required huge number of clinical test to detect disease. All existing techniques require huge number of clinical tests to diagnose eye pupil disease in children's and it's not good for children's health, so author using Pupillometry device which capture pupil diameters continuously and records that data in raw format in the file. Later we can analyse that data using Machine Learning SVM algorithm to detect presence of disease. Here author using two different SVM classifiers to train right and left eye pupil data and then performing OR operations between two classifier using ENSEMBLE VOTING classifier to get classifier with better accuracy. SVM will assign disease class label as 1 to train data if pupils size diameter is huge and if its size is normal then classifier will assign value 0.

To implement this project, Pupillometry raw data is used and perform below functions to diagnose pupils' disease.

- Upload Pupillometry Data: Using this module we will upload raw data which contains continuous recording of pupil's data.
- Filtering: Raw data contains huge number of buggy values, and we will filter that raw data to extract only useful information such as pupil min and max diameter
- Features Extraction: Using this module all pupil min and max features extracted from raw data.
- Features Reduction: Using this module we will remove unnecessary features from raw data such as camera name, position etc to reduce features set. In this module we will extract features such as Patient ID, MAX, MIN, DELTA, CH etc. Extracted data can be used to split into train and test data.
- Right SVM: Using this module we will train SVM with right pupil data.
- Left SVM: using this module we will train SVM with left Pupil data and then apply SVM on test data to calculate prediction accuracy, sensitivity, and specificity.
- Ensemble Algorithm (Left & Right SVM): Using this module we will combine both classifiers to get classifier with high prediction accuracy.
- Predict Disease: using this module we will upload test data and then apply SVM classifier to predict disease.

Below is the UI application developed for implementing proposed ensemble OR SVM-based genetic disease detection from pupillometric data.

In above screen click on 'Upload Pupillometric Dataset' button to load dataset

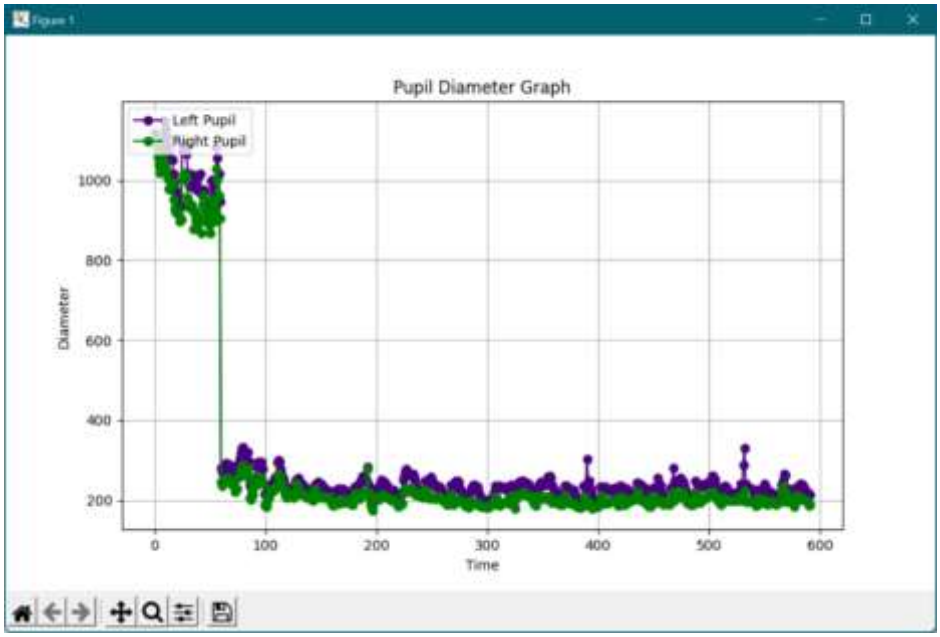


In above screen uploading 'dataset' folder and after upload will get below screen

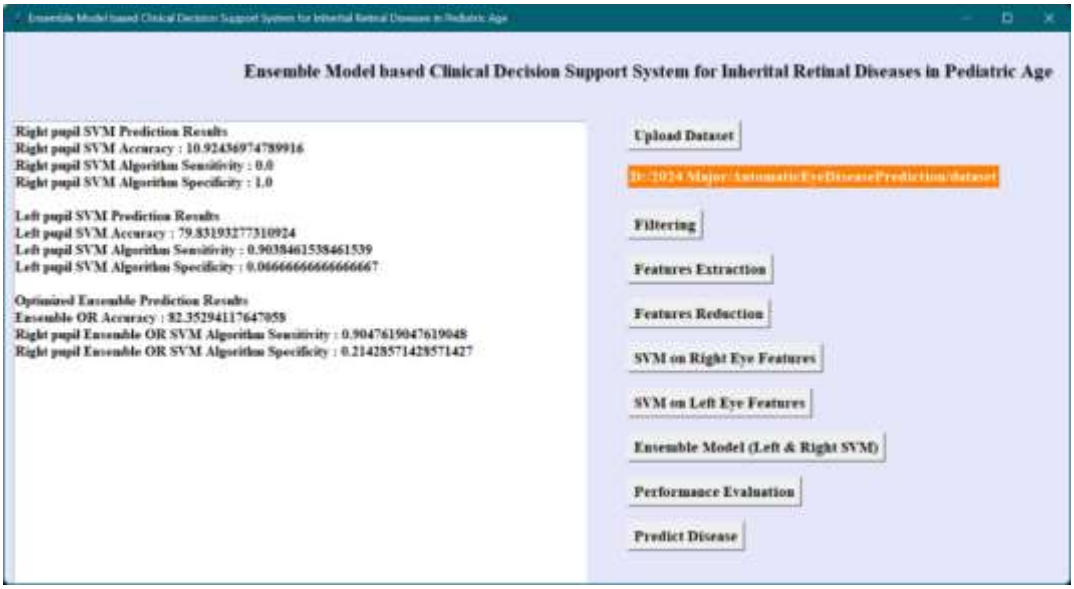
Now click on 'Run Filtering' button to perform filtering on dataset to ignore raw data

Journal of Science and Technology
ISSN: 2456-5660 Volume 8, Issue 12 (Dec -2023)
www.jst.org.in *DOI:https://doi.org/10.46243/jst.2023.v8.i12.pp46 -60*

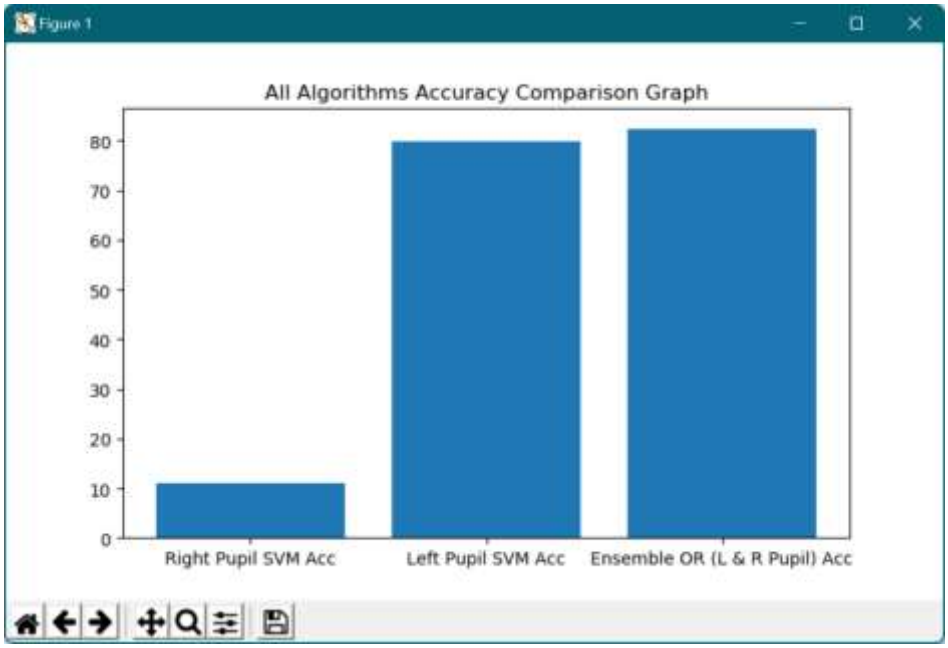
In above screen extracted features such as MIN, MAX pupil diameter etc. now clicks on 'Run Features Reduction' button to remove unimportant features and then generate train and test model for classification and to get pupil diameter graph below.



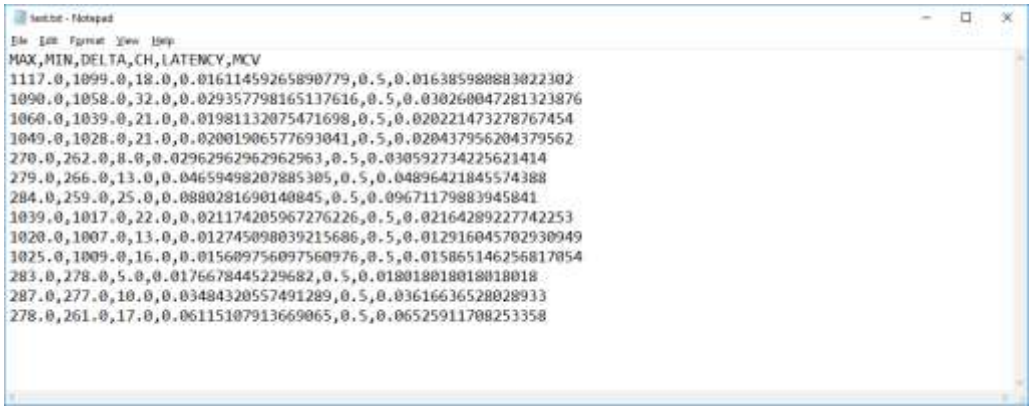
In above graph x-axis represents time of pupil capture and y-axis represents diameter of pupils. Blue line represents left pupil and green line represents right pupil. Now click on 'Run SVM on Right Eye Features' to run SVM classifier and click on 'Run SVM on Left Eye Features' button to run SVM classifier on left eye data, 'Run OR Ensemble Algorithm (Left & Right SVM)' button to combine both classifier to choose classifier with better accuracy



In above screen with ensemble OR SVM, we got 82.32% accuracy and now click on 'Accuracy Graph with Metrics' to get below accuracy graph.



In above graph x-axis represents algorithm name and y-axis represents accuracy and in all algorithms, ensemble OR SVM got high accuracy and now click on 'Predict Disease' button to upload test data and predict disease. In below test data we can see only pupil values are there but not disease information and classifier will predict disease information after applying classifier on it.



In above test data 'test.txt' we have only featured values and after uploading classifier will predict disease

In above screen uploading test data and after upload will get below screen

In above screen for each test record classifier displaying predicted result as 'disease detected' or 'no disease detected'. In above screen in square bracket, we can see TEST values and after square bracket we can see predicted result as pupillometric disease detected or not.

Here we are extracting data from binocular device data, and we are splitting train and test data as random so accuracy may vary for each run based on collected data from binocular device

5. CONCLUSION

The system was developed to clean artefacts, extract features and help the diagnosis of RP using a ML approach based on an ensemble model of two fine-tuned SVMs. Performances were evaluated with a leave-one-out cross-validation, also used to identify the best combination of internal parameters of the SVM, separately for both the left and right eyes. The class assigned to each eye were combined in the end with an OR-like approach so as to maximize the overall sensitivity of the CDSS; the ensemble system achieved 86.55% accuracy, and 92.7% sensitivity.

REFERENCES

[1] X. F. Huang, F. Huang, K. C. Wu, J. Wu, J. Chen, C. P. Pang, F. Lu, J. Qu, and Z. B. Jin, "Genotype-phenotype correlation and mutation spectrum in a large cohort of patients with inherited retinal dystrophy revealed by nextgeneration sequencing," Genetics in Medicine, vol. 17, no. 4, pp. 271–278, 2015.

[2] R. Kardon, S. C. Anderson, T. G. Damarjian, E. M. Grace, E. Stone, and A. Kawasaki, "Chromatic Pupil Responses. Preferential Activation of the Melanopsin-mediated versus Outer Photoreceptor-mediated Pupil Light Reflex," Ophthalmology, vol. 116, no. 8, pp. 1564–1573, 2009.

[3] J. C. Park, A. L. Moura, A. S. Raza, D. W. Rhee, R. H. Kardon, and D. C. Hood, "Toward a clinical protocol for assessing rod, cone, and melanopsin contributions to the human pupil response," Investigative Ophthalmology and Visual Science, vol. 52, no. 9, pp. 6624–6635, 2011.

[4] Kawasaki, F. L. Munier, L. Leon, and R. H. Kardon, ''Pupillometric quantification of residual rod and cone activity in Leber congenital amaurosis,'' Arch. Ophthalmol., vol. 130, no. 6, pp. 798–800, Jun. 2021.

[5] Iadanza, Ernesto, et al. "Automatic detection of genetic diseases in pediatric age using pupillometry." IEEE Access 8 (2020): 34949-34961.

[6] Melillo, Paolo, et al. "Toward a novel medical device based on chromatic pupillometry for screening and monitoring of inherited ocular disease: A pilot study." World Congress on Medical Physics and Biomedical Engineering 2018. Springer, Singapore, 2019.

[7] Iadanza, E., Fabbri, R., Luschi, A., Melillo, P., & Simonelli, F. (2020). A collaborative RESTful cloud-based tool for management of chromatic pupillometry in a clinical trial. Health and Technology, 10(1), 25-38.

[8] Iadanza, Ernesto, et al. "ORÁO: RESTful cloud-based ophthalmologic medical record for chromatic pupillometry." International Conference on Medical and Biological Engineering. Springer, Cham, 2019.

[9] Melillo, P., De Benedictis, A., Villani, E., Ferraro, M. C., Iadanza, E., Gherardelli, M., ... & Simonelli, F. (2019). Chromatic pupillometry for screening and monitoring of retinitis pigmentosa. Investigative Ophthalmology & Visual Science, 60(9), 4513-4513.

[10] Crippa, Sylvain V., Fatima Pedrosa Domellöf, and Aki Kawasaki. "Chromatic pupillometry in children." Frontiers in neurology 9 (2018): 669.

[11] Delfino, Higor Pereira, et al. "Techniques and equipment for automated pupillometry and its application to aid in the diagnosis of diseases: a literature review." 2020 IEEE 44th Annual Computers, Software, and Applications Conference (COMPSAC). IEEE, 2020.

[12] Najjar, Raymond P., A. V. Rukmini, Maxwell T. Finkelstein, Simon Nusinovici, Baskaran Mani, Monisha Esther Nongpiur, Shamira Perera, Rahat Husain, Tin Aung, and Dan Milea. "Handheld chromatic pupillometry can accurately and rapidly reveal functional loss in glaucoma." British Journal of Ophthalmology (2021).

[13] Sher, Ifat, Yisroel Tucker, Maya Gurevich, Amit Hamburg, Ettel Bubis, Jonathan Kfir, Shlomit Zorani, Estela Derazne, Alon Skaat, and Ygal Rotenstreich. "Chromatic pupilloperimetry measures correlate with visual acuity and visual field defects in retinitis pigmentosa patients." Translational vision science & technology 9, no. 8 (2020): 10-10.

[14] Rukmini, A. V., Dan Milea, and Joshua J. Gooley. "Chromatic pupillometry methods for assessing photoreceptor health in retinal and optic nerve diseases." Frontiers in neurology 10 (2019): 76.

[15] Rajan, Renu P., et al. "Quantification of relative afferent pupillary defect by an automated pupillometer and its relationship with visual acuity and dimensions of macular lesions in age-related macular degeneration." Indian Journal of Ophthalmology 69.10 (2021): 2746.