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AUTOMATIC DETECTION OF GENETIC EYE DISEASES IN PEDIATRIC AGE USING PUPILLOMETRY

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ABSTRACT:

Inherited retinal diseases cause severe visual deficits in children. 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 pediatric subjects. An approach that combines hardware and software is proposed: a dedicated medical equipment (pupillometer) is used with a purposely designed custom machine learning decision support system. Two distinct Support Vector Machines (SVMs), one for each eye, classify the features extracted from the pupillometric data. The designed CDSS has been used for diagnosis of Retinitis Pigmentosa in pediatric subjects. The results, obtained by combining the two SVMs in an ensemble model, show satisfactory performance of the system, that achieved 0.846 accuracy, 0.937 sensitivity and 0.786 specificity. This is the first study that applies machine learning to pupillometric data in order to diagnose a genetic disease in pediatric age.

INTRODUCTION:

nherited 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 The associate editor coordinating the review of this manuscript and approving it for publication was Asad Waqar Malik . date, which represent a remarkable obstacle to a rapid and effective diagnosis (https://sph.uth.edu/retnet/disease.htm), also considering that the same gene could cause different and heterogeneous clinical phenotypesRetinal 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 degen- erations (e.g.,

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Leber Congenital Amaurosis, Retinitis Pigmentosa, Stargardt disease, Cone Dystrophy, Acromatopsia, Choroideremia, etc.), and diseases of the inner retina, mainly retinal ganglion cell

LITERATURE SURVEY:

Genotype–phenotype correlation and mutation spectrum in a large cohort of patients with inherited retinal dystrophy revealed by next-generation sequencing

AUTHOR: X.-F. Huang, F. Huang, K.-C. Wu, J. Wu, J. Chen, C.-P. Pang, F. Lu, J. Qu, and Z.-B. Jin,

ABSTRACT:

Purpose: Inherited retinal dystrophy (IRD) is a leading cause of blindness worldwide. Because of extreme genetic heterogeneity, the etiology and genotypic spectrum of IRD have not been clearly defined, and there is limited information on genotype-phenotype correlations. The purpose of this study was to elucidate the mutational spectrum and genotype-phenotype correlations of IRD. Methods: We 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%). Moreover, novel genotype-phenotype correlations were discovered, and phenotypic trends noted. Three cases are reported, including the identification of AHI1 as a novel candidate gene for nonsyndromic retinitis pigmentosa. Conclusion: This study revealed novel genotype-phenotype correlations, including a novel candidate gene, and identified 124 genetic defects within a cohort with IRD . The identification of novel genotype-phenotype correlations and the spectrum of mutations greatly enhance the current knowledge of IRD phenotypic and genotypic heterogeneity, which will assist both clinical diagnoses and personalized treatments of IRD patients

Chromatic pupil responses. Preferential activation of the melanopsin-mediated versus outer photoreceptor-mediated pupil light reflex

AUTHOR: R. Kardon, S. C. Anderson, T. G. Damarjian, E. M. Grace, E. Stone, and A. Kawasaki,

ABSTRACT:

To weight the rod-, cone-, and melanopsin-mediated activation of the retinal ganglion cells, which drive the pupil light reflex by varying the light stimulus wavelength, intensity, and duration. Experimental study. Forty-three subjects with normal eyes and 3 patients with neuroretinal visual loss. A novel stimulus paradigm was developed using either a long wavelength (red) or short wavelength (blue) light given as a continuous Ganzfeld stimulus with stepwise increases over a 2 log-unit range. The pupillary movement before, during, and after the light stimulus was recorded in real time with an infrared illuminated video camera. The percent pupil contraction of the transient and sustained pupil response to a low- (1 cd/m(2)), medium- (10 cd/m(2)), and high-intensity (100 cd/m(2)) red- and blue-light stimulus was calculated for 1 eye of each subject. From the 43 normal eyes, median and 25th, 75th, 5th, and 95th percentile values were obtained for

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each stimulus condition. In normal eyes at lower intensities, blue light evoked much greater pupil responses compared with red light when matched for photopic luminance. The transient pupil contraction was generally greater than the sustained contraction, and this disparity was greatest at the lowest light intensity and least apparent with bright (100 cd/m(2)) blue light. A patient with primarily rod dysfunction (nonrecordable scotopic electroretinogram) showed significantly reduced pupil responses to blue light at lower intensities. A patient with achromatopsia and an almost normal visual field showed selective reduction of the pupil response to red-light stimulation. A patient with ganglion cell dysfunction owing to anterior ischemic optic neuropathy demonstrated global loss of pupil responses to red and blue light in the affected eye. Pupil responses that differ as a function of light intensity and wavelength support the hypothesis that selected stimulus conditions can produce pupil responses that reflect phototransduction primarily mediated by rods, cones, or melanopsin. Use of chromatic pupil responses may be a novel way to diagnose and monitor diseases

EXISTING SYSTEM :

‘machine learning’’ and ‘‘eye diseases’’. The number of studies decreases when it deals with systems for ‘‘rare diseases’’, ‘‘retinitis pigmentosa’’ and ‘‘pupillometry’’. Among all the found articles, the seven resumed below were chosen based on regency and variety, so as to have different views of general approaches when ML interfaces with eye diseases. Brancati et al. apply ML supervised techniques for detecting pigment signs on fundus images acquired with a digital retinal camera to study patients affected by RP. Gao et al. apply the ML random forest algorithm on optical coherence tomography (OCT) images to support the diagnosis of choroideremia by detecting intact choriocapillaris. Four more articles apply similar supervised ML algorithms to common eye diseases such as age-related macular degenerations diabetic retinopathy and glaucoma . Gargeya et al. bring a different approach to support the diagnosis of diabetic retinopathy using deep learning. The results from the studies just cited are summarized

DISADVANTAGES OF EXISTING SYSTEM :

1) Less accuracy
2)low Efficiency

PROPOSED SYSTEM :

The non-invasiveness is granted by adopting the proposed pupillometric method, which requires no spe- cific patient preparations with drugs or collyriums. If com- pared with other standard diagnostic techniques, particularly, electrorheological test, in this case no electrodes need to be placed on the patient skin: this is particularly convenient when dealing with pediatric patients. Particularly, in younger children the electrophysiological testing are usually per- formed in sedation, thus requiring a more complex clinical setting (i.e. availability of operating theater together with anesthesiologist). Chromatic pupillometry has been proven to be effective in diagnosis of RP

ADVANTAGES OF PROPOSED SYSTEM :

1) High accuracy
2)High efficiency

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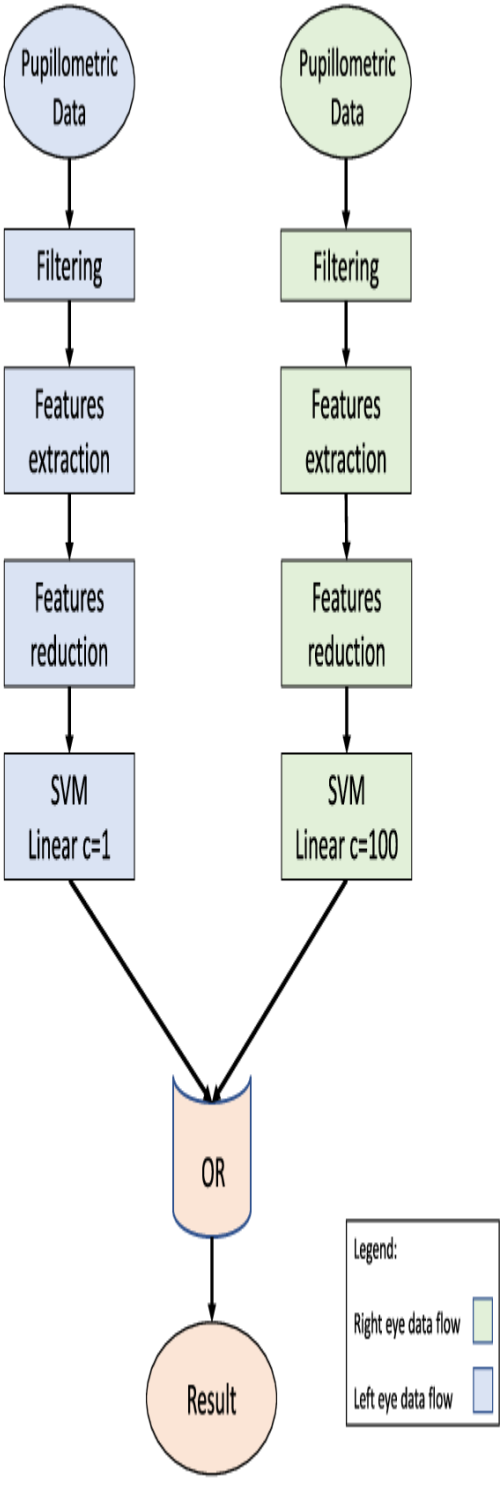
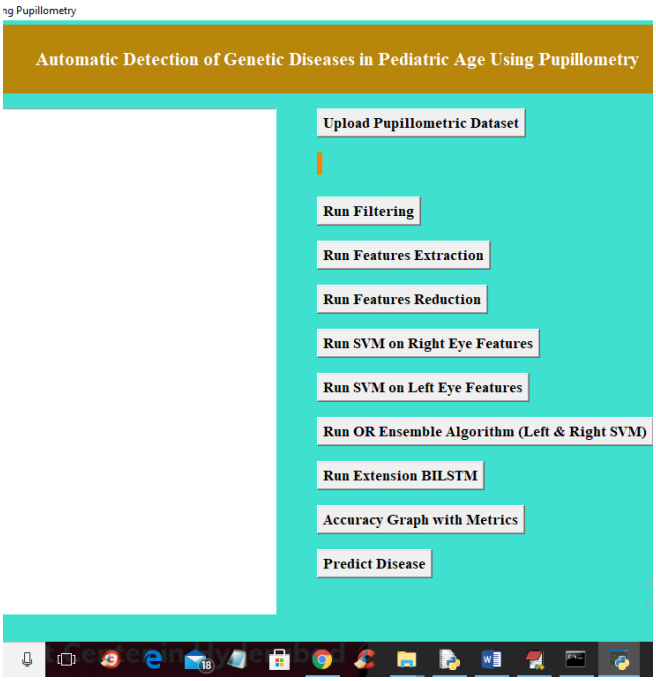
SYSTEM ARCHITECTURE :

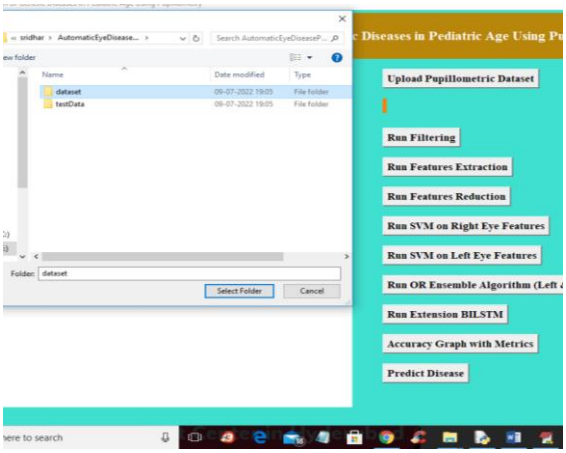


Results

To run project double click on 'run.bat' file to get below screen



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

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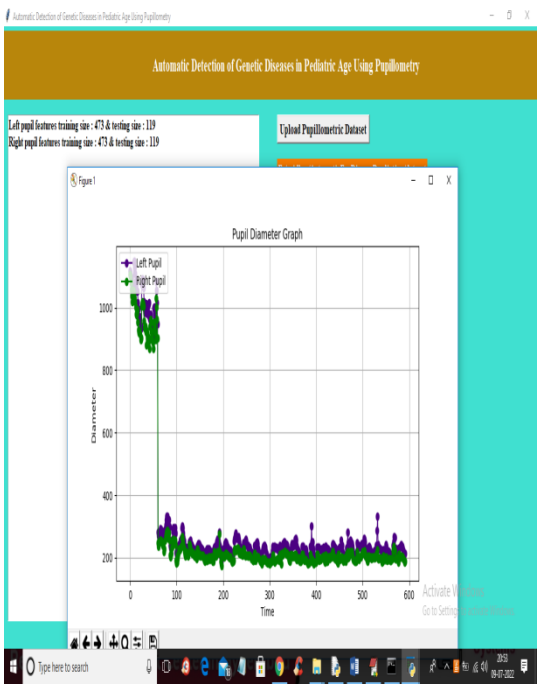
Now click on 'Run Filtering' button to perform filtering on dataset to ignore raw data

In above screen extracted features such as MIN, MAX pupil diameter etc. now click 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 screen after filtering we got 593 patients data and now click on 'Run Features Extraction' button to read features from raw file



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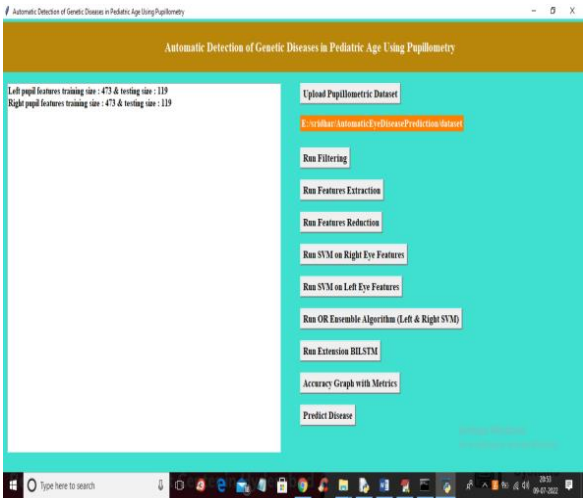
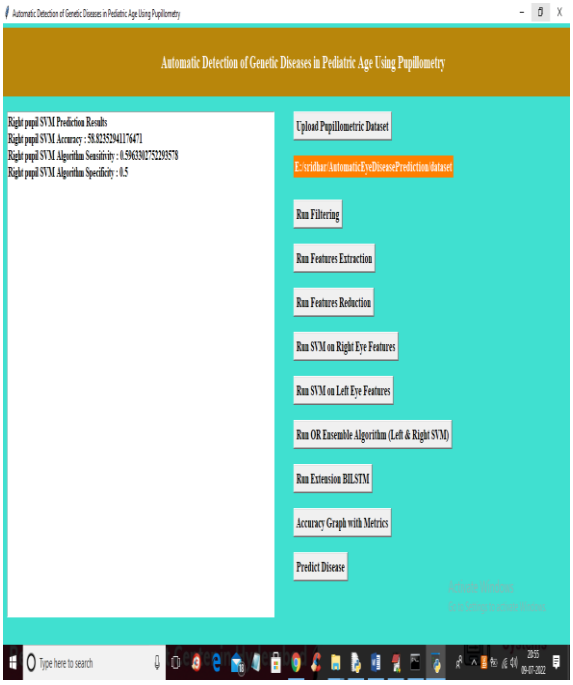
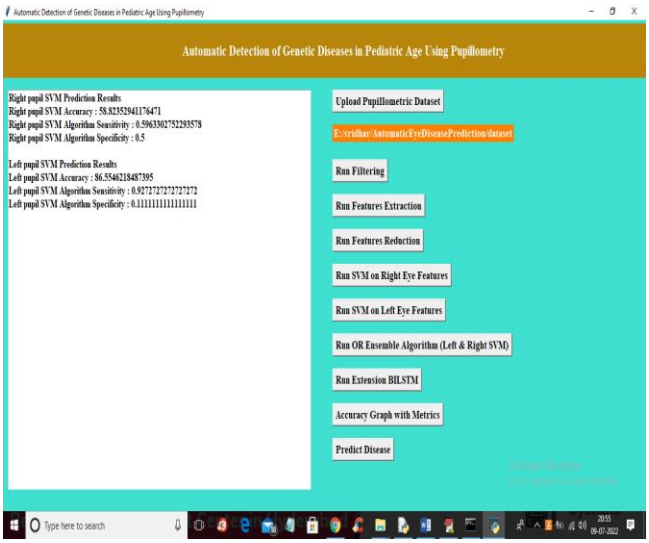
In above graph x-axis represents time of pupil capture and y-axis represents diameter of pupils. Blue line represents left pupil and green line represents right pupil. Close above graph to get below screen



In above screen application using 473 records for training and 119 records for testing from total 593 records. Now click on 'Run SVM on Right Eye Features' to run SVM classifier



In above screen with right pupil SVM got 58% accuracy and now click on 'Run SVM on Left Eye Features' button to run SVM classifier on left eye data



In above screen with left pupil data we got 86% accuracy and now click on '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 86% accuracy and now click on 'Run

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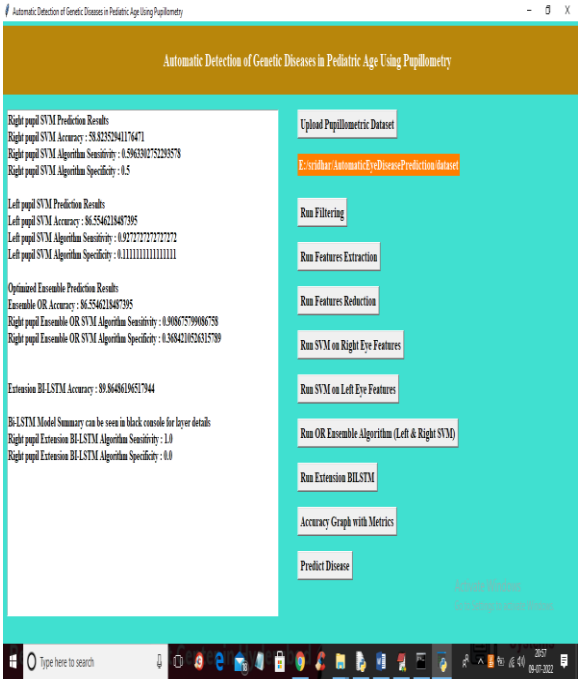
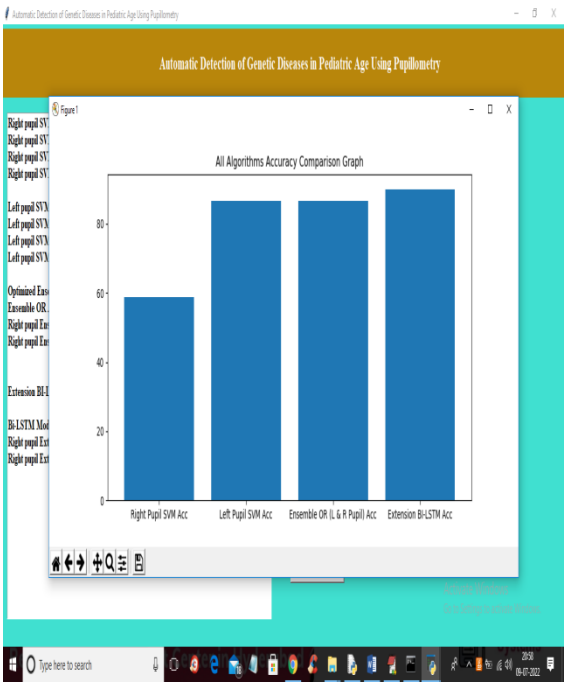
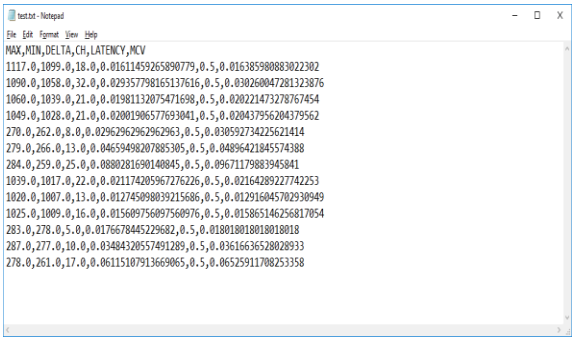
Extension BILSTM' button to run BILSTM algorithm and get below output



In above screen with extension 'BILSTM' we got 89% 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 extension BILSTM 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 features values and after uploading classifier will predict disease

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

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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 pupillometri 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 data.

CONCLUSION:

This paper describes a new approach for supporting clinical decision for diagnosis of retinitis pigmentosa starting from analysis of pupil response to chromatic light stimuli in pedi- atric patients. 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 84.6% accuracy, 93.7% sensitivity and 78.6% speci- ficity. The small amount of data available for this work, calls for further tests with a larger data pool for validating the performance of the system. Future scope includes testing the same approach with different devices

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