

Review Article

GRAVITATIONAL SEARCH ALGORITHM BASED RNFL SEGMENTATION FOR EARLY STAGE ALZHEIMER'S DETECTION

Nishi S. Das¹, S. Palanikumar²

¹Department of Electronics and Communication, Noorul Islam Centre for Higher Education, Thuckalay, Kumaracoil, Tamil Nadu, India. nishidas@gmail.com

²Department of Information Technology, Noorul Islam Centre for Higher Education, Thuckalay, Kumaracoil, Tamilnadu, India. palanikumarcsc@yahoo.com

Received: 16.12.2019

Revised: 08.01.2020

Accepted: 03.02.2020

Abstract

Alzheimer's disease (AD) is a harmful form of dementia occurred in elderly people. AD is a neuro degenerative brain disease. There are no pills and drugs exist for AD. Therefore, early diagnosis can delay progression of AD. Image segmentation used to analyze and visualize the image more precisely. It plays a vital in medical image analysis. Segmented Retinal Nerve Fiber Layer (RNFL) edges give structural framework for visualization. Segmented RNFL poses large information which is useful in AD diagnosis early. Segmentation refers to the labeling of pixels into different regions. In this work introduced a new system to automatically detect the RNFL using retinal images. Initially, the images pre-processed using Bilateral filter, then detected the edge of the RNFL, after that they identified and characterize the true retinal boundaries based on the Gravitational Search (GSA) algorithms. They segmented the interior and exterior boundaries with the Gravitational Search of retinal structure. They automatically segment the retinal images without the intervention of human and accurately detecting the RNFL edges.

Keywords: Alzheimer's Disease, RNFL, Bilateral Filter, Gravitational Search (GSA) Algorithms.

© 2019 by Advance Scientific Research. This is an open-access article under the CC BY license (<http://creativecommons.org/licenses/by/4.0/>) DOI: <http://dx.doi.org/10.31838/jcr.07.04.42>

INTRODUCTION

Dementia is a group of more than ten brain disorders. Alzheimer's Disease (AD) is a progressive, brain disorder. Recent studies indicated that many people are living with AD around the world. The death of cells in brain cause change in one's behavior. Sign and symptoms of AD are memory loss, poor judgment and confusion with time and place. Future to this, Aging is the major cause of AD. However, ageing is not only that contributes to the development of AD. Family history also causes AD. People with mild cognitive impairment are likely to have AD. Epidemiological reports and experts estimate the prevalence of dementia to 24.3 million by the end of the year 2013. Every 20 years people suffering from AD will double and reach to 81.1 million by 2040[2]. Developing countries with the highest population are having a high risk of dementia. In India, at current, about 1.5 million people are diagnosed with dementia, about 70% of the cases attributed to AD. The rate of increase in the number of dementia cases in India between 2001 and 2040 is estimated to be around 300%. Research studies showed that AD affects not only brain cells but also in retinal images [17-19]. This fact motivated us to develop a system that can differentiate AD from normal patients based on retinal image features.

Several vision issues such as loss of colour vision, changes in visual activity and contrast, visual evoked potentials, reading problems and recognition of objects are faced by AD patients [4]. A majority of these issues are controversial with conflicting information found in survey and no particular loss can be considered for AD diagnosis. Also, some pathological changes have been observed. The optometrist has significant role in AD diagnosis [5]. The standard approach many histological studies show a notable reduction in the number of Retinal Ganglion Cells (RGCs) and it's axons present in the optic nerves of the AD patients, which can be a preferential damage or maybe the large diameter of neurons clinical studies of Optic Nerve Head (ONH) and Retinal Nerve Fiber Layer (RNFL) depicts that an occurrence of optic neuropathy with RNFL abnormalities is a factor of AD. Therefore, the disease

analysis can be carried out using an optic disc, blood vessels, retinal nerve fiber for identification of the disease at an early stage. So, the purpose research is to get a clear picture of the disease process in humans and find new ways to diagnose or predict AD early, and thereby improve the life of the AD patients. Thus, this research focuses on the detection of AD using retinal abnormalities[6].

Computer-aided Alzheimer's Detection general step by step process of the system. A novel automated segmentation method Geodesic distance weighted by an exponential function is introduced by Duan et al [7] to segment tangled retinal structures and other deformity caused by the deformity. The quantitative and qualitative analyses in clinical trials were done in 2D and 3D images. While comparing the proposed 2D segmentation result with Parallel Double Snake (PDS) and Chiu's graph search method, Geodesic Distance Method (GDM) indicate better performance in detecting retinal boundaries. Odstrcilik et al [8,9] proposed the Gaussian Local binary pattern for and Markov random field for feature extraction and then for detecting the RNFL edge Matched filtering approach is used. Hayashi et al [10], suggested Morphological filtering for preprocessing. Then the preprocessed images are enhanced by Gabor filtering. Finally finding the RNFL edge Statistical region merging algorithm is used, here 71% of NFLDs with an average 3.2 false positives were detected Chandrappa et al [11] explained the preprocessing and RNFL edge detection based on Median filter algorithm and Image adjustment method. Finally, the result shows the actual boundaries of RNFL. Gabor et al [12] proposed nonlinear complex diffusion filter, Shadow gram technique Power spectrum method to measure fractal dimension of IRT. Vinodhini et al [13] suggested Gaussian filter and Image gradient techniques for image enhancement [19]. Canny edge detection Custom-built software (OCTRIMA) is used for segmentation procedure. Here CL+IPL layer is obtained and texture features are extracted [17]. The authors proposed various algorithms for preprocessing and segmentation of RNFL edges. In

this work, novel techniques are proposed. Initially, the image of the retina is given as the input. The second block of the system extracts the essential features. The essential features extracted are fed to the segmentation block where it gets segmented. Section 1 describes the introduction and the review of literature and section 2 demonstrates the methodology work of the proposed technique. Section 3 presents the outcomes of segmentation and section 4 gives major findings of the work.

PROPOSED WORK

An automatic fundus image analysis involves various processes including image acquisition, preprocessing, segmentation, feature extraction and classification. Image acquisition is done by fundus camera. Preprocessing helps to improve the quality of the input image. In this work, bilateral filter employed to remove noise from the input image. Segmentation is defined the process of grouping an image into many segments based on some attributes like intensity, color and texture features. Gravitational Search Algorithm (GSA) is used to segment retinal image. The overall framework of the developed system is depicted in figure.1.

Image acquisition

Image analysis is an interesting topics of research that has caught more attention from researchers. The goal of medical image analysis is develop an efficient tool which will help the physician to visualize, analyse and make correct decision about the image. The procedure of taking fundus images starts by dilating the pupil with pharmaceutical eye drops. After that, the patient is asked to stare at a fixation device in order to steady the eyes. While taking the pictures, the patient will see a series of bright flashes. The entire process takes about five to ten minutes, the eye fundus images of diabetic patients must be examined at least once a year.

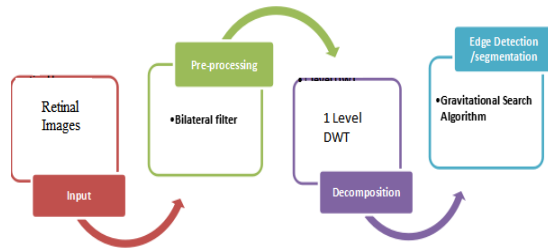


Figure 1: Overall Block Diagram

Image preprocessing

Preprocessing method is the preliminary step in the diagnosis. The input fundus images are preprocessed before it is applied to the segmentation process. As an initial preprocessing step, the blurred images are rectified.

Bilateral filter

Bilateral filter was first introduced by Tomasi et al. in 1998. The idea of bilateral filter was also presented in the Smallest Unvalued Segment Assimilating Nucleus (SUSAN) Filter and the neighborhood filter in different earlier methods. Bilateral filter is a type of non-linear, noise removing and edge smoothing filter. It uses both spatial domain and intensity domain information for processing an image. The pixel value in an image is replaced by a weighted mean of value of nearby pixels. The weight value depends on both Euclidean and radiometric distances. Therefore, bilateral filter can preserve edges than other filters [18]. Bilateral filter can be expressed as:

$$I_{filtered}(X) = \frac{1}{W_p} \sum_{x_i \in \omega} I(X_i) f_r(|I(X_i) - I(X)|) g_s(|X_i - X|) \quad (1)$$

Where the normalization term,

$$W_p = \sum_{x_i \in \omega} f_r(|I(X_i) - I(X)|) g_s(|X_i - X|) \quad (2)$$

Where, $I_{filtered}$ is the filtered image, I is the original input image to be filtered, X_i are the coordinate of the current pixel to be filtered, R is the window centered with x , f_r is the range kernel for ,

smoothing differences in intensities. This action can be a Gaussian function is the spatial kernel.

1-LEVEL DISCRETE WAVELET TRANSFORM

A wavelet is a powerful tool to analyses signal or image. It is used to analyse the signal or image in multi resolution. Discrete wavelet transform is formed from other wavelet transform is formed from other wavelet, but with time and frequency in separate phase. The connection among wavelets in spatial domain and frequency domain in multi resolution analysis it can describe the wavelet transform in this work. Mallet's presented that it is possible to construct wavelets Ψ such that the translated family.

For Multi Resolution Analysis (MRA) the DWT is used. The MRA can be used for the signals which are non-stationary and nonlinear. The DWT decomposes the given function $f(t)$ into the approximation and element coefficients. The feature $f(t)$ satisfy some conditions and it could be expressed as

$$f(t) = \sum_{j=1}^l \sum_{k=-\infty}^{\infty} d(j, k) \cdot \varphi(2^{-j}t - k) + \sum_{l=-\infty}^{\infty} a(l, k) \varphi(2^{-l}t - k) \quad (3)$$

Where the $\theta(t)$ scaling is function, $\omega(t)$ is the mother wavelet, $d(j, k)$ is the detail coefficient at scale j and $a(l, k)$ is the approximation coefficient at scale l . The expression for element coefficients and approximation are given underneath

$$d(j, k) = \frac{1}{\sqrt{2^j}} \int_{-\infty}^{\infty} f(t) \cdot \varphi(2^{-j}t - k) \quad (4)$$

$$a(l, k) = \frac{1}{\sqrt{2^l}} \int_{-\infty}^{\infty} f(t) \cdot \varphi(2^{-l}t - k) \quad (5)$$

The DWT is the method which uses a filtering approach by using high pass (wavelet) filter and a low pass (scaling) filter. Those filters use one-of-a-kind layers, inside the first layer the DWT decomposes the signal into two bands which offers an excessive skip model of the sign and a low bypass model. The excessive skip filtered signal provides the parts or great rate deviations at the equal time as the low pass sign offers the approximate illustration of the signal. Inside the 2nd degree of decomposition, the low skip signal obtained from the primary stage is decomposed into bands an excessive pass version of the sign and a low pass model of this low skip sign. There are different forms of Wavelet remodel.

To compute the detail coefficients and the approximation the above 2 equation (4) and (5) give a mathematical relationship. This procedure is seldom approved. To use Mallet's Fast Wavelet Transform procedure more practical approach is found. In truth, a classical arrangement in the signal treating community, so-called a double channel sub-band coder the treatment of conjugate quadrature filters or quadrature mirror filters (QMF) is the Mallet's set of rules for discrete wavelet transforms (DWT).

Segmentation

Image segmentation is a crucial step in medical image analysis. It is utilized to separate the useful information from its background. Several segmentation algorithms such as ANN, Fuzzy have been proposed. Each algorithm has its own characteristics. In this GSA algorithm is used for segmentation.

GSA algorithm

GSA is a type metaheuristic algorithms, proposed by Rashedi et al. in 2009. GSA is motivated by mass interactions and gravity law. Gravitation is the attraction of masses by other masses, which is depends on masses and their distance.

GSA is consists of several search agents that interact each other through gravity force. The agents are assumed as objects and their performance is evaluated by their masses. The gravity force

causes a global movement where all objects move towards other objects with heavier masses. The slow movement of heavier masses guarantees the exploitation step of the algorithm and corresponds to good solutions. Equation (6) and Equation (7) represents gravity law and motion law respectively.

$$F = G(M_1 M_2 / R^2) \quad (6)$$

$$a = F / M \quad (7)$$

Where, F- gravitational force, R- distance, G-constant, M1- Mass of first object and M2- Mass of second object.

In GSA, search agent poses 4 main variables such as position, inertial mass, active gravitational mass and passive gravitational mass. Position corresponds to the solution, inertial and gravitational masses are computed by cost function. The detailed steps of GSA are given below:

Step 1: Initialization:

Initialize search agents, N randomly

$$X_i = (x_i^1, \dots, x_i^d, \dots, x_i^n), \text{ for } i = 1, 2, \dots, N. \quad (8)$$

where, x_i^1 -position of i^{th} agent and n-dimension.

Step 2: Cost function computation:

Minimization problems

$$\text{best}(t) = \min \text{fit}_j(t) \quad j \in \{1 \dots N\} \quad (9)$$

$$\text{worst}(t) = \max \text{fit}_j(t) \quad j \in \{1 \dots N\} \quad (10)$$

Maximization problems

$$\text{best}(t) = \max \text{fit}_j(t) \quad j \in \{1 \dots N\} \quad (11)$$

$$\text{worst}(t) = \min \text{fit}_j(t) \quad j \in \{1 \dots N\} \quad (12)$$

fit $j(t)$ fitness value of the j^{th} agent at iteration t , best (t) - best case and worst (t) - worst case at t .

Step 3: compute gravitational constant (G):

G can be computed as:

$$G(t) = G_0 e^{(-\alpha t / T)} \quad (13)$$

G_0 and α initialized at the starting and then decreased to optimize accuracy. T- iteration.

Step 4: Calculate agent's masses:

Agent's masses can be expressed as:

$$M_{ai} = M_{pi} = M_{ii} = M_i \quad i = 1, 2, \dots, N.$$

$$m_i(t) = \frac{\text{fit}_i(t) - \text{worst}(t)}{\text{best}(t) - \text{worst}(t)} \quad (14)$$

$$m_i(t) = \frac{m_i(t)}{\sum_{j=1}^N m_j(t)} \quad (15)$$

Where, M_{ai} -active mass, M_{pi} -passive mass and M_{ii} - inertia mass.

Step 5: Accelerations of agents computation:

Acceleration of the i^{th} agents is computed.

$$a_i^d = F_i^d(t) / M_{ii}(t) \quad (16)$$

$F_i^d(t)$ total force acting on i^{th} agent calculated as:

$$F_i^d(t) = \sum_{j \in K, \text{best}, j \neq i} \text{rand} F_{ij}^d(t) \quad (17)$$

Kbest set of first K agents with the best fitness value and biggest mass. **Kbest** will decrease linearly with time and at the end there will be only one agent applying force to the others. $F_{ij}^d(t)$ is computed as the following equation:

$$F_{ij}^d(t) = G(t) \cdot (M_{pi}(t) \times M_{aj}(t) / R_{ij}(t) + \epsilon) \cdot (x_j^d(t) - x_i^d(t)) \quad (18)$$

$F_{ij}^d(t)$ is the force acting on agent i from agent j at d^{th} dimension and i^{th} iteration. $R_{ij}(t)$ is the Euclidian distance between two agents i and j at iteration t . $G(t)$ is the computed gravitational constant at the same iteration while ϵ is a small constant

Step 6: Calculate velocity and position:

Velocity and the position of the agents are calculated using equations:

$$V_i^d(t+1) = \text{rand}_i x v_i^d(t) + a_i^d(t) \quad (19)$$

$$x_i^d(t+1) = x_i^d(t) + V_i^d(t+1) \quad (20)$$

Step 7: Repeat steps 2 to 6

Steps 2 to 6 are repeated until the iterations reach their maximum limit. The best fitness value at the final iteration is computed as the global fitness while the position of the corresponding agent at specified dimensions is computed as the global solution of that particular problem. Process of GSA is given in figure.2.

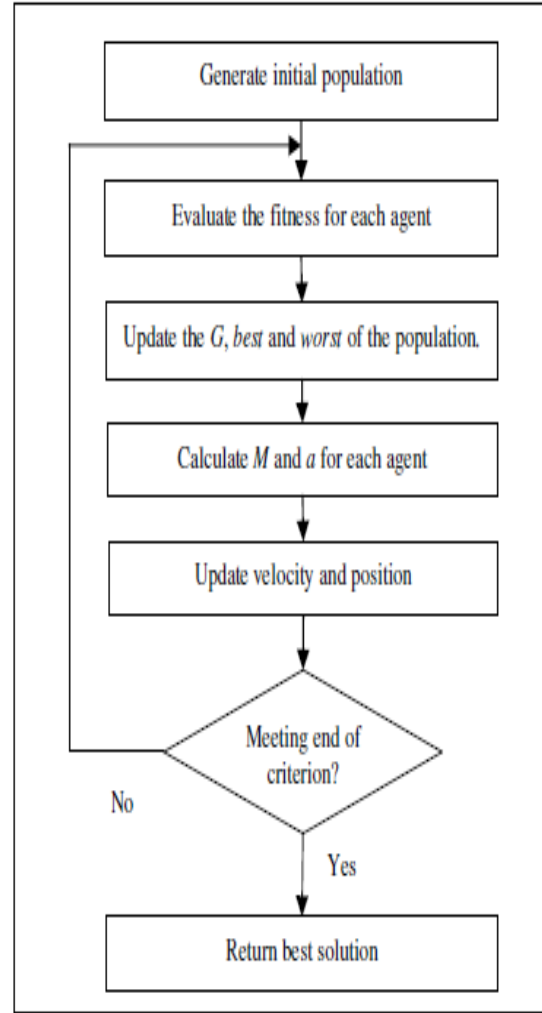


Figure 2: GSA process

EXPERIMENTAL RESULTS

In this model, fundus images are collected for processing. Preprocess method is employed for removing noise. Here the bilateral filter is utilized as preprocessing tool which can reduce the noise completely. The result of the preprocessed image is compared with the average filtered, median filtered and wiener filtered technique. Compared with these techniques the bilateral image gives a better result. Preprocessed image is shown in Figure.3.

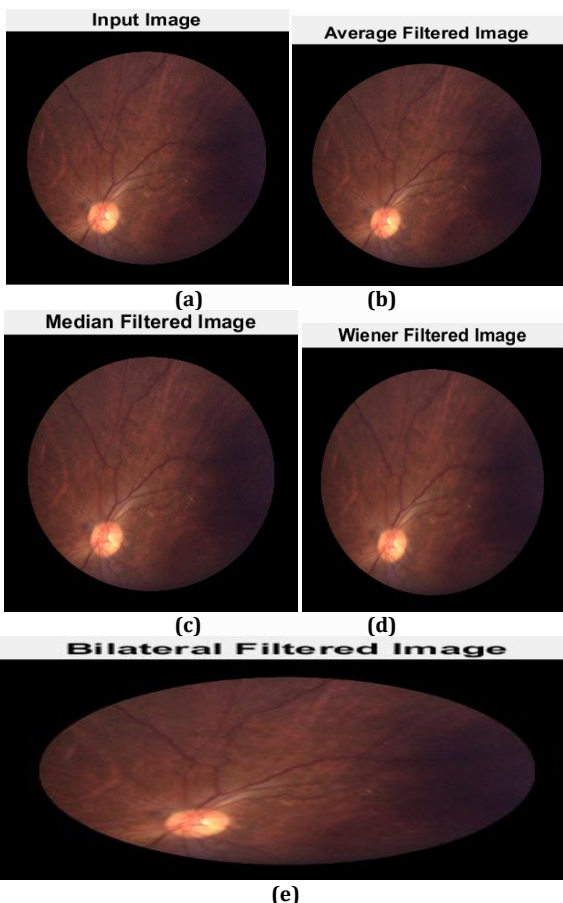


Figure 3: (a) Input image, (b-e) Pre-processed results of average filtered, median filtered, wiener filtered technique and bilateral filtered image

After the preprocessing model using the DWT technique, the decomposition is performed. This decomposition model uses a high pass and low pass technique. Figure 4 shows the decomposed result, here 4(a) represents the decomposed DWT image, 4(b) represents the low pass image, 4(c) represents the multilevel BF image and 4(d) shows the binarized result. Following decomposition using the GSA algorithm the separation of RNFL from preprocessed image is done. This process show good outcome. Figure.5 shows the segmentation results.

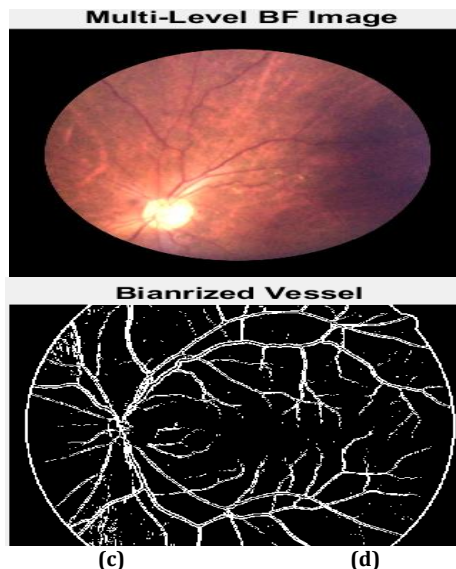
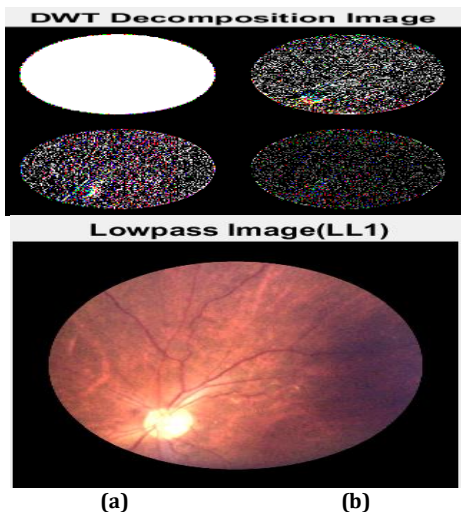


Figure 4: Decomposition result (a) decomposed image, (b) low pass image, (c) multilevel BF image, (d) binarized result

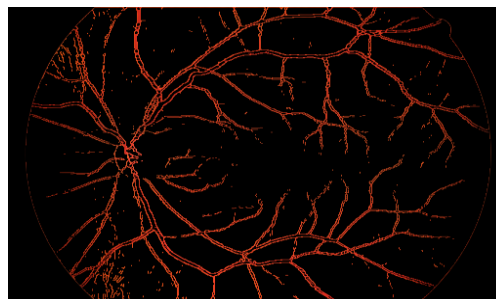


Figure 5: RNFL segmented image

Threshold values obtained with several metaheuristic algorithms are tabulated in Table. 1. from the Table 1, it is observed that MB-GSA provides outstanding performance when compared to other algorithms. For better analysis, statistical comparison is plotted for GA-GSA, GSA, PSO, MB-GSA in Figure.6, Figure.7, Figure.8 and Figure.9 respectively.

Table 1: Result of uniformity value for GA-GSA, GSA, PSO, MB-GSA for different images

Images	GA-GSA	GSA	PSO	MB-GSA
Lenna 2	0.8166	0.8067	0.7967	0.8422
Lenna 3	0.8785	0.8476	0.8374	0.8993
Lenna 4	0.881	0.8486	0.8439	0.9237
Lenna 5	0.918	0.8744	0.8615	0.9455
Pepper2	0.8061	0.7865	0.7865	0.8359
Pepper3	0.8742	0.8561	0.8086	0.9122
Pepper4	0.9657	0.9636	0.9619	0.9911
Pepper5	0.9716	0.9667	0.9627	0.9946

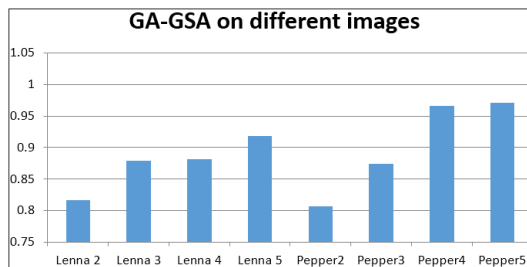


Figure 6: Statistical Comparison of GA-GSA Based Method

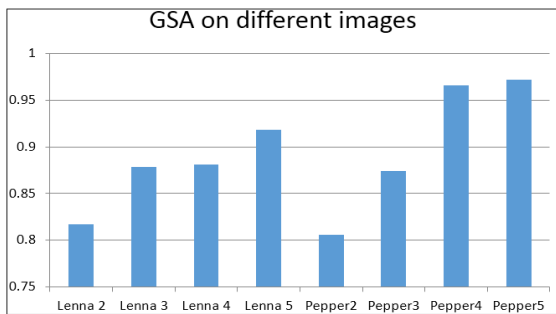


Figure 7: Statistical Comparison of GSA Based Method

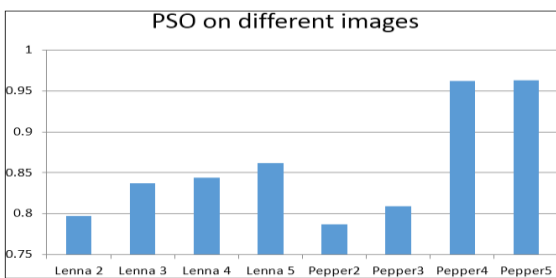


Figure 8: Statistical Comparison of PSO Based Method

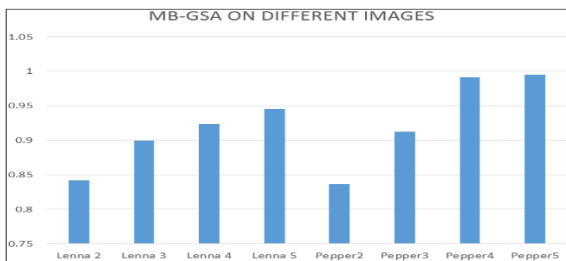


Figure 9: Statistical Comparison of MB-GSA Based Method

Widely used algorithm to solve complex problems. Standard PSO is applied and results are observed. For a better analysis of the result, it is plotted in figure 10.

Table 2: Result of MB-GSA in Different fundus Images

Images	MB-GSA
Fundus1	0.8886
Fundus2	0.9438
Fundus3	0.9682
Fundus4	0.9956
Fundus5	0.8846

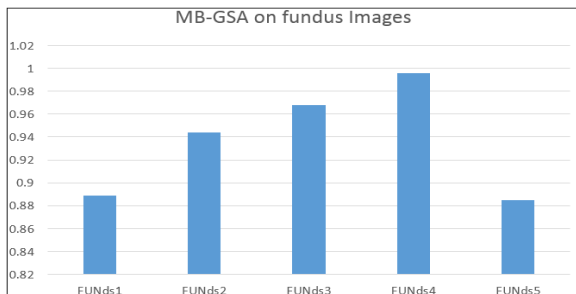


Figure 10: Statistical Comparison of results obtained using GSA Based Method

CONCLUSION

This paper has proposed a novel method for detecting RNFL edges using Gravitational search algorithm for AD diagnosis at an early stage. GSA employed for separating RNFL from its background.

The pre-processing of the retinal images are performed by a bilateral filter and enhanced by 1-level DWT method. Subsequently, the RNFL regions are separated by GSA which accurately determines the most important regions. Results showed that the efficacy of proposed method is superior to other algorithms.

REFERENCES

- Akar Gokcen et al. (2014) 'Retinal nerve fiber layer thickness in cases with mild cognitive impairment and Alzheimer-Type Dementia', Biomedical Research pp. 597-602
- Anat London, Inbal Benhar and Michal Schwartz,(2012) 'The retina as a window to the brain-from eye research to CNS disorders', Nature Reviews Neurology, pp. 100-110.
- Blanks JC, Torigoe Y, Hinton DR, Blanks RH. (1996) 'Retinal pathology in Alzheimer's disease. I. Ganglion cell loss in foveal/parafoveal retina', Neurobiol Aging, pp. 377-384.
- C. Paquet, M. Boissonnot, F. Roger, P. Dighiero, R. Gil, and J. Hugon,(2007) 'Abnormal retinal thickness in patients with mild cognitive impairment and Alzheimer's disease', Neuroscience Letters, Vol. 420, No. 2, pp. 97-99.
- Cronin-Golomb A, Corkin S, Rizzo JF, Cohen J, Growdon JH, Banks KS,(1991) 'Visual Dysfunction in Alzheimer's Disease: Relation to Normal Aging', American Neurological Association, Vol. 29, No. 1, pp.41-52.
- Vincenzo Parisi, Rita (2001), 'Morphological and functional retinal impairment in Alzheimer's disease patients', Vol. 112, No. 10, pp: 1860-1867.
- Jinming Duan, Christopher Tench, Irene Gottlob, Frank Proudlock, Li Bai, (2016), 'Automated Segmentation of Retinal Layers from Optical Coherent Tomography Images Using Geodesic Distance,' arXiv Computer Science, pp.01-20.
- Odstrcilik J, Kolar R, Tornow R P, Jan J, Budai A, Mayer M, Vodakova M, (2015), 'Analysis of the Retinal Nerve Fiber Layer Texture Related to the Thickness Measured by Optical Coherence Tomography', Springer, Development in Medical Image Processing and Computational Vision, pp. 19-40.
- Odstrcilik J, Kolar R, Tornow RP, Jan J, Budai A, Mayer M, Vodakova M, Laemmer R, Lamos M, Kuna Z, Gazarek J, Kubena T, Cernosek P, Ronzhina M, (2014), 'Thickness related textural properties of retinal nerve fiber layer in color fundus images,' Computerized medical imaging and graphics: the official journal of the Computerized Medical Imaging Society, Vol. 38, No. 6, pp. 508-16.
- Mohamed Saleem TS, Jain A, Tarani P, Ravi V, Gauthaman K. "Aliskiren: A Novel, Orally Active Renin Inhibitor." *Systematic Reviews in Pharmacy* 1.1 (2010), 93-98. Print. doi:10.4103/0975-8453.59518
- Yoshinori Hayashi ,Yuji Hatanaka, Akira Aoyama, Masakatsu Kakogawa, Takeshi Hara, Hiroshi Fujita, Tetsuya Yamamoto(2007), 'Detection of retinal nerve fiber layer defects in retinal fundus images using Gabor filtering', Proceedings of SPIE, Medical Imaging, Computer-Aided Diagnosis, Vol. 65142, pp.1-8.
- Chandrappa. S, Dharmanna Lamani, Ranjan Kumar H.S (2015). 'Segmentation of Retinal Nerve Fiber Layer in Optical Coherence Tomography (OCT) Images using Statistical Region Merging Technique for Glaucoma screening', International Journal of Computer Application, Vol.128, No.10, pp.32-35
- Gabor Mark Somfai, Erika Tatrai, Lenke Laurik, Boglarka E Varga, Vera Olvedy, William E Smiddy, Robert Tchtitnga, Aniko Somogyi and Delia Cabrera DeBuc.(2014), 'Fractal-based analysis of optical coherence tomography data to quantify retinal tissue damage,' BMC Bioinformatics, pp: 1-10.
- R. Vinodhini, N. Padmasini, R. Uma Maheshwar, Mohammed Yacin,(2016), 'Feature Extraction And Segmentation Of RNFL from SDOCT Retinal Images For The Diagnosis Of Diabetic Retinopathy,' International Journal of Research and

- Reviews in Applied Sciences And Engineering (IJRRASE), Vol 8. No.1, pp. 85-91.
15. Vijay Kumar, Jitender Kumar Chhabra , Dinesh Kumar "Automatic cluster evolution using gravitational search algorithm and its application on image segmentation" Eng. Appl. Artif. Intel.(2013), Elsevier
 16. Mohamed M. Dessouky, Mohamed A. Elrashidy, Taha E. Taha, and Hatem M. Abdelkader, "Computer-Aided Diagnosis System for Alzheimer's Disease Using Different Discrete Transform Techniques"sagepub.com/journalsPermissions.nav DOI: 10.1177/1533317515603957.
 17. Rajeesh, J and Moni, RS and Palanikumar, S and Gopalakrishnan, "Noise reduction in magnetic resonance images using wave atom shrinkage" International Journal of Image Processing (IJIP), volume=4, number=2, pages=131-141, year=2010
 18. Augustin, M Besita and Juliet, Sujitha and Palanikumar, "Motion and feature based person tracking in surveillance videos", 2011 International Conference on Emerging Trends in Electrical and Computer Technology, pages=605-609, year=2011, IEEE 2011
 19. Rajeesh, J., Moni, R.S., Kumar, S.P., & Gopalakrishnan, T. (2010, October). Rician noise removal on MRI using wave atom transform with histogram based noise variance estimation. In 2010 International Conference On Communication Control And Computing Technologies (PP. 531-535). IEEE.
 20. Palanikumar, S., Sasikumar, M., & Rajeesh, J. (2011). Palmprint Enhancement Using Discrete Curvelet Transform. International Journal of Computer Science Issues (IJCSI), 8(4), 313.
 21. Li, Y., Zhang, L., Zhang, L., Zhang, H., Zhang, N., Yang, Z., Gao, M., Yang, X., Cui, L.High-dose glucose-insulin-potassium has hemodynamic benefits and can improve cardiac remodeling in acute myocardial infarction treated with primary Percutaneous coronary intervention: From a randomized controlled study(2010) Journal of Cardiovascular Disease Research, 1 (3), pp. 104-109.
DOI: 10.4103/0975-3583.70899