A complex system for the automatic screening of diabetic retinopathy

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International Medical Informatics and Telemedicine – IMIT 2014,
13-14 April 2014, Geneva, Switzerland

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Introduction

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Debrecen, the second largest city of Hungary, is one of the most vivid and cosiest nooks: it is a unique whirlpool of a dynamic intellectual and cultural heritage and of an effective and successful economic life. The centuries' old traditions and the most recent technical and scientific innovations enhancing each other make Debrecen a nationally and internationally renowned city.

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Introduction

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The **University of Debrecen** was formed, on 1 January 2000, through the (re)merging of several hitherto autonomous institutions. Its historical roots stretch back to the foundation of the Reformed College of Debrecen (1538). With a student body of 30,000, including 20,000 full-time students, and a 1,700-strong teaching staff, the University of Debrecen is one of the largest higher-education institutions in the country, and with its 15 faculties, two independent institutes and 23 doctoral schools, it also offers the widest range of educational and research opportunities.

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Introduction

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The **Faculty of Informatics** boasts the only accredited university-level educational program for IT specialists in the east-Hungarian region. Its six departments represent a formidable pool of intellectual potential, which has earned recognition even at international level. There are currently 2350 students studying academic programs. The **Image Processing Group of Debrecen** and **Bioinformatics Research Group** of the Faculty can offer contribution in R&D activities including *image processing with specialization in the clinical domain, machine vision, data mining, scientific visualization, visual analytics, big data analysis, decision making human-machine interaction also with a strong theoretical modelling background.*

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Advantages/Importance

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- Retinal image analysis is an important tool for diagnosis and treatment of many eye diseases.
  - age-related macular degeneration,
  - diabetic retinopathy,
  - glaucoma are the leading disabling diseases and the causes of preventable blindness in the world.
- 2D and 3D fundus imaging provides a basis for quantitative methods to identify clinically relevant structures such as blood vessels, optical nerve head, and retinal lesions.
- Automated methods for retinal image analysis are important for mass screening of the population.
- Retinal atlases are important for the research community for quantitative evaluation and comparison of retinal image analysis methods.

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Advantages/Importance

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- Processing of retinal images is a standard clinical practice
- Changes in the nerve fiber layer is associated with glaucoma
- Earliest sign of macular degeneration are the appearance of yellowish spots (drusens) on the retina
- The vascular system is observable in a non-invasive way
  - hypertonia can be detected (tortured vessels)
- Diabetes can be detected/monitored via finding corresponding lesions

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Main Topics

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- image quality quantification,
- segmentation of anatomical structures on the retina (vessels, fovea, optic disc),
- segmentation of pathological structures on the retina (microaneurysms, exudates, haemorrhages, neovascularization, cottonwool spots, drusens, etc.),
- quantitative assessment of algorithm performance,
- evaluation of automatic screening systems,
- other modalities (optical coherence tomography),
- retinal image databases and atlases.

8th International Symposium on Image and Signal Processing and Analysis (ISPA 2013), Special Session on Retinal Image Analysis
September 4-6, 2013, Trieste, Italy

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Diabethic Retinopathy

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One of the most important challenges in retinal image analysis is to create **automatic** screening systems.

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Diabetes - Overview

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DM: insufficient level of insulin, high blood sugar level

Epidemiology:

- 17 million patients in 2000, 2,8% of the population (WHO)
- USA, above 60 years 18,3% = 8,6 million (American Diabetes Association)
- Growing prevelency, ~ 300 million for 2030
- Fastest in Africa and Asia
- 1/3 will suffer from diabetes among born after 2000 (CDC)

DM affects: kidney, vessels, nerves,
eye - diabetic retinopathy (DR)

DR screening: developing an automatic screening system to recognize DR based on digital fundus (retinal) images

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Diabetic retinopathy

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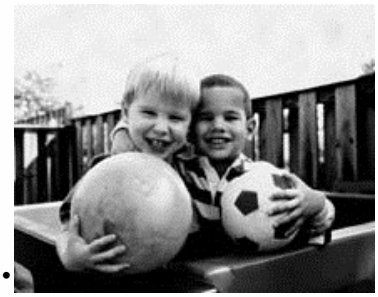
- **Reason:** deterioriation of the wall of the nervic membrane
- **Symptons:** initially no symptoms, then fast vision loss, blindness



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DR screening programmes

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- After 10 years of diabetes 80% DR
- Sysmptoms can be reversed/stabilized in 90%
- Large burden on medical doctors

- In Hungary frequent controll
- ***Digital screening programmes:***
- English National Screening Programme for Diabetic Retinopathy (UK)
- Vanderbilt Ophthalmic Imaging Center (USA)

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Simple screening decision

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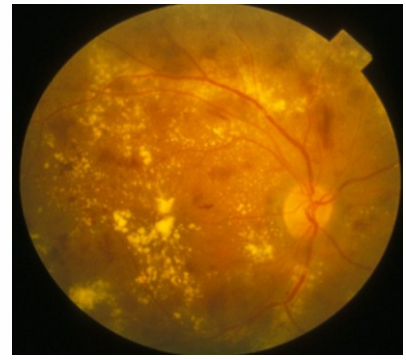
Healthy



DR, macular oedema, hard exudates, haemorrhages, aneurysms

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Anatomical parts/lesions

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Healthy retina

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Microaneurysms (early sign)

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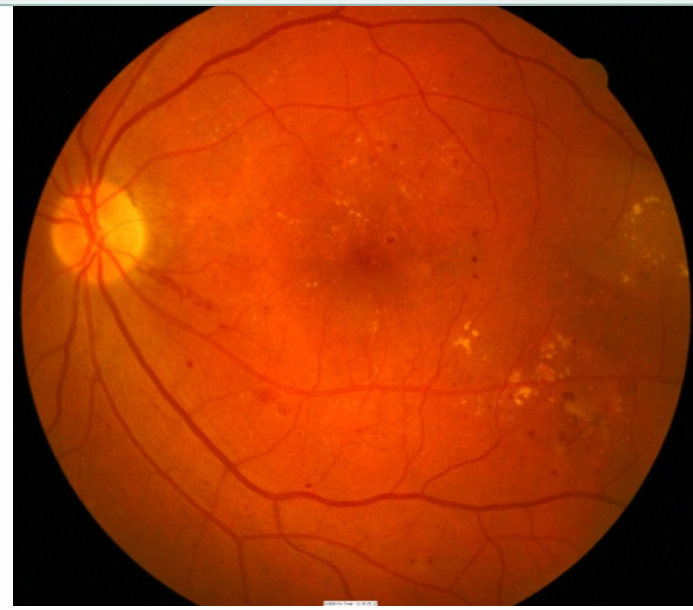

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Haemorrhages

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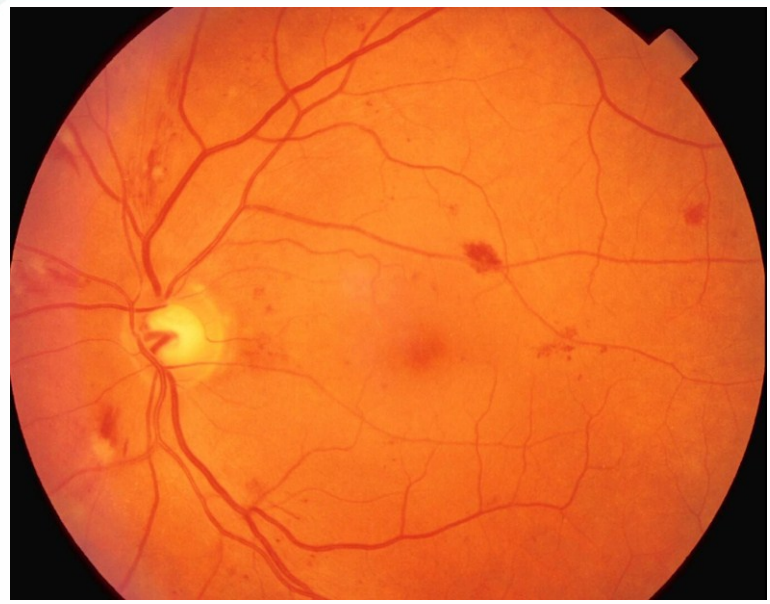

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Exudates

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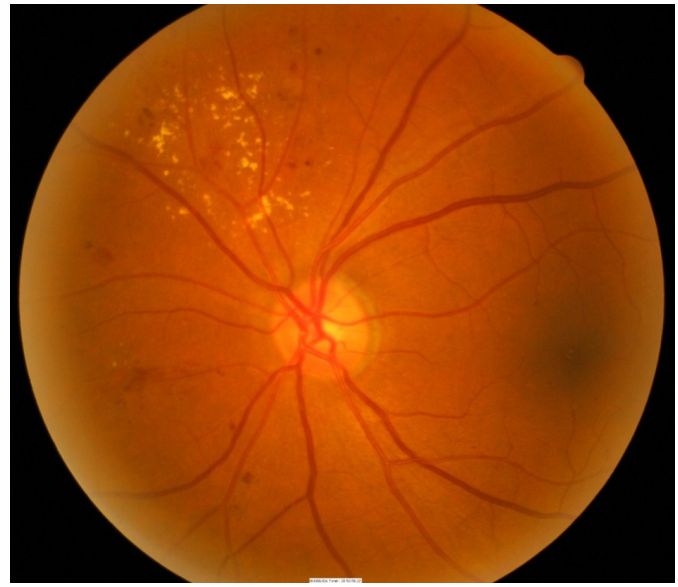

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Steps of a screening approach

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- Prefiltering
- Preprocessing
- Detecting anatomical parts
  - Vascular system
  - Temporal arcade
  - Optic disc
  - Macula/fovea
- Detecting lesions
  - Aneurysms/haemorrhages
  - Exudates
- Decision, diagnostics

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Prefiltering

Main motivation is to immediately classify images without detailed processing as:

- Healthy
- Non-healthy

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Classifying images

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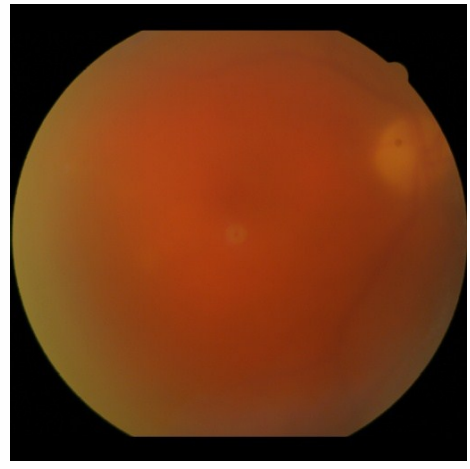
- Non-retinal images (outliers)
- Bad quality – ungradable



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Classifying images

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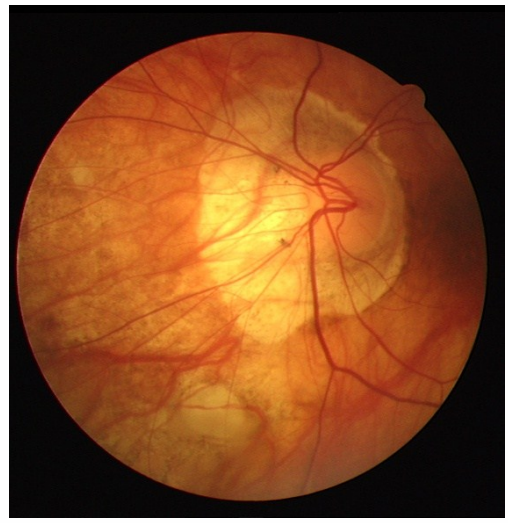
- Abnormal retina



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Classifying images

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- To be processed further

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Preprocessing

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Adaptive histogram equalization

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Adaptive histogram equalization

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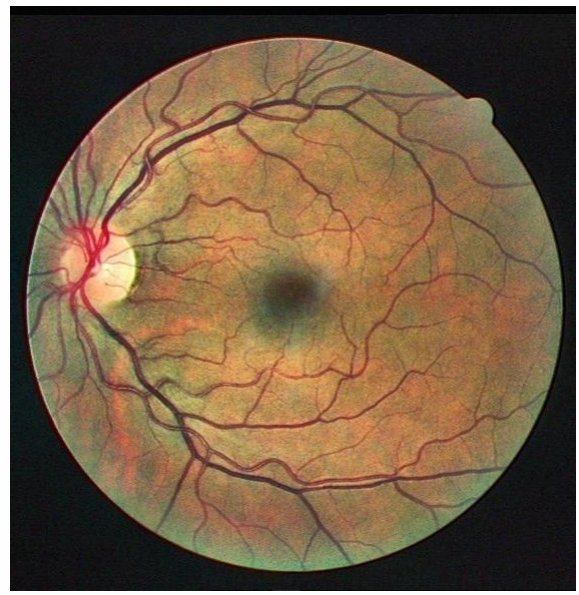

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Detecting main anatomical features

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Retinal fundus images and main anatomical features

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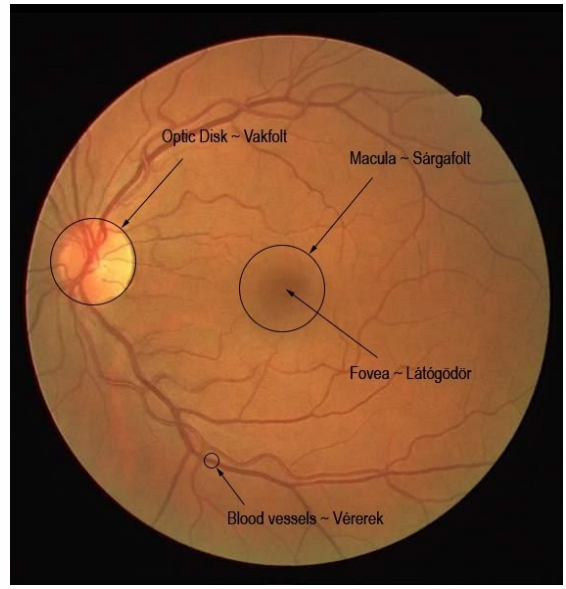

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Description of algorithms used for detecting optic disc and macula

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Detecting the optic disc

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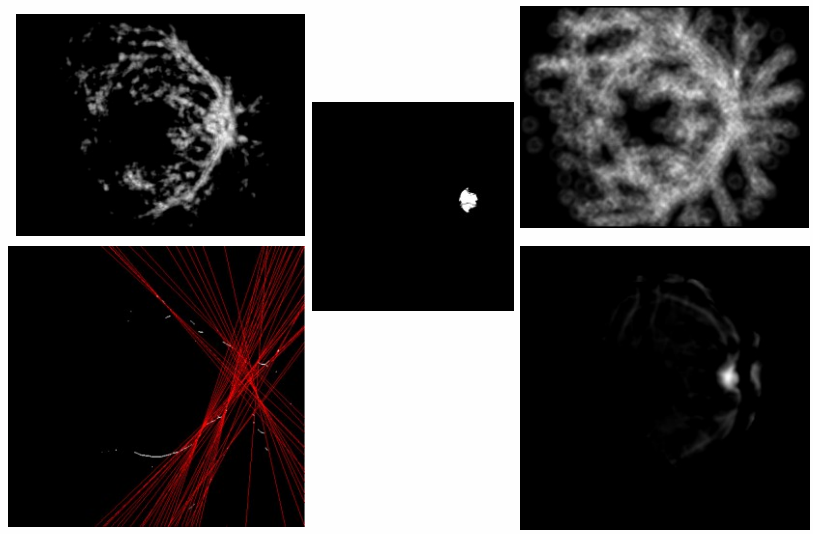

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Detecting the optic disc

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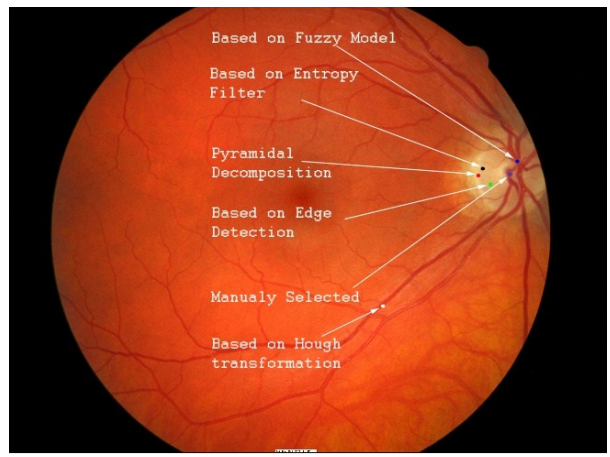
1. Simple majority voting



B. Harangi, R. J. Qureshi, A. Csutak, T. Peto, A. Hajdu: Automatic Detection Of The Optic Disc Using Majority Voting In A Collection Of Optic Disc Detectors, 7th IEEE International Symposium on Biomedical Imaging (ISBI 2010), Rotterdam, The Netherlands, 2010, pp. 1329-1332.

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Detecting the macula

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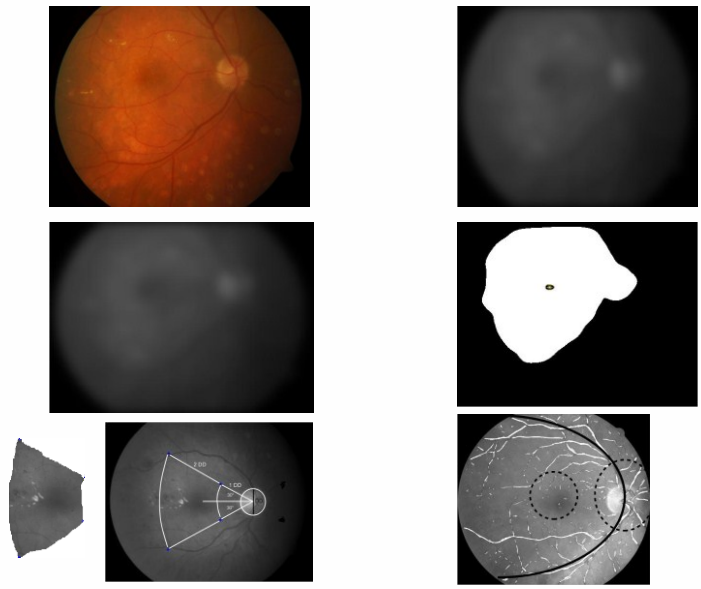

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Vessel segmentation

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Vessel segmentation

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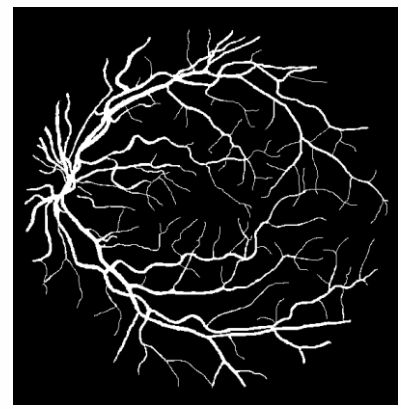
- The main objective is to extract the vascular system to enhance the accuracy and specificity of microaneurysm detection



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Detecting lesions

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Detecting microaneurysms

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Microaneurysm Detection

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- In order to prevent the damage of the retina, it is very important to diagnose diabetic retinopathy and provide appropriate treatment to minimize further deterioration as early as possible.
- Microaneurysms are the earliest sign of Diabetic Retinopathy, a frequently observed complication in both type 1 and type 2 diabetes.
- Our goal is to develop algorithms are able to detect this lesions.

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Microaneurysm Detection

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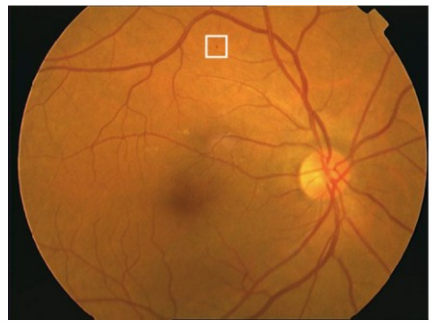

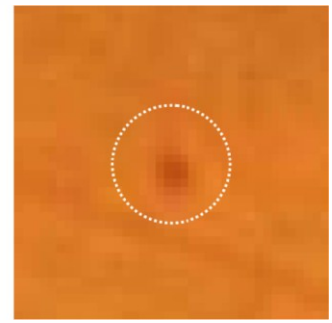

Example for a microaneurysm on a fundus image

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Microaneurysm Detection

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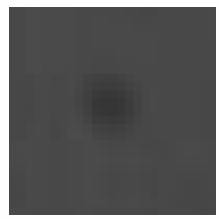
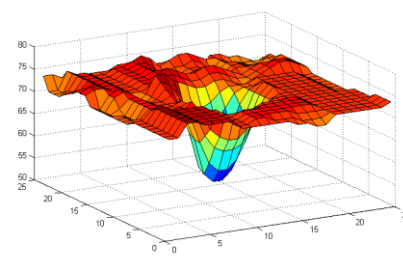
- Processing of color retinal images is usually conducted in its green channel since microaneurysms have the highest contrast with its background here.



A microaneurysm in a color retinal image in green channel



A microaneurysm illustrated with the corresponding mesh plots

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Microaneurysm Detection

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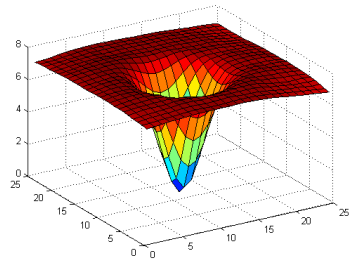
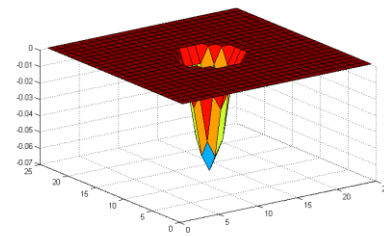
As can be seen, microaneurysms exhibit a Gaussian shape.



Mean of 3000 microaneurysm



A gaussian kernel

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Clustering MAs

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- We classified the microaneurysm into 5 classes
- The centroids of the classes represents the microaneurysms belongs to it
- The elements of the classes correlate well with the corresponding centroids

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Microaneurysm classes

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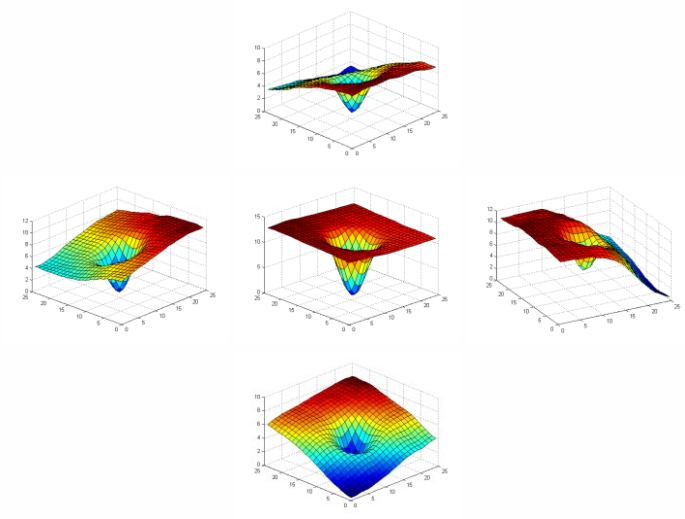
Centroids of the classes



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Results on MA detection

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TABLE I. RESULTS ON THE TEST DATABASE DIARET0

	TP	FP
Walter	423	11973
Spencer	186	2626
Hough	34	16692
Lazar	464	7074
Proposed	**618**	**15501**

TABLE II. RESULTS ON THE TEST DATABASE DIARET1

	TP	FP
Walter	390	8894
Spencer	5	2312
Hough	23	13069
Lazar	352	5325
Proposed	**458**	**11232**

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An Ensemble-based System For Detecting Microaneurysms

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The usual steps of MA detection

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Preprocessing

↓

Candidate extraction

↓

Classification

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The usual steps of MA detection

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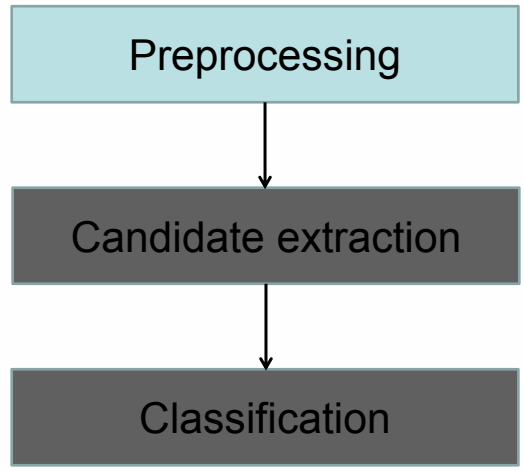

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Preprocessing

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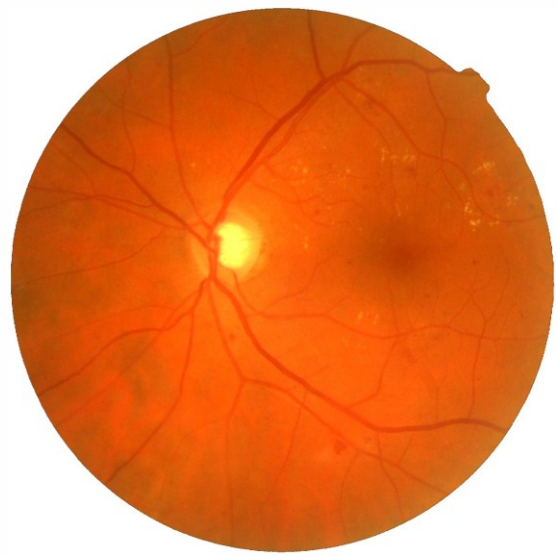

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Preprocessing

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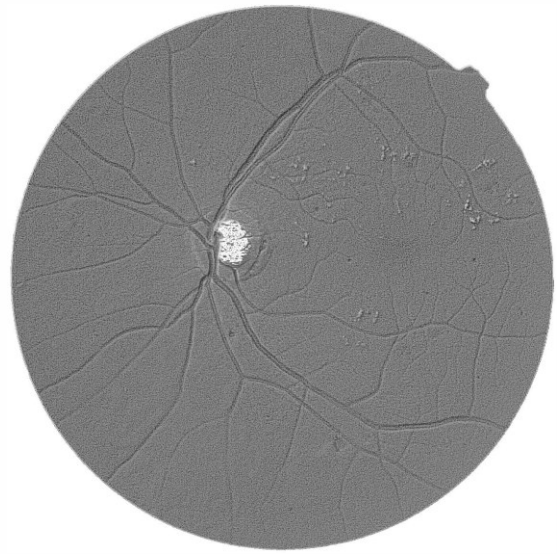

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The usual steps of MA detection

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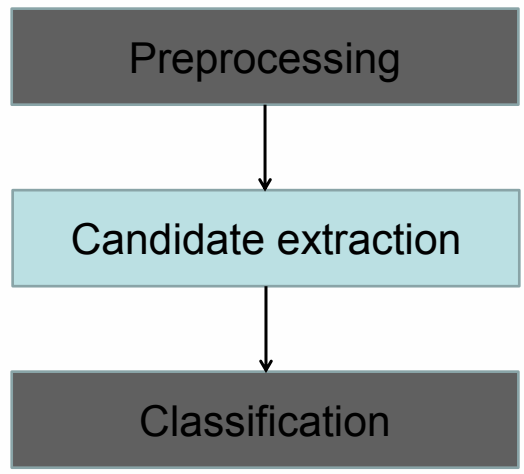

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Candidate Extraction

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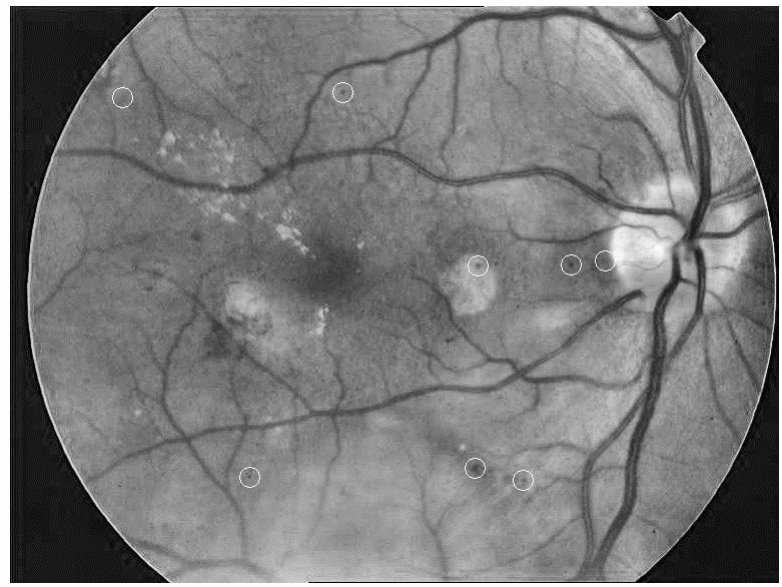

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The usual steps of MA detection

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Preprocessing

↓

Candidate extraction

↓

Classification

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Classification

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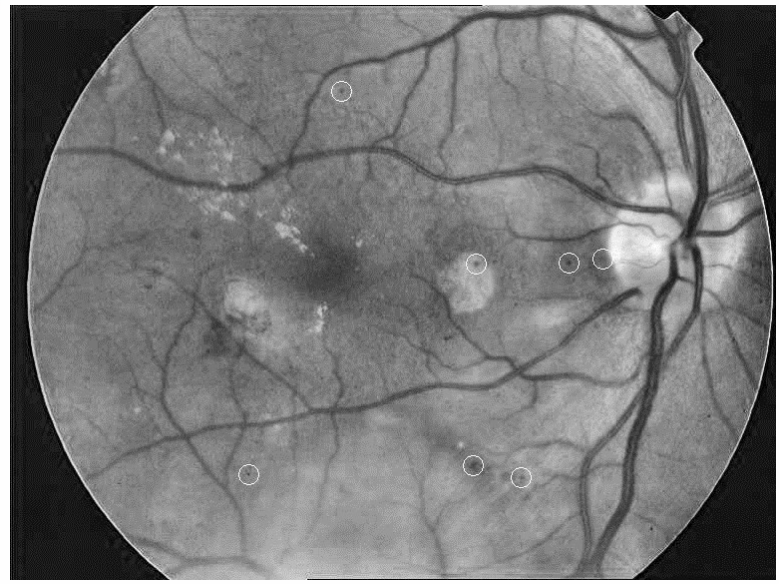

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Problems with usual MA detection

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- We have evaluated the state-of-the-art methods
- There are too many false positives
- And there are too few true positives
- The classification step has little influence in the whole process

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Hypothesis

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The ratio of the true and false MA detections can be improved by applying majority voting among several MA detectors.

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Diversity of MA candidate extractors

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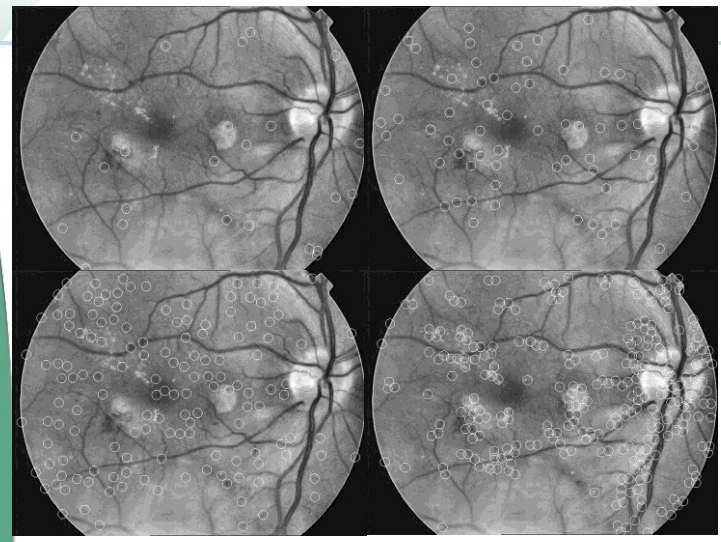

(a) Lazar (b) Walter
(c) Spencer (d) Hough

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Majority Voting

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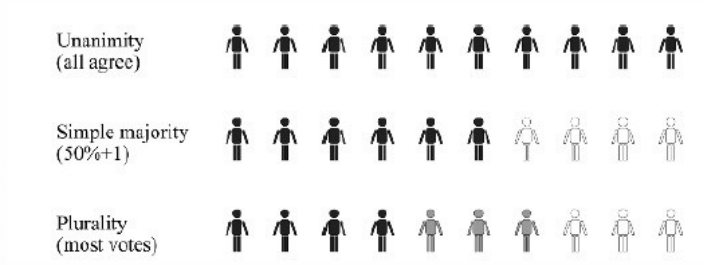

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After Majority Voting

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Results

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The ratio of the true and false MA detections is improved by the proposed method. However, it still does not good enough for clinical use.

How can we detect more true MAs?

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Preprocessing Methods

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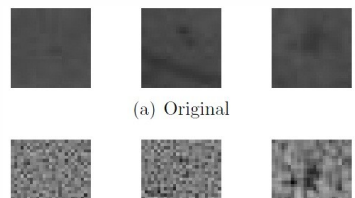
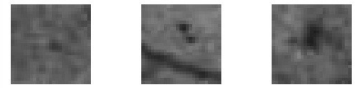
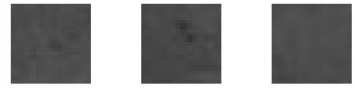


(a) Original

(b) Walter-Klein constrast enhancement



(c) CLAHE



(d) Vessel removal and extrapolation

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Hypothesis

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The detectors detect different MAs when different pre-processing steps are applied. Thus, we can create more diversity among MA detectors if we use different preprocessing methods => the sensitivity of MA detection can be improved this way.

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Results

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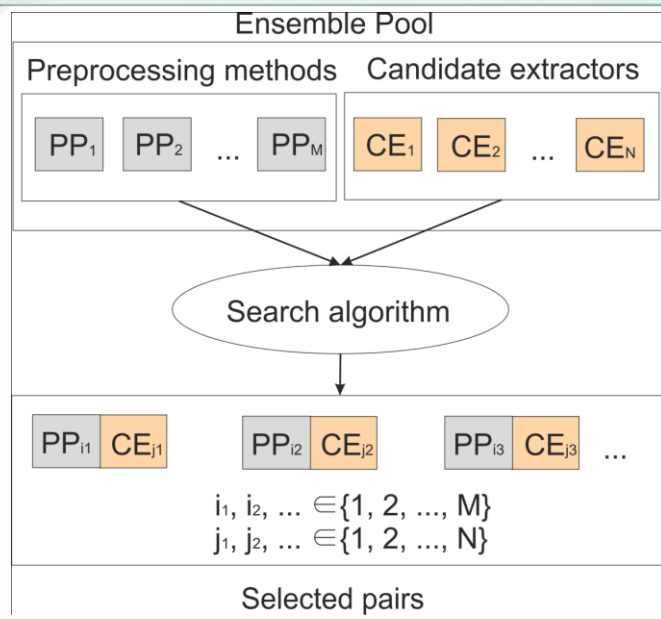

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Pairs included in the ensemble

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Preprocessing \ Candidate extractor	Walter	Spencer	Hough	Lazar	Zhang
Walter-Klein					•
CLAHE	•			•	
Vessel Removal				•	•
Illumination equalization				•	
No preprocessing	•			•	•

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Confidence levels assigned to MA detections

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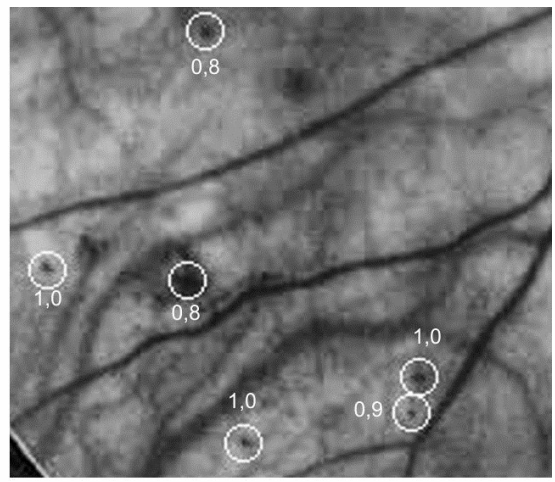

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Results

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We have tested our approach to MA detection on several public and private databases. Our experimental results show that the proposed ensemble-based MA detector outperforms the current individual approaches in MA detection. Our main results is achieved in the Retinopathy Online Challenge, where the presented algorithm is currently ranked as first.

B. Antal, A. Hajdu: An *Ensemble-based* System for Microaneurysm Detection and Diabetic Retinopathy Grading, IEEE Transactions on Biomedical Engineering, vol.59, no.6, pp.1720-1726, June 2012.

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Retinopathy Online Challenge

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	1/8	1/4	1/2	1	2	4	8	avg.
DRSCREEN	**0.173**	**0.275**	**0.380**	**0.444**	**0.526**	**0.599**	**0.643**	**0.434**
Niemeijer et al.	0.243	0.297	0.336	0.397	0.454	0.498	0.542	0.395
LaTIM	0.166	0.230	0.318	0.385	0.434	0.534	0.598	0.381
OKmedical	0.198	0.265	0.315	0.356	0.394	0.466	0.501	0.357
Lazar et al.	**0.169**	**0.248**	**0.274**	**0.367**	**0.385**	**0.499**	**0.542**	**0.355**
GIB	0.190	0.216	0.254	0.300	0.364	0.411	0.519	0.322
Fujita	0.181	0.224	0.259	0.289	0.347	0.402	0.466	0.310
IRIA	0.041	0.160	0.192	0.242	0.321	0.397	0.493	0.264
ISMV	0.134	0.146	0.202	0.249	0.286	0.345	0.430	0.256
Waikato	0.055	0.111	0.184	0.213	0.251	0.300	0.329	0.206

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Exudate detection

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What is an exudate?

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- Deposits of cholesterol or other fats (proteins) from the blood that have leaked into the retina.
- There are tiny yellow patches on the retina.

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Exudate detection

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Exudate detection

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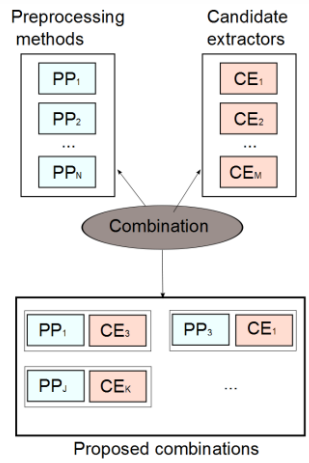
1. Ensemble-based detection



B. Nagy, B. Harangi, B. Antal, A. Hajdu: Ensemble-based exudate detection in color fundus images, 7th International Symposium on Image and Signal Processing and Analysis (ISPA 2011), Dubrovnik, Croatia, 2011, pp. 700-703.

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Exudate detection

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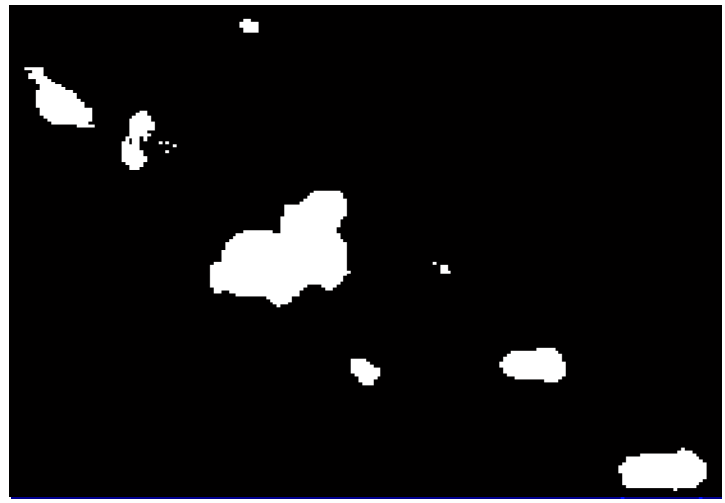
1. Ensemble-based detection



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Grading Retinal Images

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Grading of Diabetic Retinopathy (DR)

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MA is the earliest sign of DR. Why don't we use the MA detector to indicate the presence of DR? The results: 76% sensitivity, 88% specificity and 82% accuracy on a publicly available dataset.

How can we improve it?

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Clinical Grades

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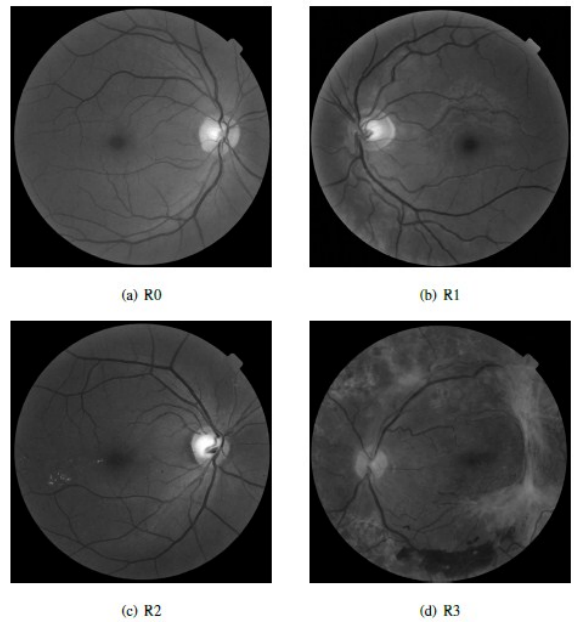

(a) R0 (b) R1

(c) R2 (d) R3

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Decision Process

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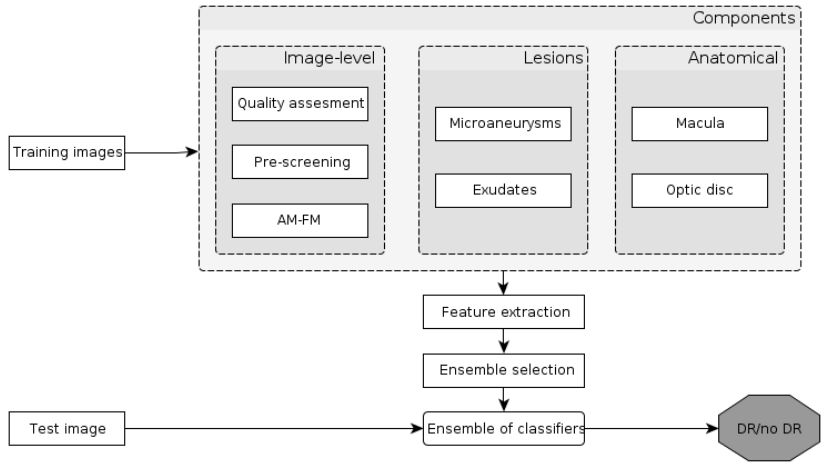

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Results of the final decision

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The results show that compared to the DR grading performance of the MA-only early detection framework, the improvement using the final decision framework is significant: the most accurate result achieved by the MA detector achieved 76% sensitivity, 88% specificity and 82% accuracy, opposed to the 94% sensitivity, 90% specificity and 90% accuracy of the latter approach. Thus, the more resource-demanding final decision approach is also more reliable in DR grading.

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Results of the final decision

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	ALL	FORWARD	BACKWARD
majority	99%/67%/81%	100%/0%/45%	98%/71%/83%
weighted majority	98%/67%/80%	100%/0%/45%	100%/0/%45%
avg	94%/79%/85%	**91%/83%/86%**	94%/77%/85%
mul	**94%/80%/86%**	**91%/86%/86%**	93%/78%/85%
max	60%/91%/77%	**93%/80%/86%**	64%/92%/71%
min	100%/52%/73%	86%/84%/85%	100%/54%/74%

B. Antal, A. Hajdu: An ensemble-based system for automatic screening of diabetic retinopathy, *Knowledge-Based Systems (Elsevier)* **60** (April 2014), 20-27, IF=4.104.

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Thank you for your attention!

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