Medical Image Analysis

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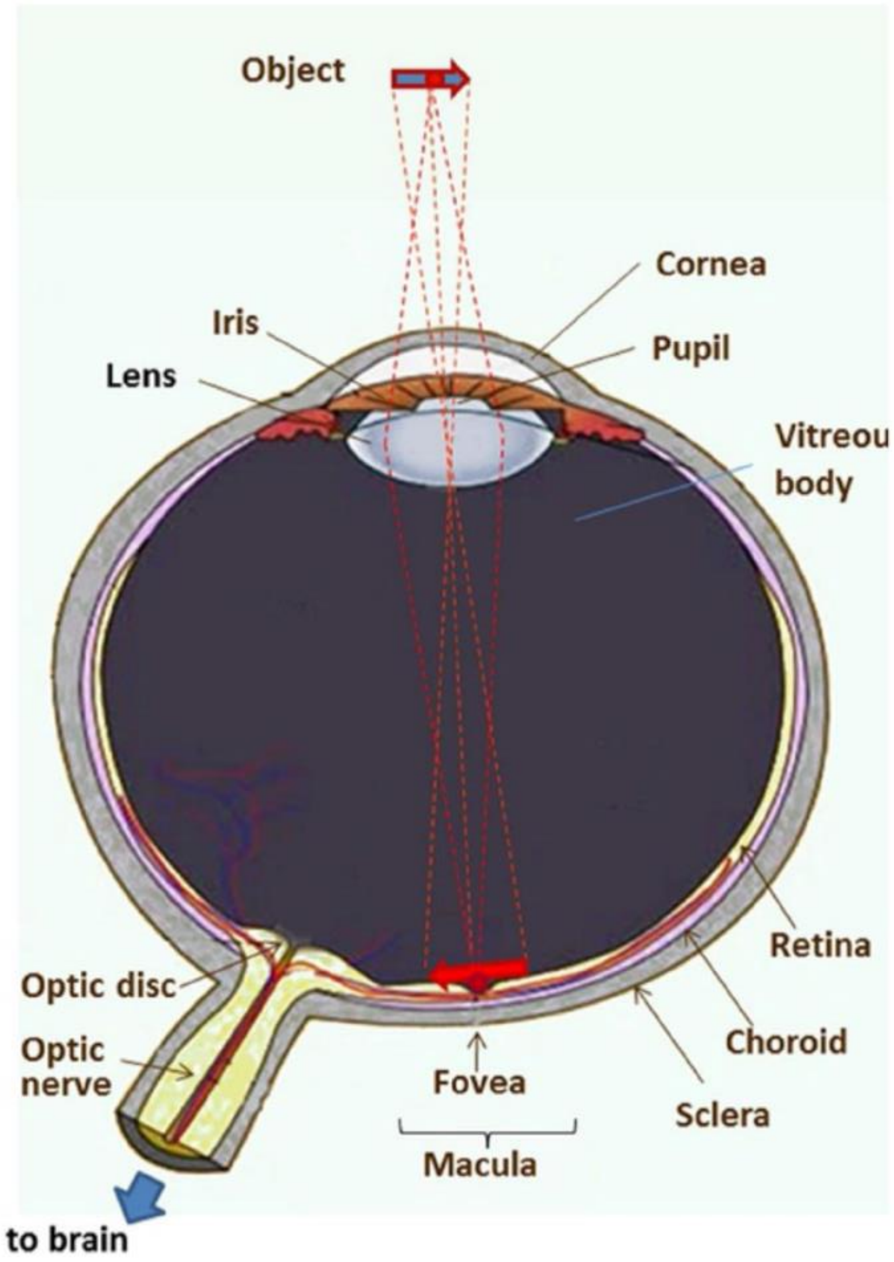
Retinal Image Analysis

The Human Eye



https://doi.org/10.1007/s11042-020-09041-y
Multimedia Tools and Applications (2020) 79:22389–22421

Why Retinal Image Analysis?

- Retinal pathologies are responsible for millions of blindness cases worldwide
- Major causes
  - Glaucoma
  - Age-related macular degeneration (AMD)
  - Diabetic retinopathy (DR)
- Early diagnosis is critical
  - Retinal image analysis may be helpful

Why Retinal Image Analysis using AI Techniques?

- AI algorithms have been used to assist in areas of diagnosis by
  - Big data and imaging analysis
  - Resident education
  - Patient scheduling
  - Imaging analysis
  - Disease risk prediction
  - Hospital management

Why Retinal Image Analysis using AI Techniques?

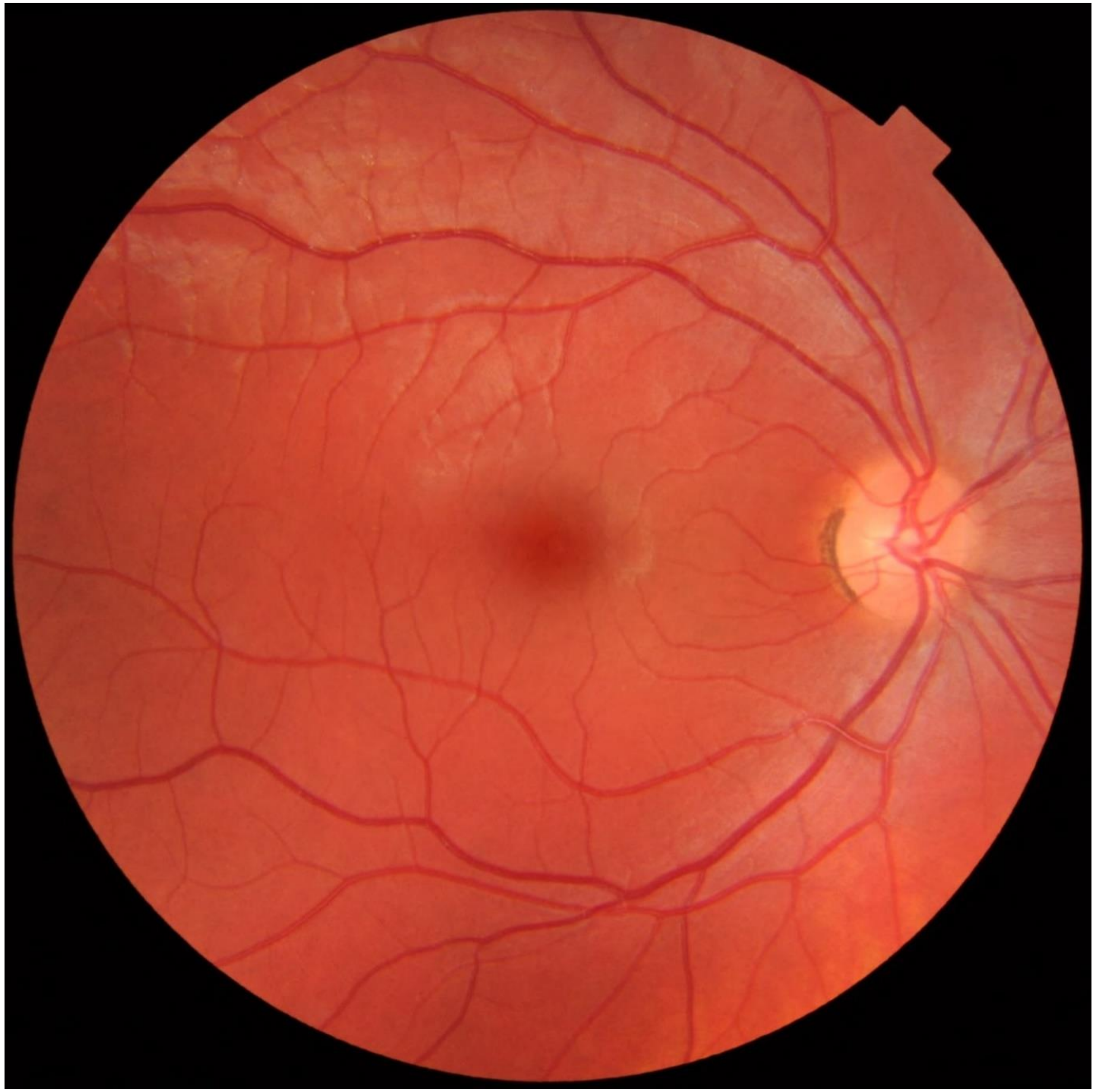
- Survey in Australia and New Zealand (305 ophthalmologists)
  - Glaucoma progression analysis
  - Optical coherence tomography (OCT) assessment
  - DR image assessment
  - Intraocular lens power calculation
- The majority of ophthalmologists agreed with the statement that "ophthalmology will improve with the introduction of AI"
- Major impact in next few years

Retinal Fundus Image

- Photographing the rear of an eye (fundus)

- Specialized fundus cameras
  - Consists of an intricate microscope attached to a flash enabled camera
  - Central and peripheral retina, optic disc and macula
  - Specialized dyes including fluorescein and indocyanine green may be used

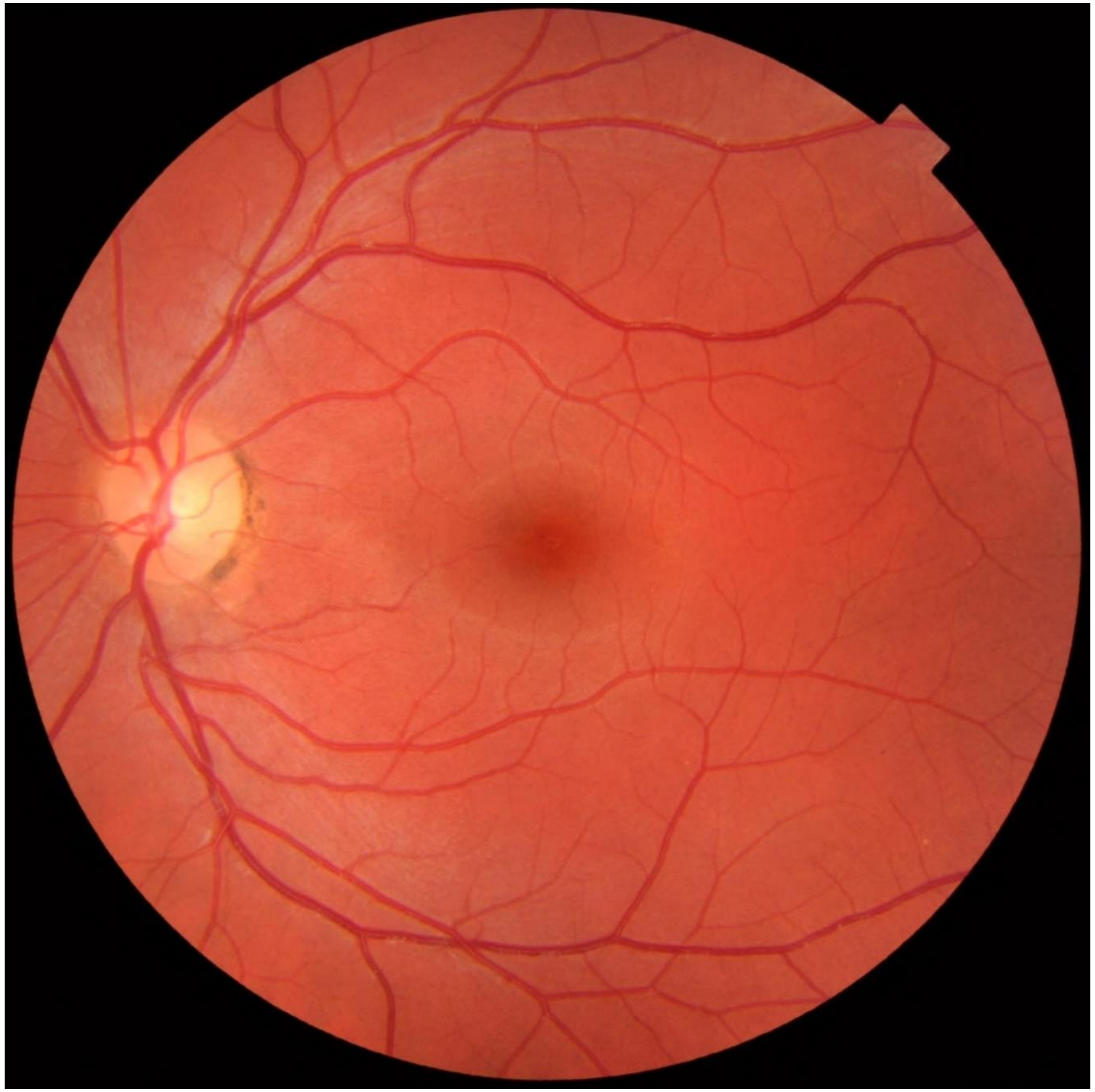
Retinal Fundus Image



Right eye

Retinal Fundus Image

Left eye

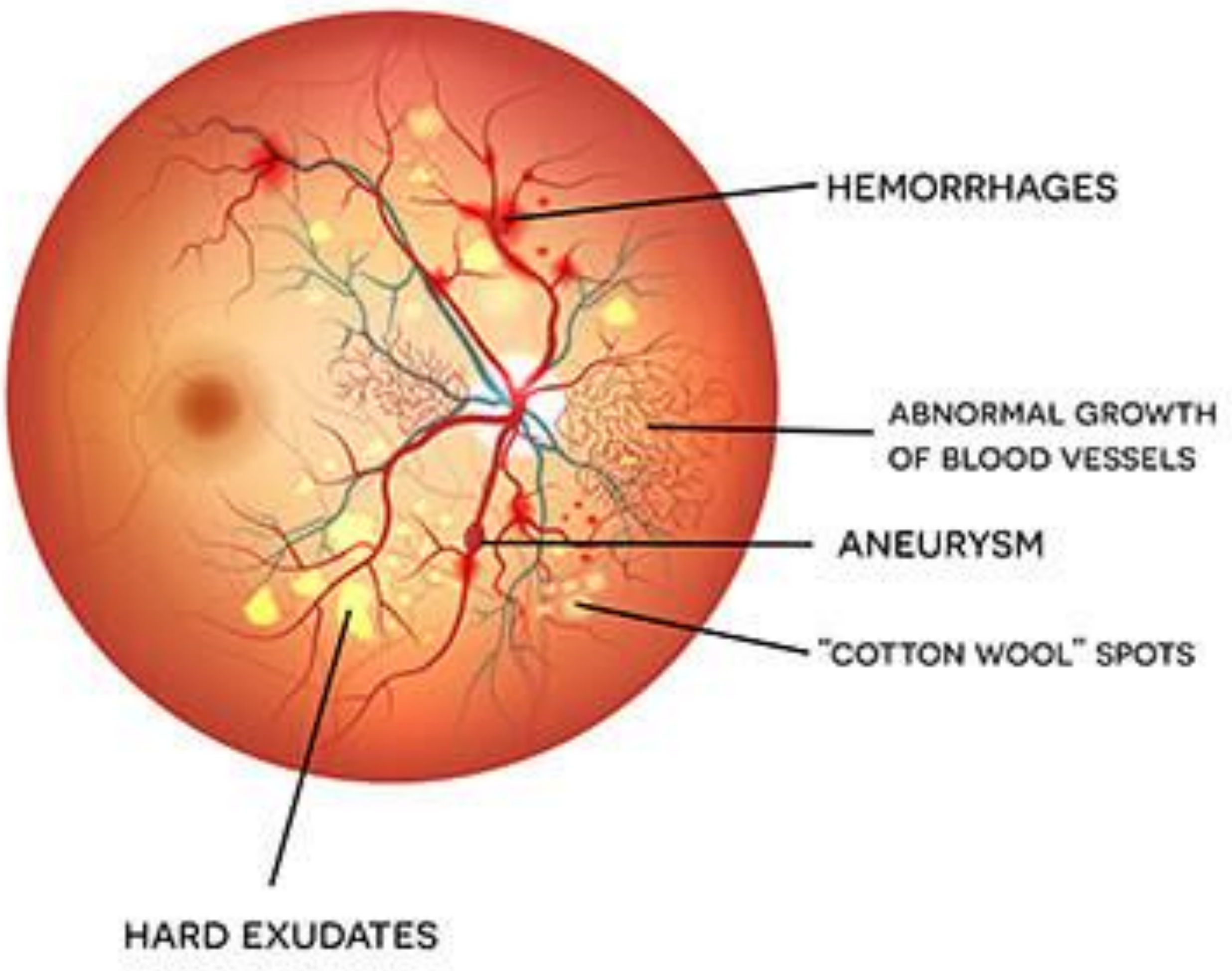


Retinal Fundus Image: Diabetic Retinopathy

Retinal Fundus Image: Diabetic Retinopathy

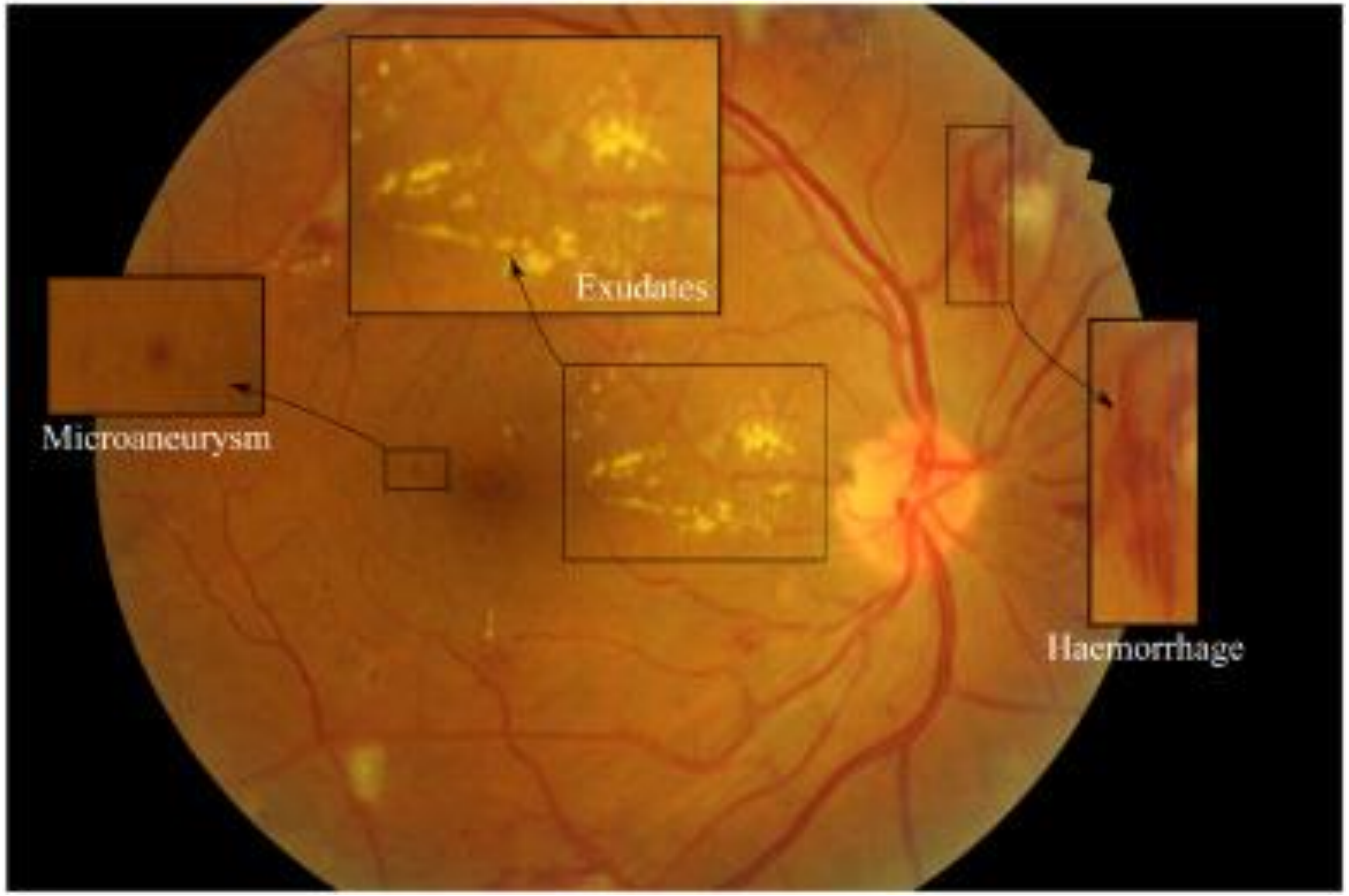
- Characteristics of diabetic retinopathy can be observed
  - Macular edema
  - Microaneurysms
  - Retinal details may be easier to visualize in fundus images as opposed to with direct examination

Retinal Fundus Image: Diabetic Retinopathy



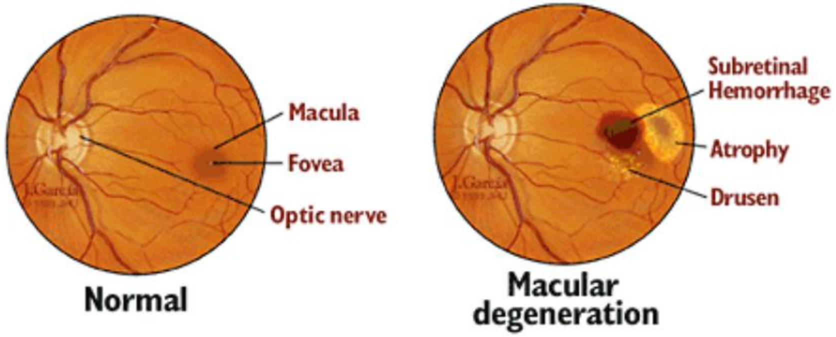
https://starretina.com/diabetic-retinopathy/

Retinal Fundus Image: Diabetic Retinopathy



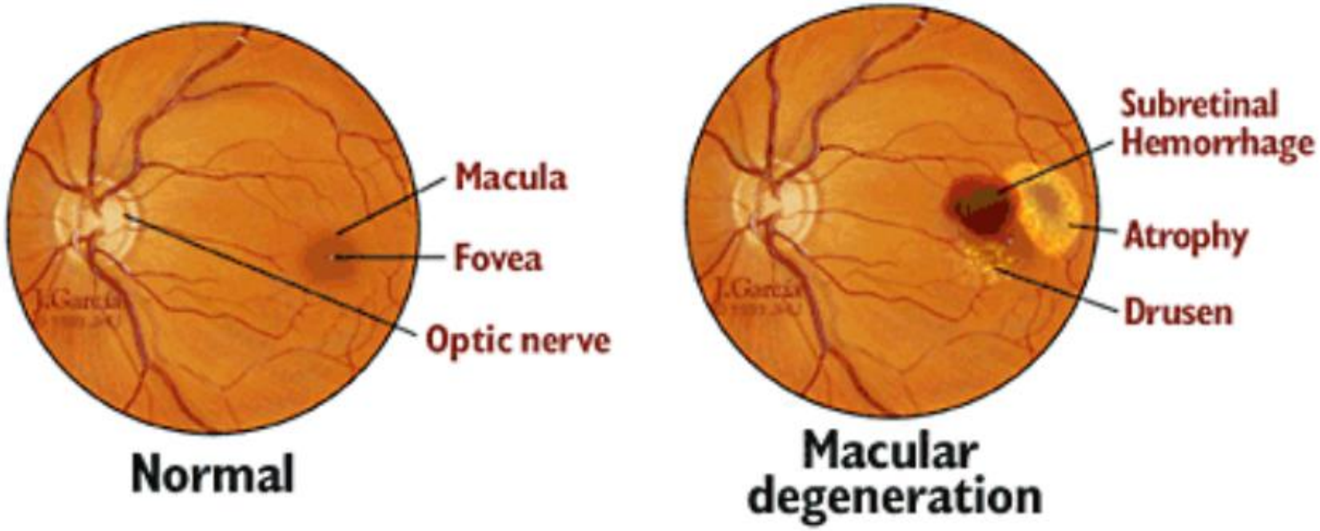
Retinal Fundus Image: Age-related macular degeneration (AMD)

- Most common cause of severe loss of eyesight in 50 and older
- Dry: most common
- Wet: most severe
- The presence of drusen, which are tiny yellow deposits in the retina, is one of the most common early signs of age-related macular degeneration

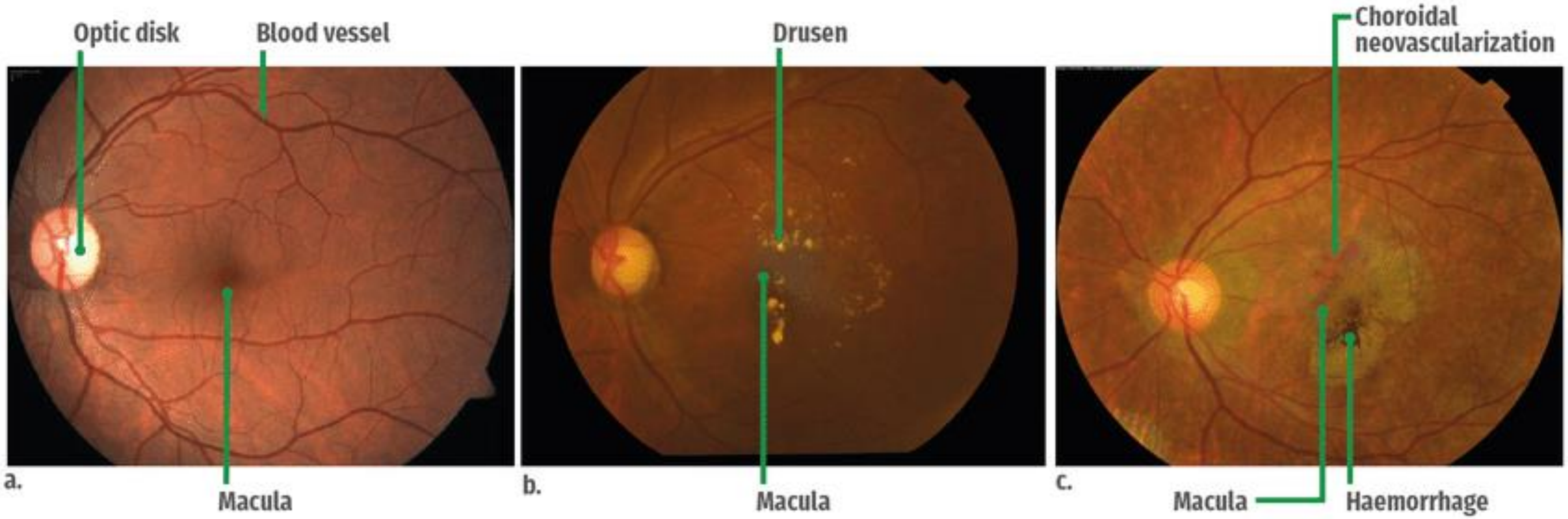


https://www.hopkinsmedicine.org/health/conditions-and-diseases/agerelated-macular-degeneration-amd

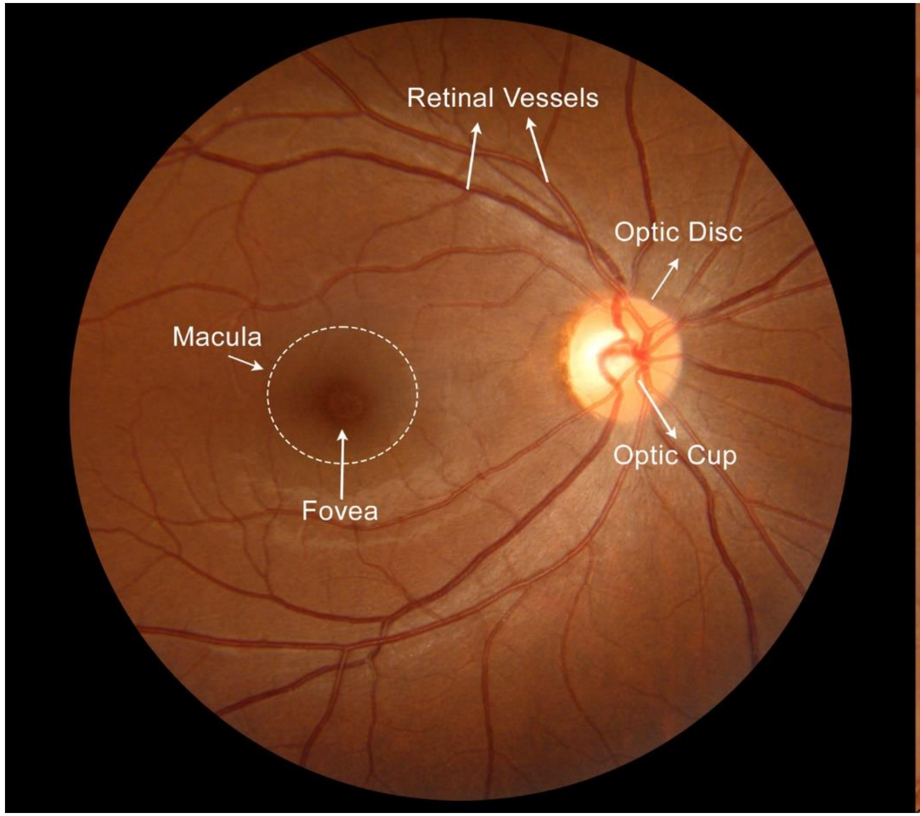
Retinal Fundus Image: Age-related macular degeneration (AMD)

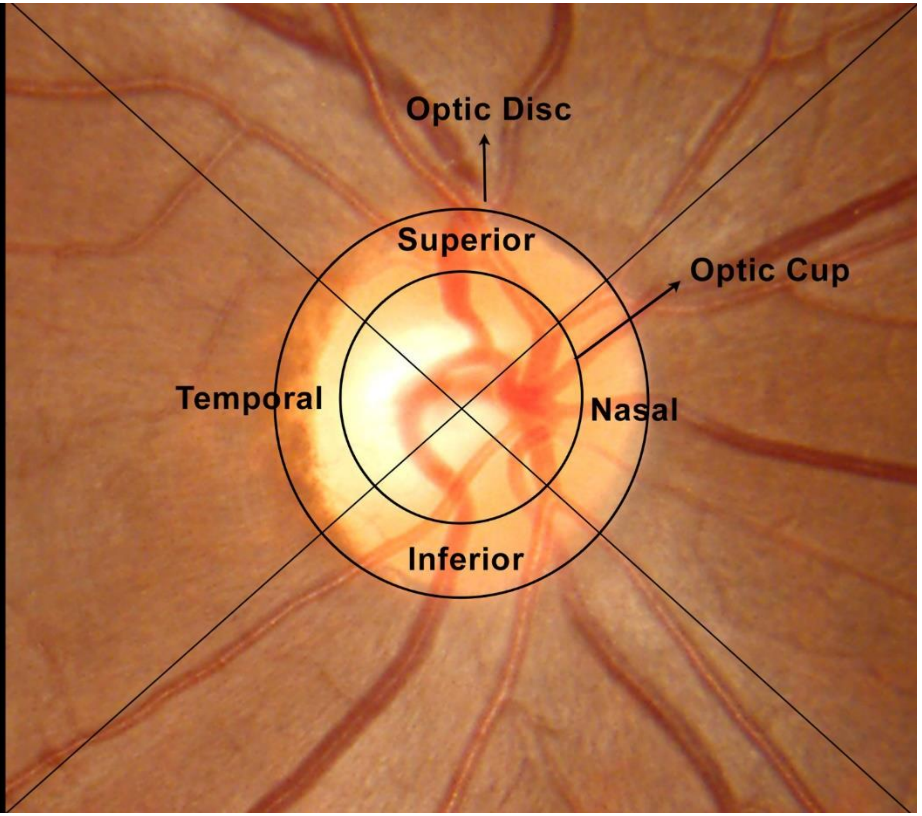


Retinal Fundus Image: Age-related macular degeneration (AMD)



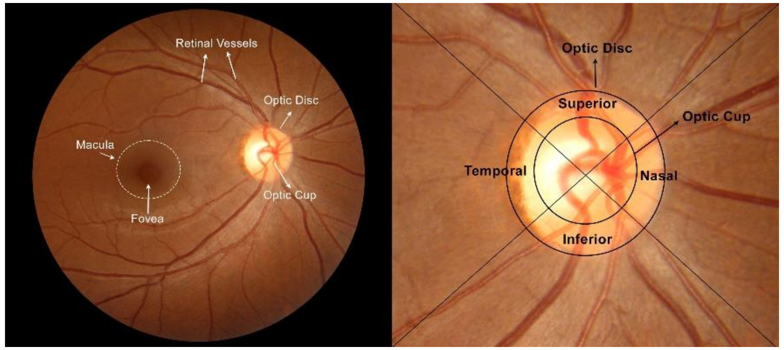
Retinal Fundus Image: Glaucoma





Healthy Eye

Retinal Fundus Image: Glaucoma

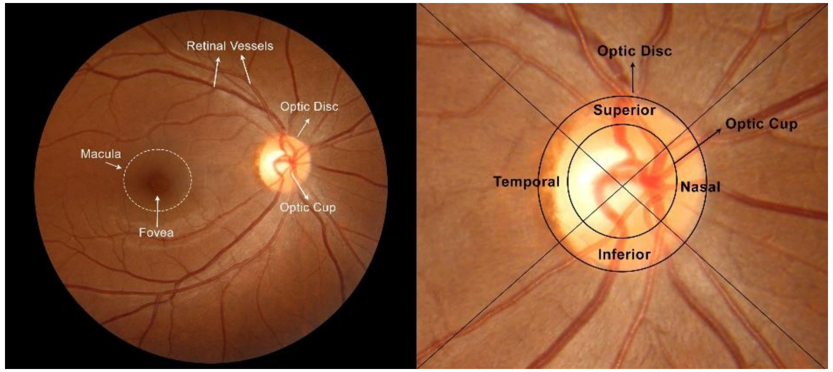


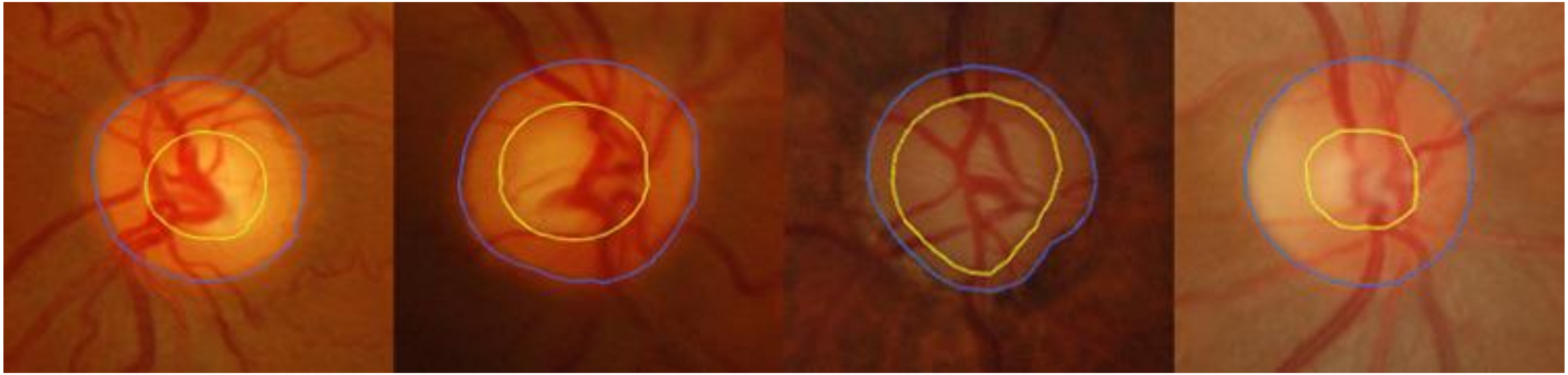
Healthy Eye

- Glaucoma is a chronic progressive optic neuropathy in which changes in the structure of the optic nerve head (ONH) and retinal nerve fiber layer (RNFL) are associated with visual defects
- Structural changes are manifested by a slow, yet progressive, narrowing of the neuroretinal rim, indicating degeneration of retinal ganglion cells axons, and astrocytes of the optic nerve
- To evaluate the narrowing of the neuroretinal rim (NRR) the clinician needs to identify the boundary contours of the cup and disc

Retinal Fundus Image: Glaucoma

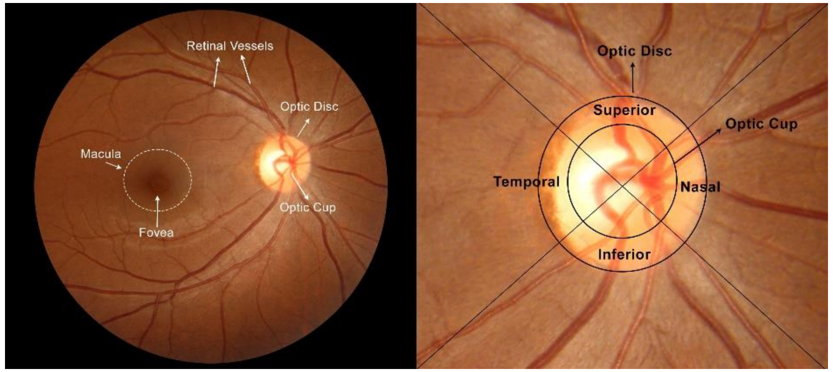
- Cup to disc ratio
- Detect the contour of cup and disc





Retinal Fundus Image: Glaucoma

- Cup to disc ratio
- Detect the contour of cup and disc



The vCDR is defined as:

$$vCDR = \frac{Vertical\ Cup\ Diameter}{Vertical\ Disc\ Diameter}$$

The ACDR is defined as:

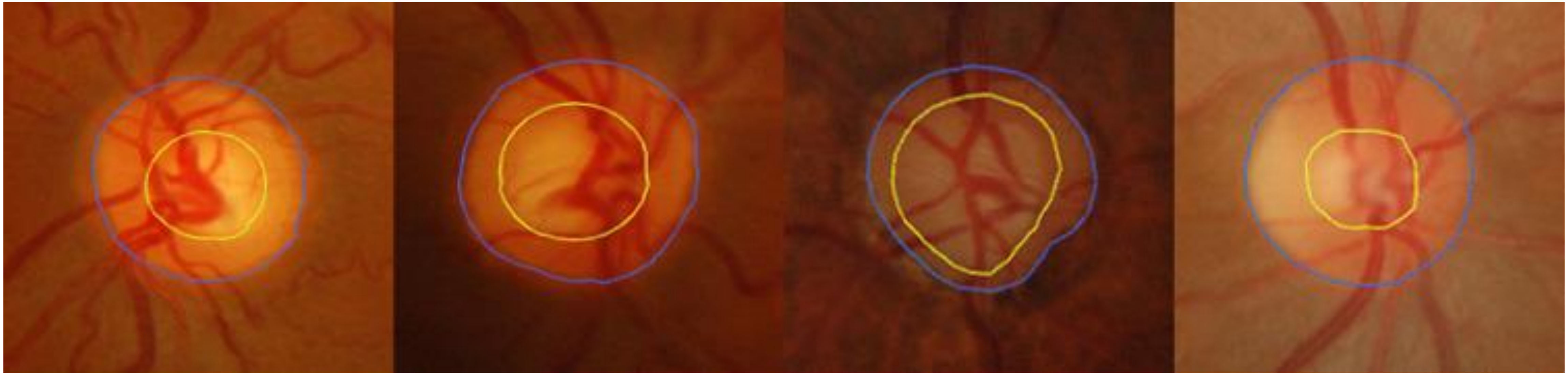
$$ACDR = \frac{Area\ of\ Cup}{Area\ of\ Disc}$$

(a) (b) (c) (d)

Retinal Fundus Image: Glaucoma

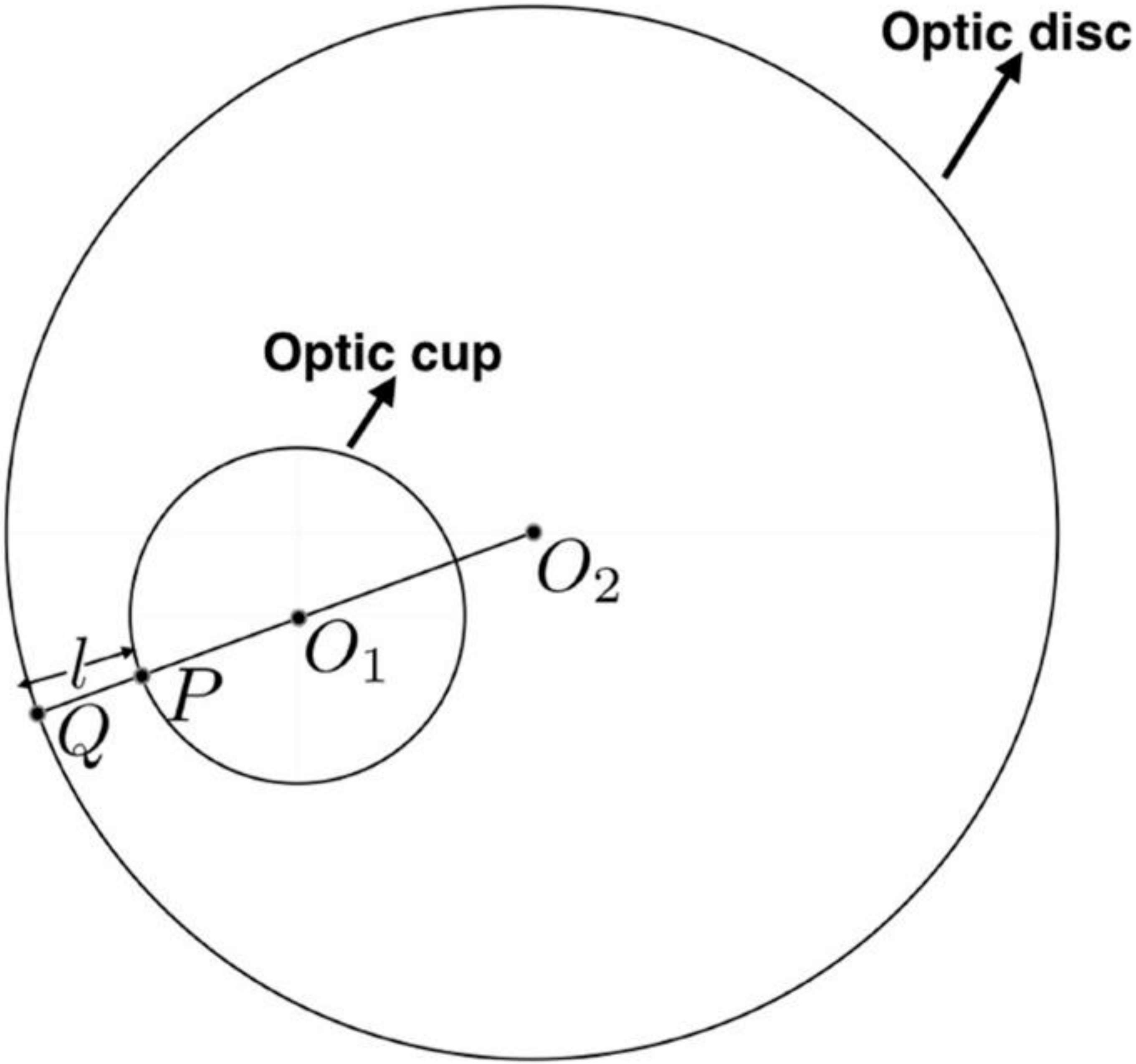
- Nueroretinal rim area ratio

$$\mathrm{NRR} = \frac{\mathit{Area\ in\ Inferior\ Quadrant} + \mathit{Area\ in\ Superior\ Quadrant}}{\mathit{Area\ in\ Nasal\ Quadrant} + \mathit{Area\ in\ Temporal\ Quadrant}}$$



Retinal Fundus Image: Glaucoma

- Disk damage likelihood scale
- Measures the minimum rim width

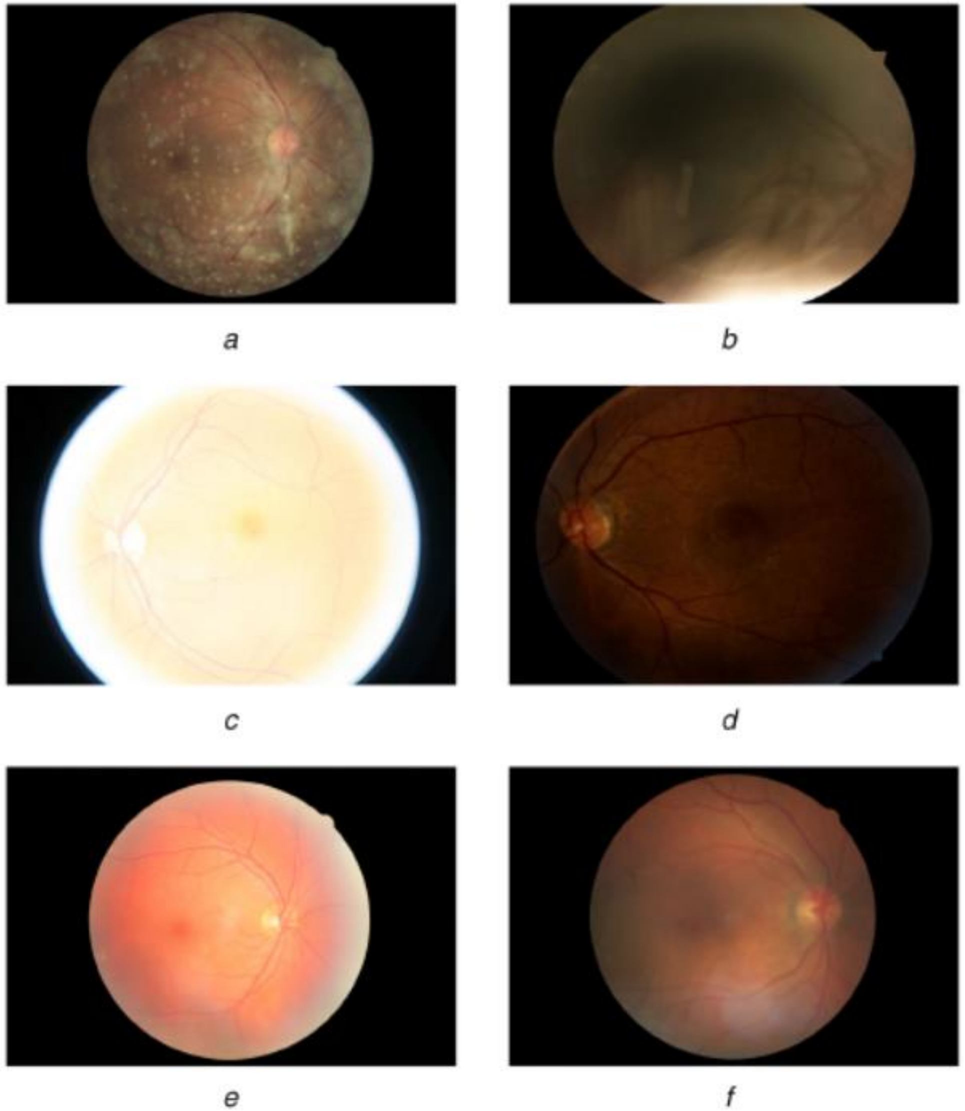


Retinal Fundus Image: Glaucoma

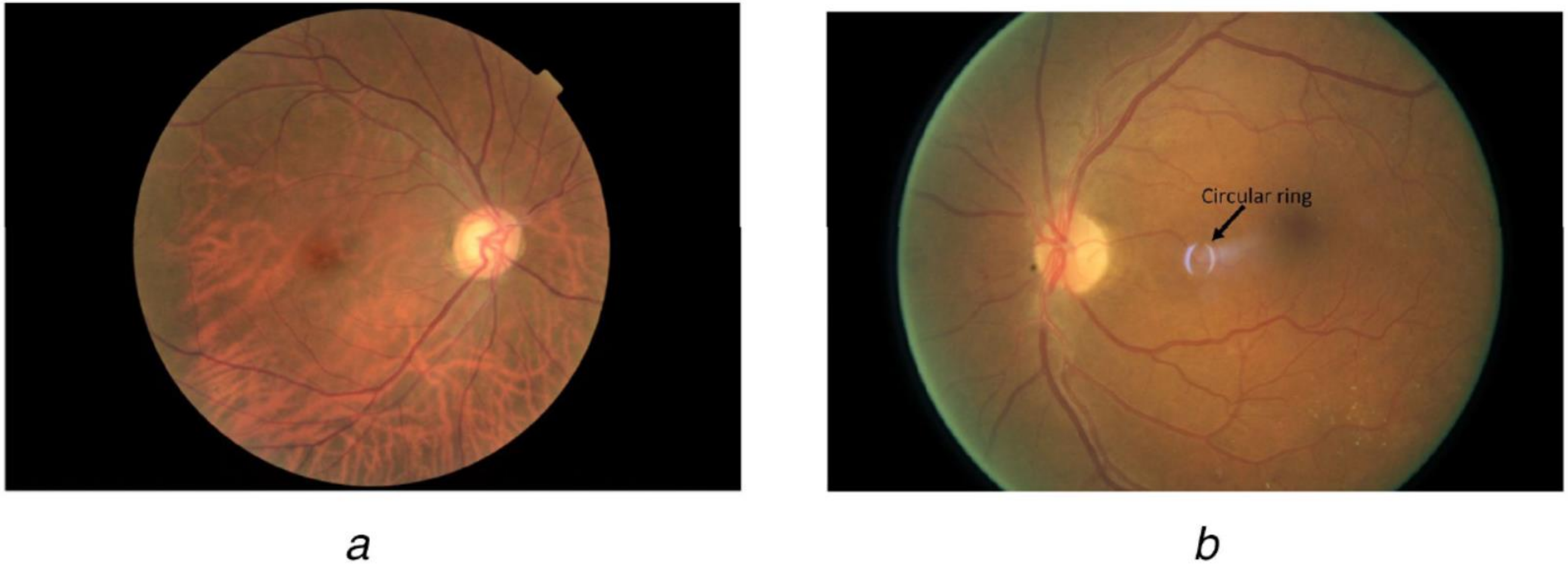
New DDLS stage	Narrowest width of rim (rim/disc ratio)			
	For small disc <1.50 mm	For average size disc 1.50–2.00 mm	For large disc >2.00 mm	Old DDLS stage
1	0.5 or more	0.4 or more	0.3 or more	0a
2	0.4 to 0.49	0.3 to 0.39	0.2 to 0.29	0b
3	0.3 to 0.39	0.2 to 0.29	0.1 to 0.19	1
4	0.2 to 0.29	0.1 to 0.19	less than 0.1	2
5	0.1 to 0.19	less than 0.1	0 for less than 45°	3
6	less than 0.1	0 for less than 45°	0 for 46° to 90°	4
7	0 for less than 45°	0 for 46° to 90°	0 for 91° to 180°	5
8	0 for 46° to 90°	0 for 91° to 180°	0 for 181° to 270°	6
9	0 for 91° to 180°	0 for 181° to 270°	0 for more than 270°	7a
10	0 for more than 180°	0 for more than 270°		7b

Factors Affecting Quality of Fundus Images

(a)Light flares, (b) Total eye blink, (c) Overexposed, (d) Underexposed, (e) Uneven illumination, (f) Blur



Factors Affecting Quality of Fundus Images



Samples of fundus images with red colour ‘leopard’ print and circular ring [48](a) Leopard print, (b) Circular ring

Methods for Assessing the Quality of Fundus Images

- Similarity based methods
  - Evaluates the similarity of some image attribute between target image and a set of good quality reference images
- Correlation between intensity histograms
  - **What is the drawback?**

Methods for Assessing the Quality of Fundus Images

- Similarity based methods
  - Evaluates the similarity of some image attribute between target image and a set of good quality reference images
- Correlation between intensity histograms
  - Does not capture structural similarities

Methods for Assessing the Quality of Fundus Images

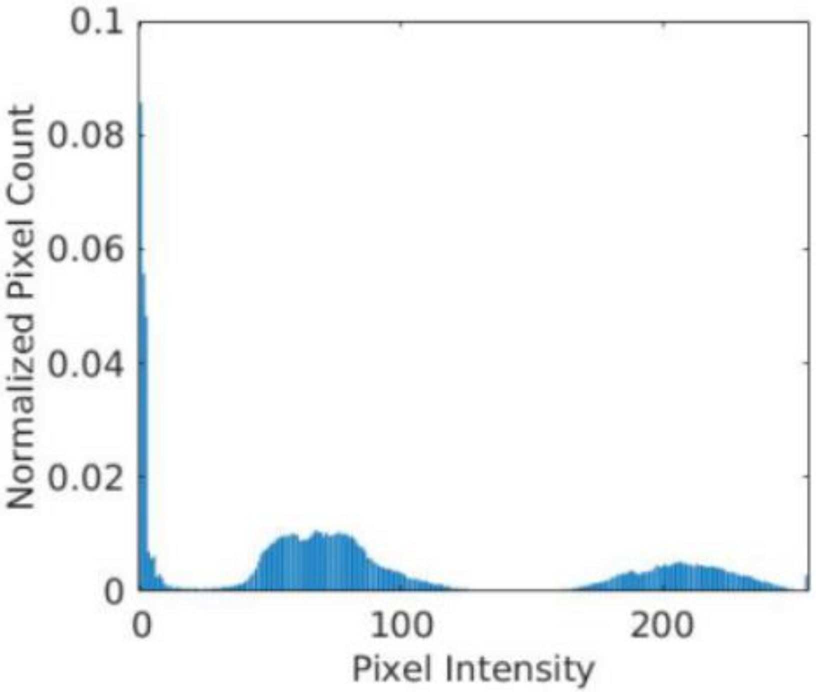


Fig. 8 *Normalised histogram of both fundus images*

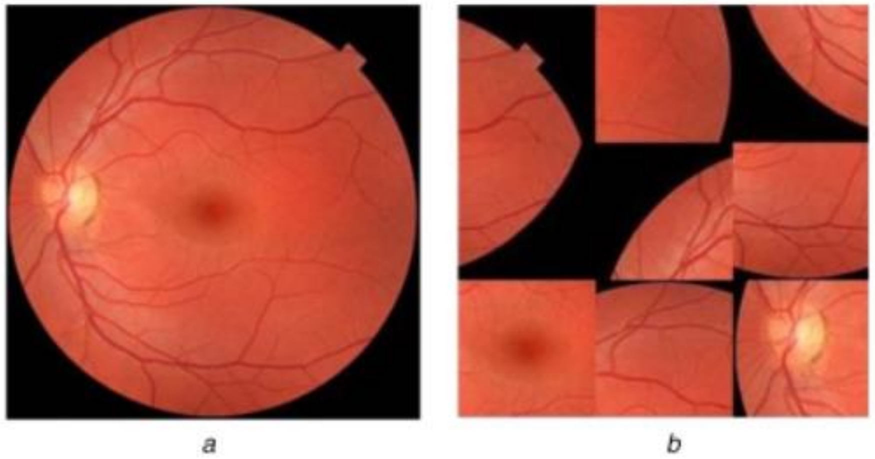


Fig. 9 *Sample fundus images*
(a) Good quality, *(b)* Poor quality

Methods for Assessing the Quality of Fundus Images

- Pen and paper assignment (time 5 min)
  - Write pseudocode foe calculating correlation between the histograms of target and reference images

Methods for Assessing the Quality of Fundus Images

- Similarity based methods
- Distribution of edge magnitude and local intensity distribution
- Edge magnitude histogram
  - Squared distance between the edge magnitude histograms of two images
- Local intensity distribution
  - Mean image from several good quality images
  - Segmenting the target image in several regions using histogram splitting
  - For each region in target image
    - Compare the histograms of target image and men image of that region

$$d_{intensity}(I_{Target}, I_{Mean}) = \sum_{i=1}^{Nb\,regions} Size_i \cdot W(HR_i^{(I_{Target})}, HR_i^{(I_{Mean})})$$

Methods for Assessing the Quality of Fundus Images

- Segmentation based methods
- Segmentation of blood vessels
  - Counting the number of vessel pixels
  - More the number, better the image

- Segmentation of blood vessels and macula
  - Small number of blood vessels exist around the macula
  - Visibility of blood vessels around the macula: a quality measure
  - Location and diameter of the optical disc and visibility of the region within the two disk diameters

Methods for Assessing the Quality of Fundus Images

- ML-based methods
- Feature extraction
  - Structural analysis
    - Use of filters, calculation of local vessel density, visibility of optical disk and blood vessels, etc.
  - Generic image statistics
    - Colour, focus, contrst, sharpness, etc.
  - CNN features
- Training & validation (usually with two classes: good, poor)
- Testing

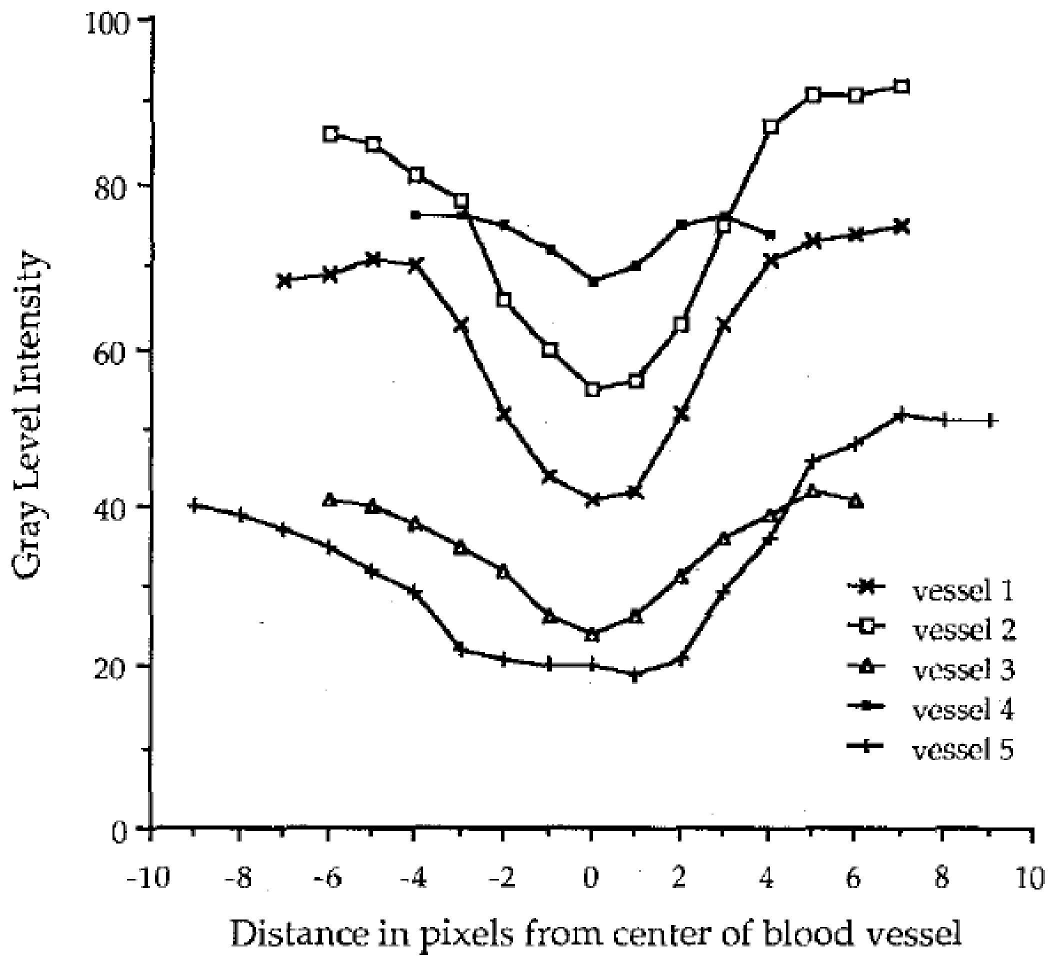
Retinal Image Processing: Pre-processing

- Denoising
- Contrast enhancement
- Deblurring
  - Reduces blur caused by camera defocus
- Vessel enhancement
  - Matched filter

Vessel Enhancement using Matched Filter

- Blood vessels usually have small curvatures, the anti-parallel pairs may be approximated by piecewise linear segments
- Since the vessels have lower reflectance compared to other retinal surfaces, they appear darker relative to the background.
- Vessels almost never have ideal step edges. Although the intensity profile varies by a small amount from vessel to vessel, it may be approximated by a Gaussian curve
- Intensity profile can be assumed to be symmetrical about the straight line passing through the center of the vessel

Vessel Enhancement using Matched Filter

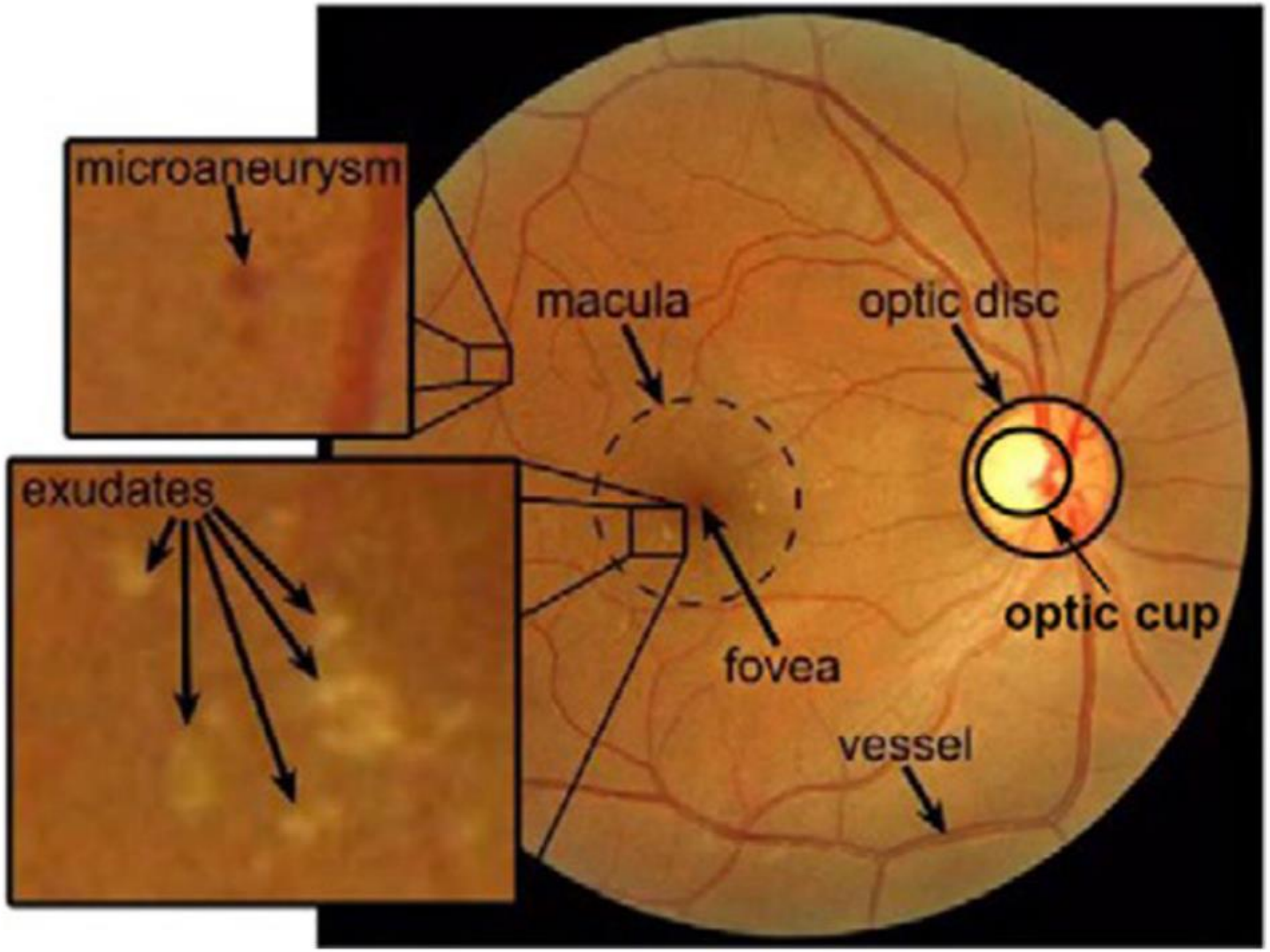


Vessel Enhancement using Matched Filter

- $s_o(t) = \int H(f)\{s_{in}(f) + \eta(f)\} \exp(j2\pi f t)\, df$
  - $H(f)$ that maximizes output SNR is $H(f) = s_{in}^*(f)$
  - Optimal filter must have the same shape as that of the input intensity profile
- Vessel may be aligned at any angle θ
- To have matched filter peak, filter must be aligned at $\theta \pm \frac{\pi}{2}$
  - Filter to be rotated at all possible angle for each pixel
  - Only the max response has to be recorded
- Matching number of cross-sections of the vessel simultaneously
  - Along its length

Segmentation & Localization of Retinal Landmarks

- Optic disc and optic cup localization and segmentation
  - May be based on
    - The intensity and shape features of OD
    - The location and orientation of the vasculature



Optic Disc and Optic Cup Localization and Segmentation

- PCA
  - Clustering on the training dataset based on high-intensity pixels
  - PCA to project a new image
  - Location of the OD centre was found using minimum distance between original image and its projection
- Variance of intensity
  - Between the optic disc and the adjacent blood vessels
- Directional pattern
  - Retinal vessels originate from the optic disc and follow a similar directional pattern in all images
  - The parametric geometric model can describe the typical direction of the retinal vessels as they converge on the optic disc

Optic Disc and Optic Cup Localization and Segmentation

- Attention Models

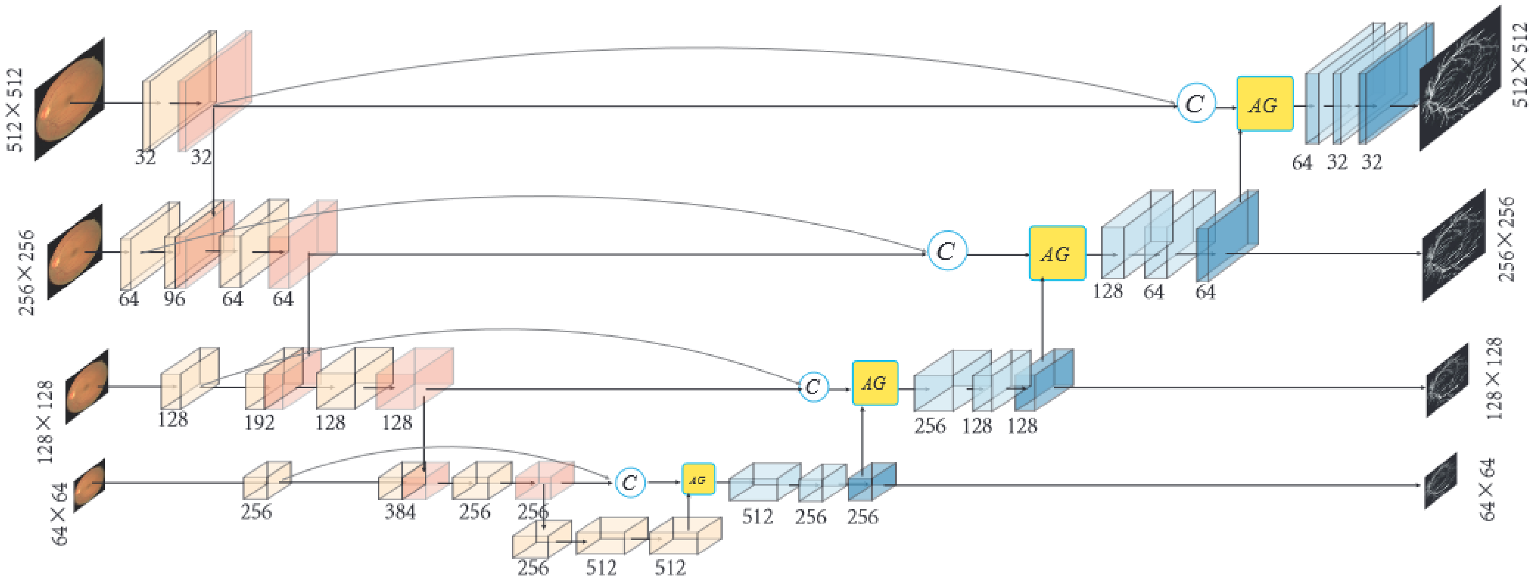


Fig. 1: Architecture of proposed AG-Net. Our AG-Net is based on M-Net [3], which is a multi-scale multi-label segmentation network. The block AG represents our attention guided filter and the operator C is the concatenation. In our AG-Net, the attention guided filter is used as a structural sensitive skip-connection to replace the skip-connection and upsampling layer for better information fusion.

Zhang S, Fu H, Yan Y, Zhang Y, Wu Q, Yang M, Tan M, Xu Y (2019
intervention. Springer, Berlin, pp 797–805 22420 Multimedia Tools and Applications (2020) 79:22389–22421
https://github.com/HzFu/AGNet

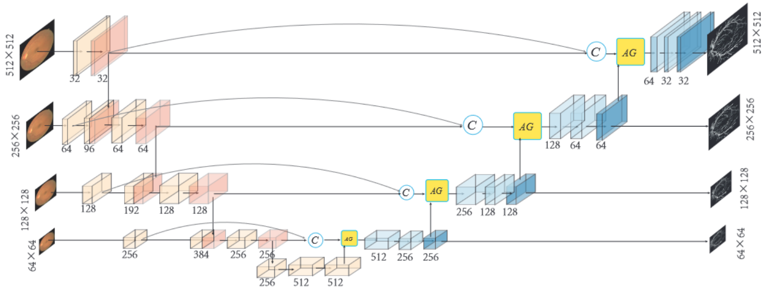
Optic Disc and Optic Cup Localization and Segmentation

- Preserves structural information

- Guided filter as an expanding path to transfer structura information extracted from low-level feature maps to high-level ones

- Guided filter: edge preserving filter

- Attention in guided filter



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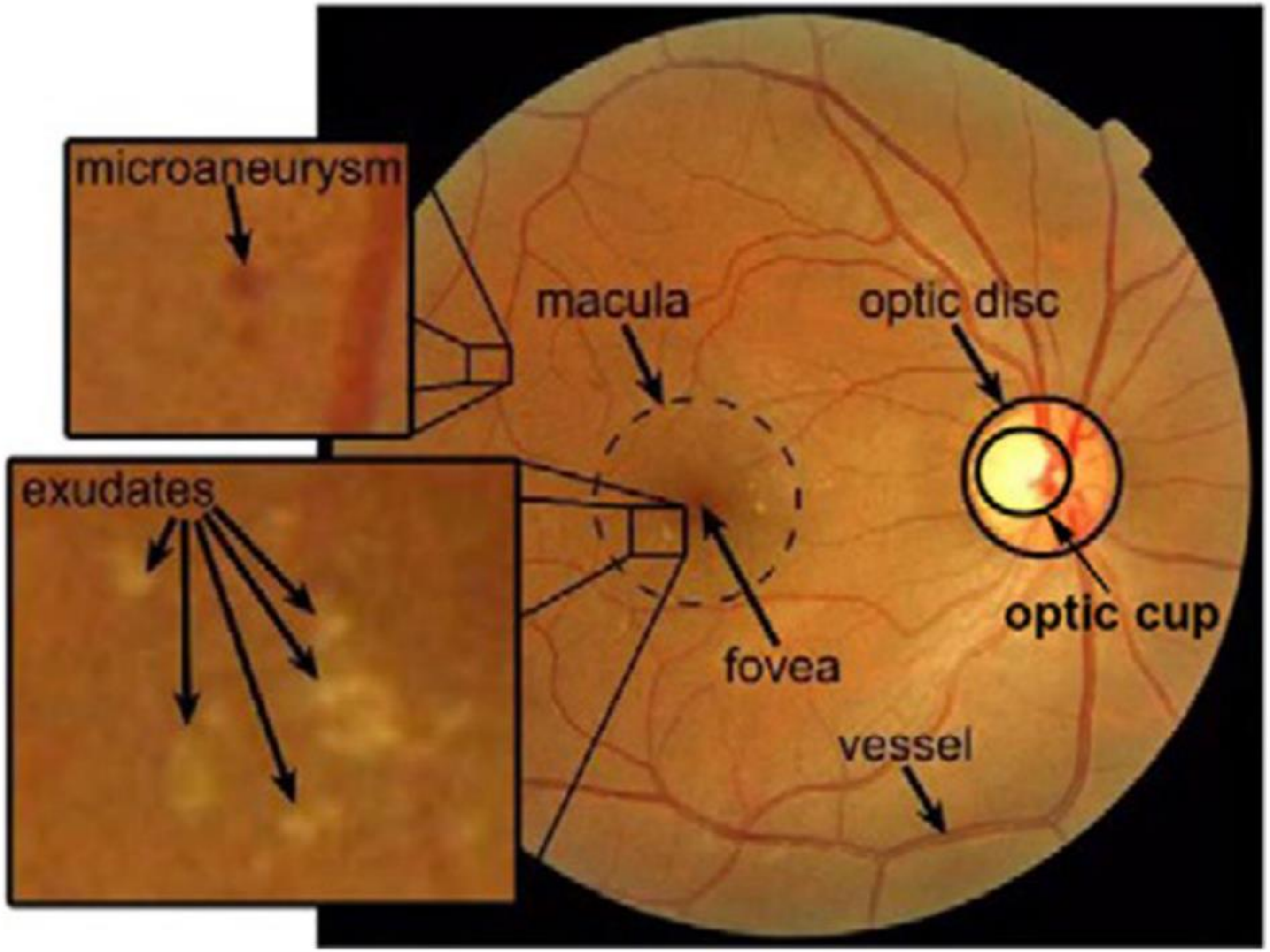
Segmentation & Localization of Retinal Landmarks

- Macula and fovea cup segmentation
  - Macula is an oval-shaped pigmented area near the centre of the retina of the human eye. It is the centre for sharp vision.
  - The fovea is the centre of the macula and contains the largest concentration of cone cells.



Macula and Fovea Cup Segmentation

- Model-based method
  - The position of the fovea was estimated by fitting a parabola curve with the OD as the centre. Then the points on the main blood vessels were extracted by a modified active model.
- Intensity-hue-saturation transformation method
  - The location of the fovea was chosen as the maximum correlation position between the intensity image (through intensity-hue-saturation transformation) and a model template.
- Vessel density-based method
  - The fovea was localized as a region of minimum vessel density in the approach used

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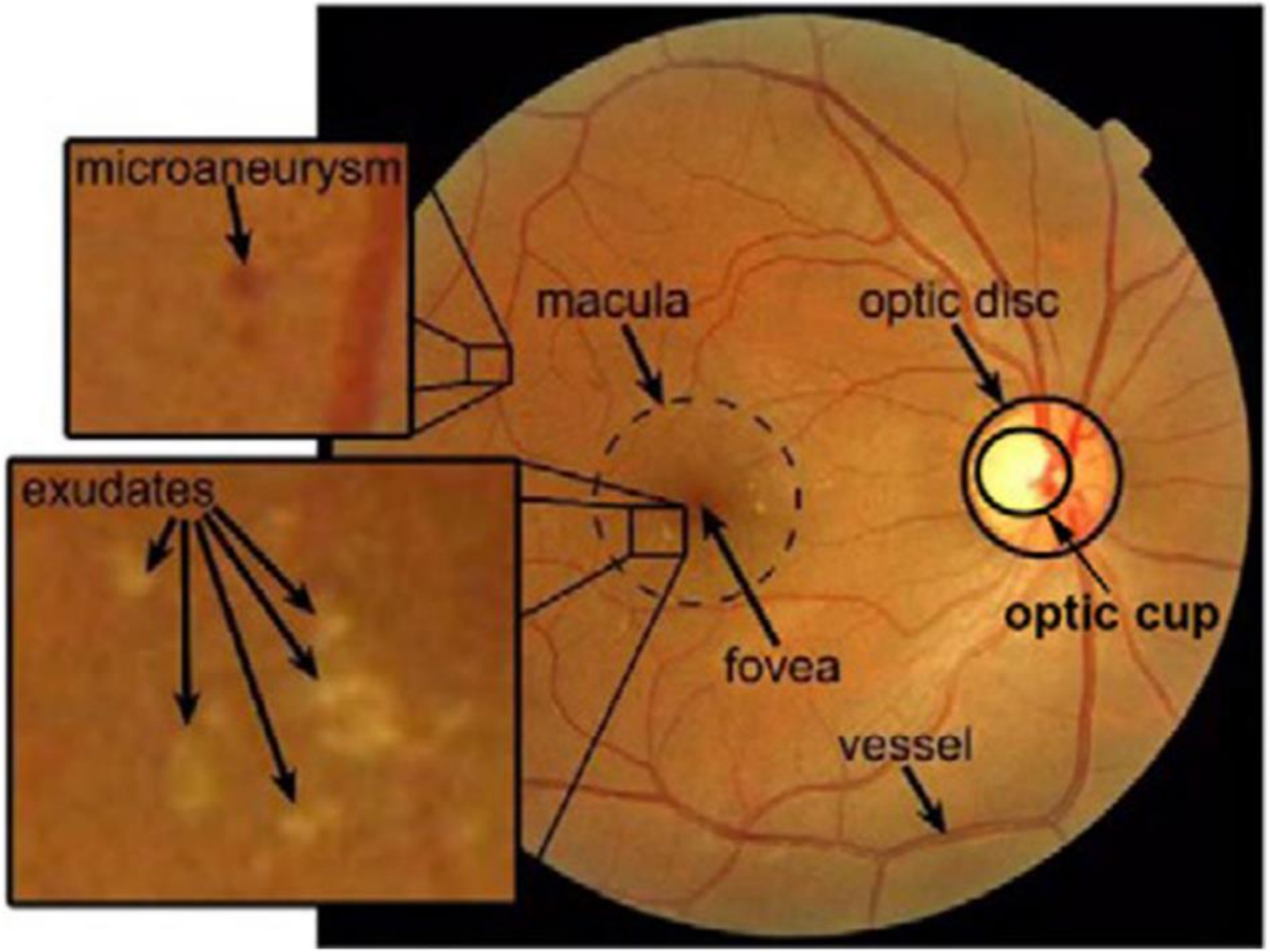
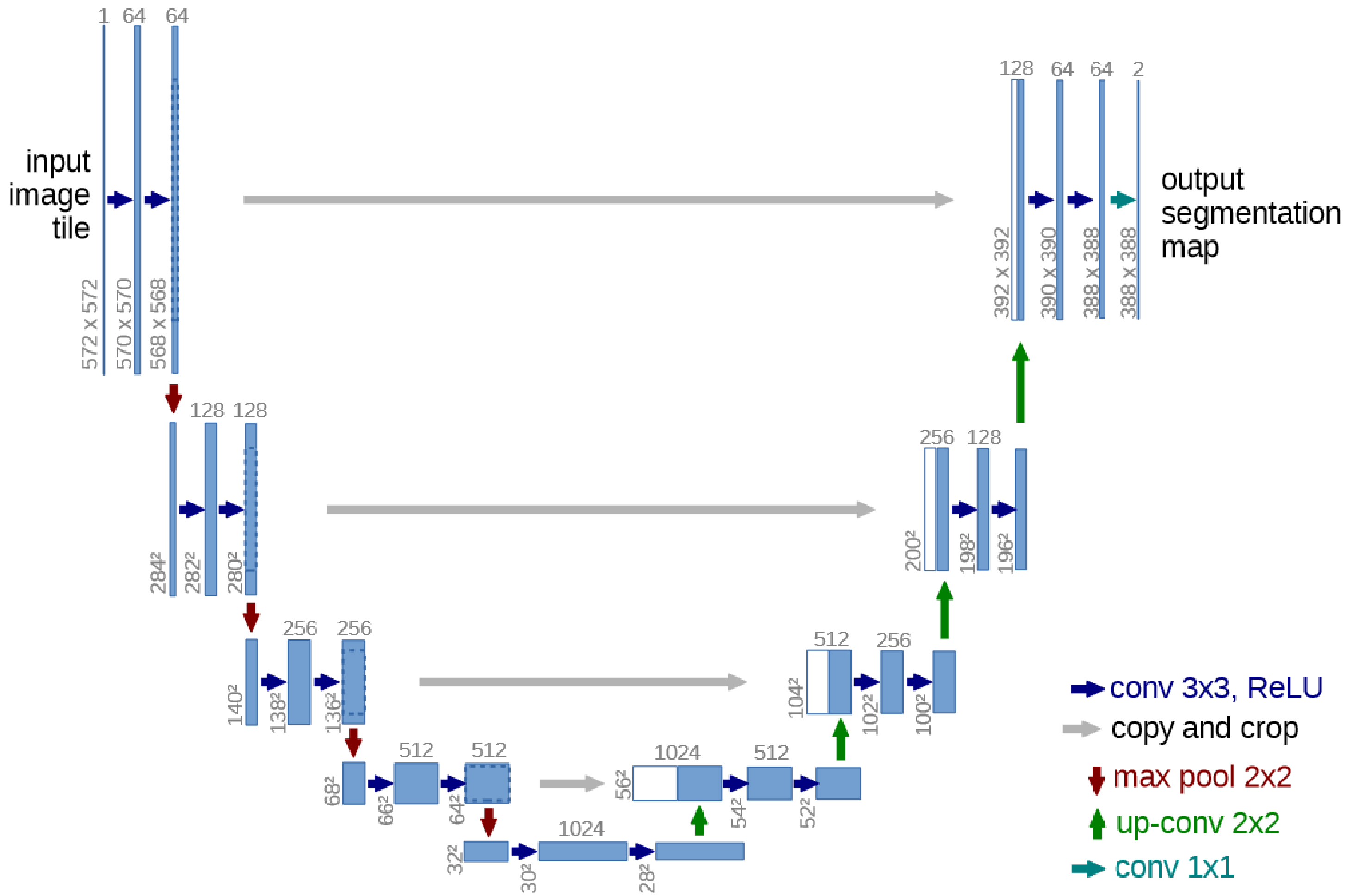
Segmentation & Localization of Retinal Landmarks

- Retinal Blood Vessel Segmentation
  - Classical Methods
  - Deep Methods



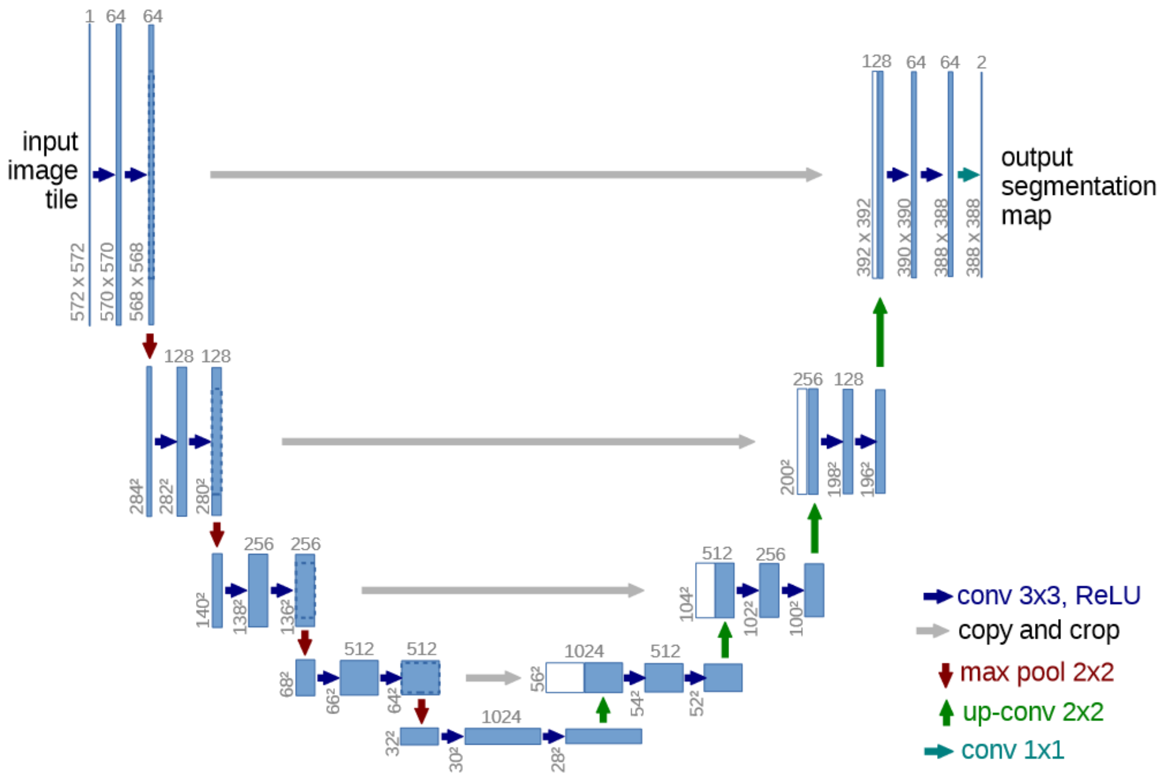
Deep Learning for RBVS

- U-Net

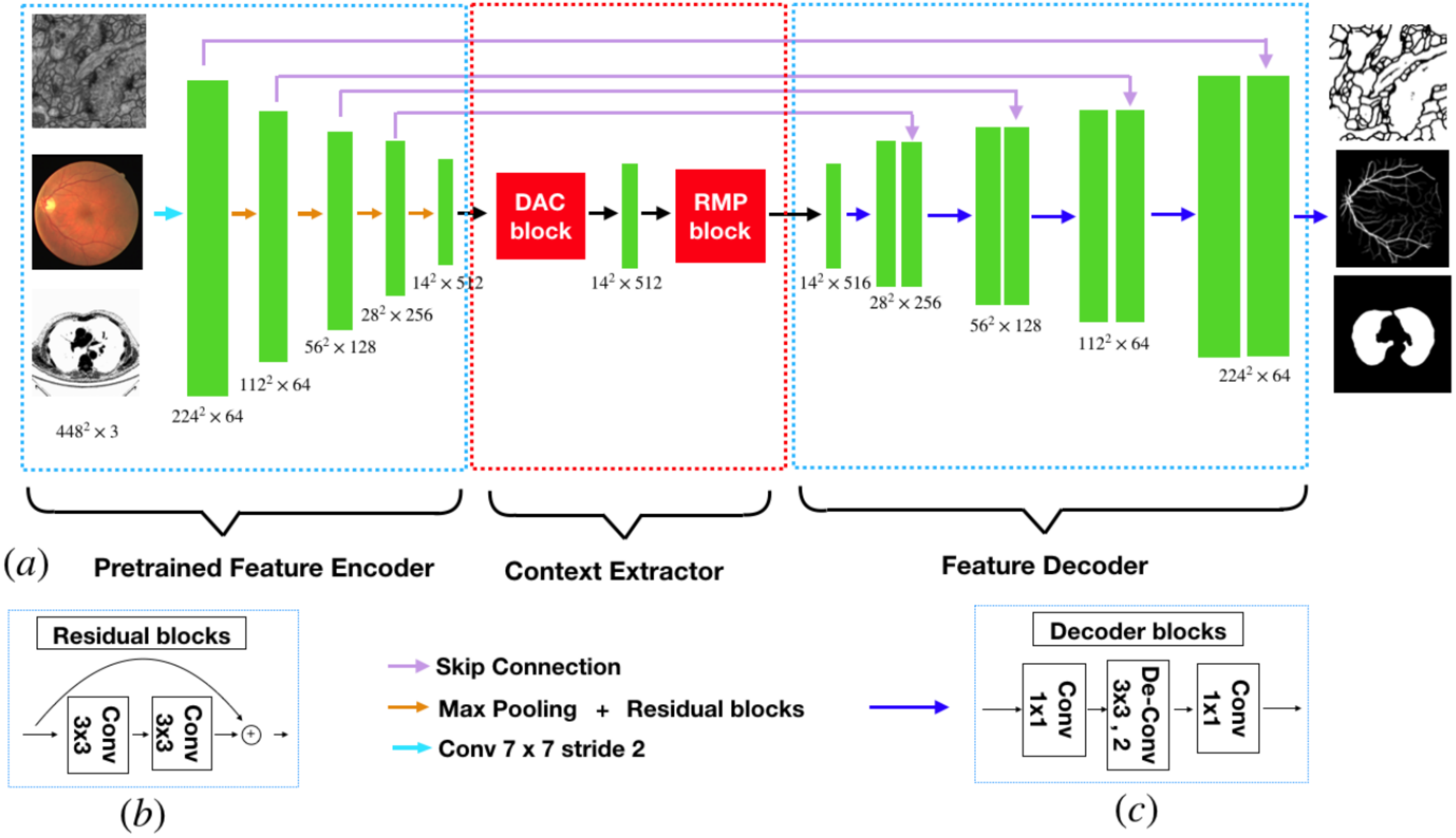


U-Net

- U-Net
- Fully convolutional
- The architecture consists of a contracting path to capture context
- A symmetric expanding path that enables precise localization

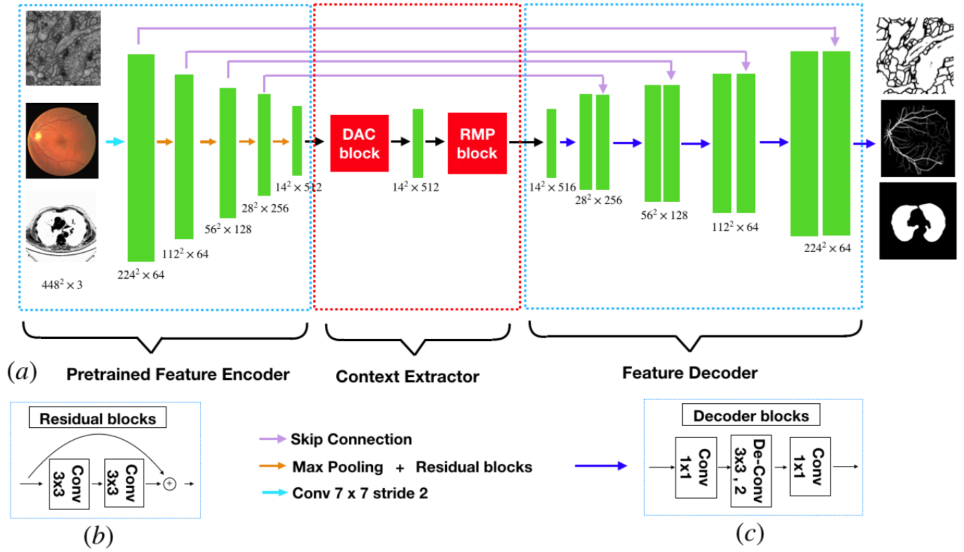


Context Encoder Network (CE-Net)



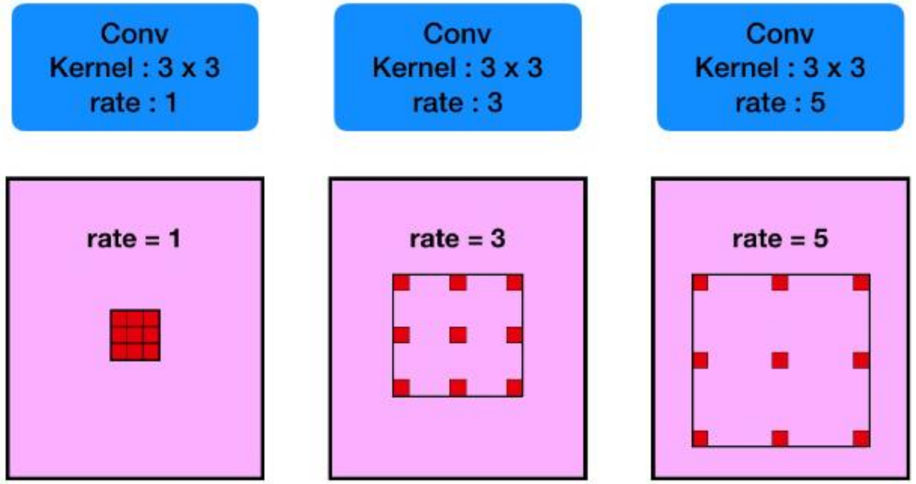
Context Encoder Network (CE-Net)

- Capture more high-level information and preserve spatial information for 2D medical images
- Three major components: a feature encoder, module, a context extractor and a feature decoder module
- Pretrained ResNet block as the fixed feature extractor
- Context extractor module: formed by a dense atrous convolution (DAC) block and residual multi-kernel pooling (RMP) block



CE-Net: Context Encoder Network for 2D Medical Image Segmentation

Atrous Convolution



- Better capturing of context

CE-Net: Context Encoder Network for 2D Medical Image Segmentation

Dense Atrous Convolution

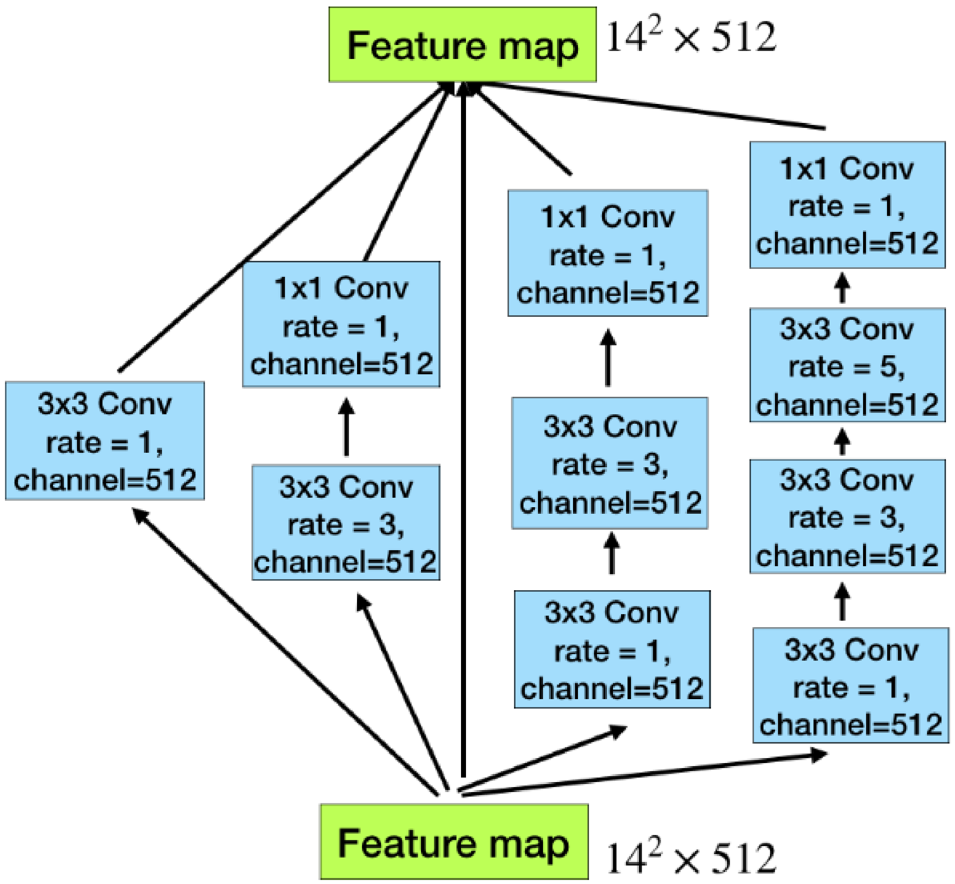


Fig. 3. The illustrations of dense atrous convolution block. It contains four cascade branches with the gradual increment of the number of atrous convolution, from 1 to 1, 3, and 5, then the receptive field of each branch will be 3, 7, 9, 19. Therefore, the network can extract features from different scales.

Residual Multi Kernel Pooling

- relies on multiple effective field-of-views to detect objects at different sizes

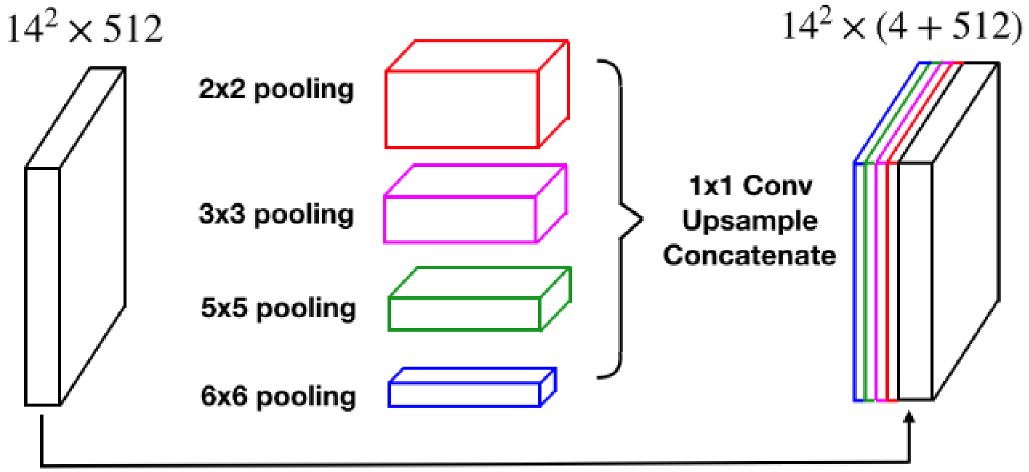
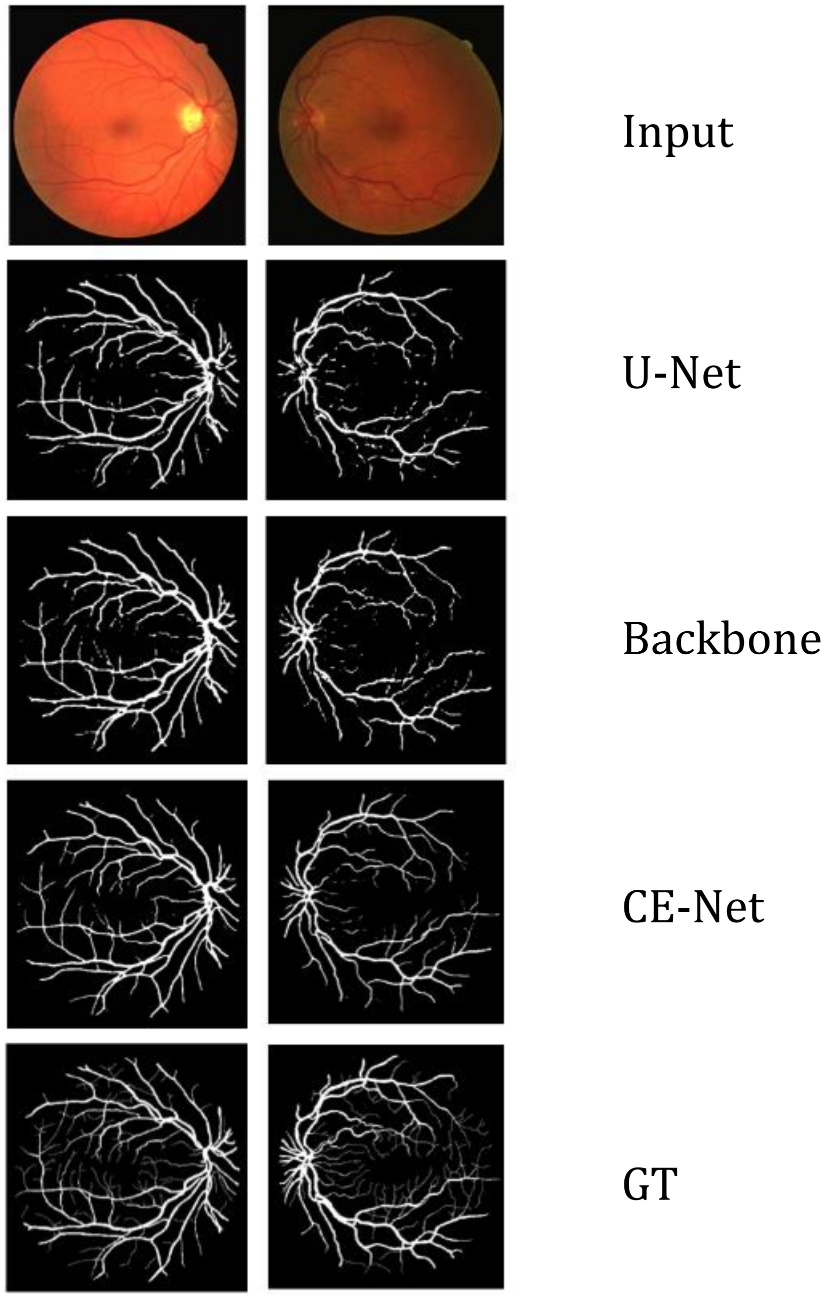


Fig. 4. The illustrations of residual multi-kernel pooling (RMP) strategy. The proposed RMP gather context information with four different-size pooling kernels. Then features are fed into 1×1 convolution to reduce the dimension of feature maps. Finally, the upsampled features are concatenated with original features.

Context Encoder Network (CE-Net)



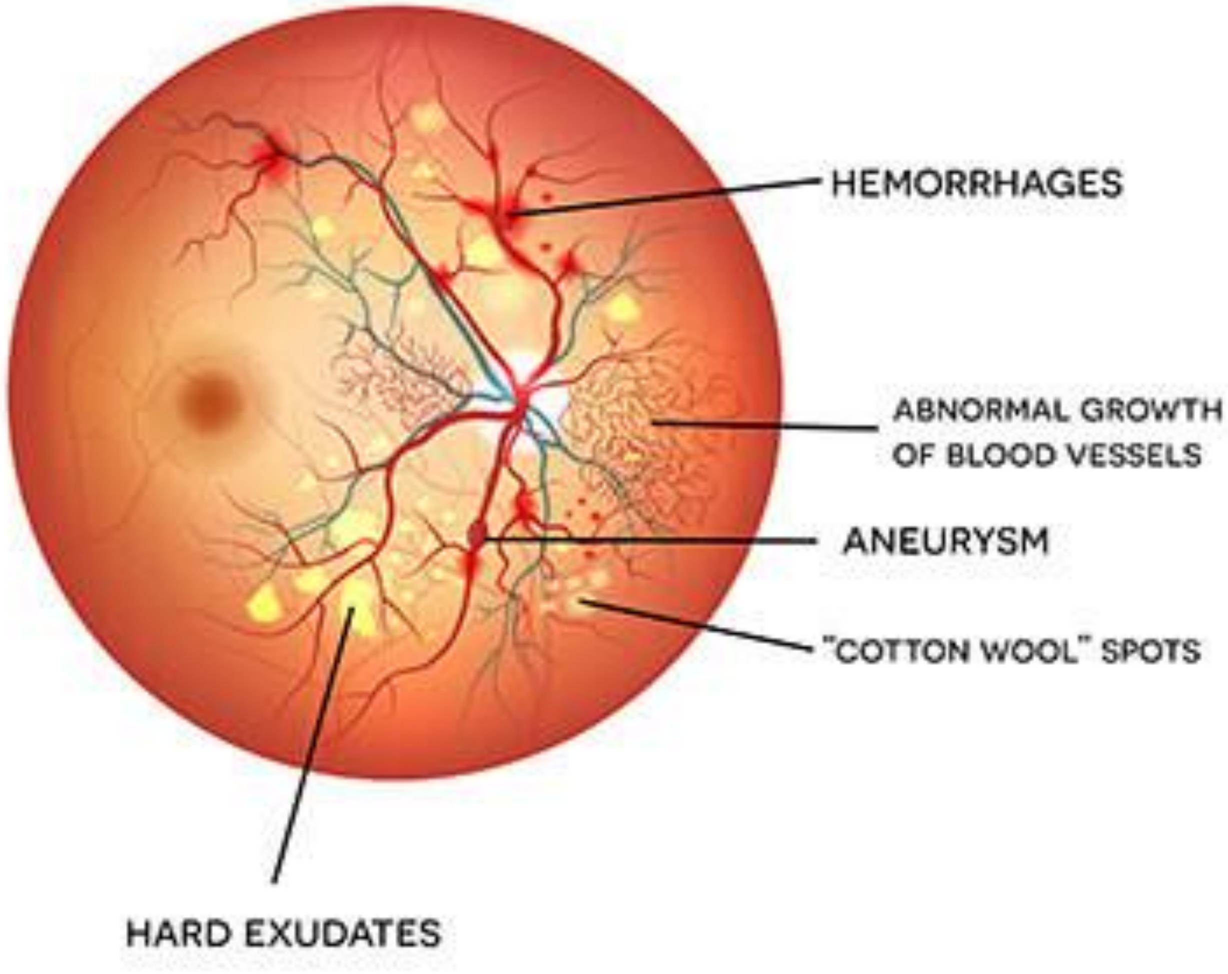
Segmentation by Vessel Tracking

- Segment blood vessels by tracking vessels
- Starts with a set of seed points and then use them to trace the retinal vasculature based on the local intensity or texture information.
- The tracing follows a tree-like structure as the vessels are connected
  - Kalman filter
  - Other algorithms
- Advantage: provide accurate vessel widths
- Disadvantage: dependency on the pre-processing step, as the pre-processing phase involves the vessel enhancement of all the vessels of varying sizes and orientations

Presentation

- Kalman Filter and a possible application in MedIA

Retinal Fundus Image



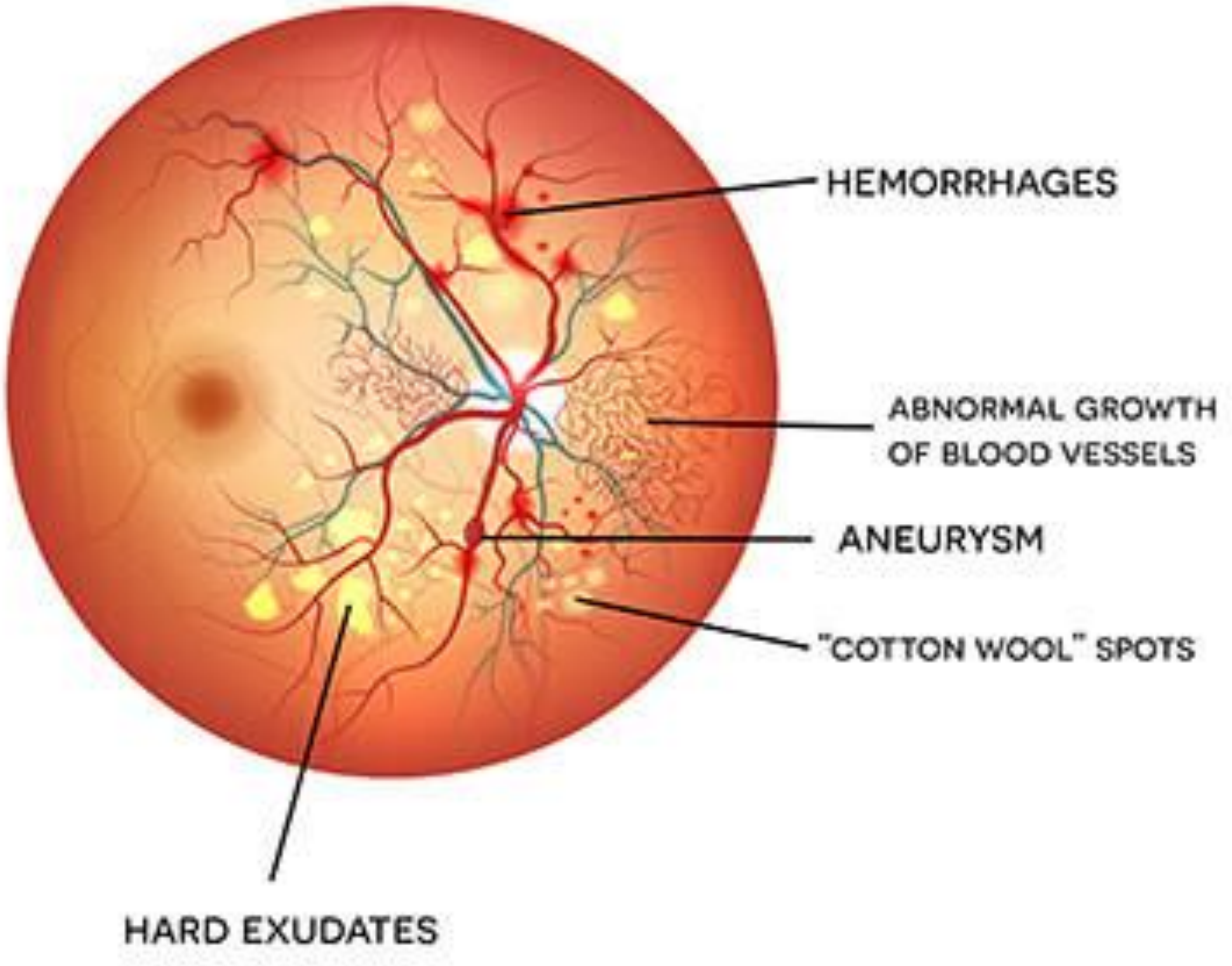
https://starretina.com/diabetic-retinopathy/

Detection of Retinal Lesions: Microaneurysms and hemorrhages

- Microaneurysms: Red dot, hemorrhages: red regions

- Microaneurysms detection (high contrast in green channel)
  - Thresholding
  - Matched filter
  - Pixel classification
  - Circular Hough transform
  - Neural networks
  - Candidate detection followed by tree-based ensemble classifier

Retinal Fundus Image



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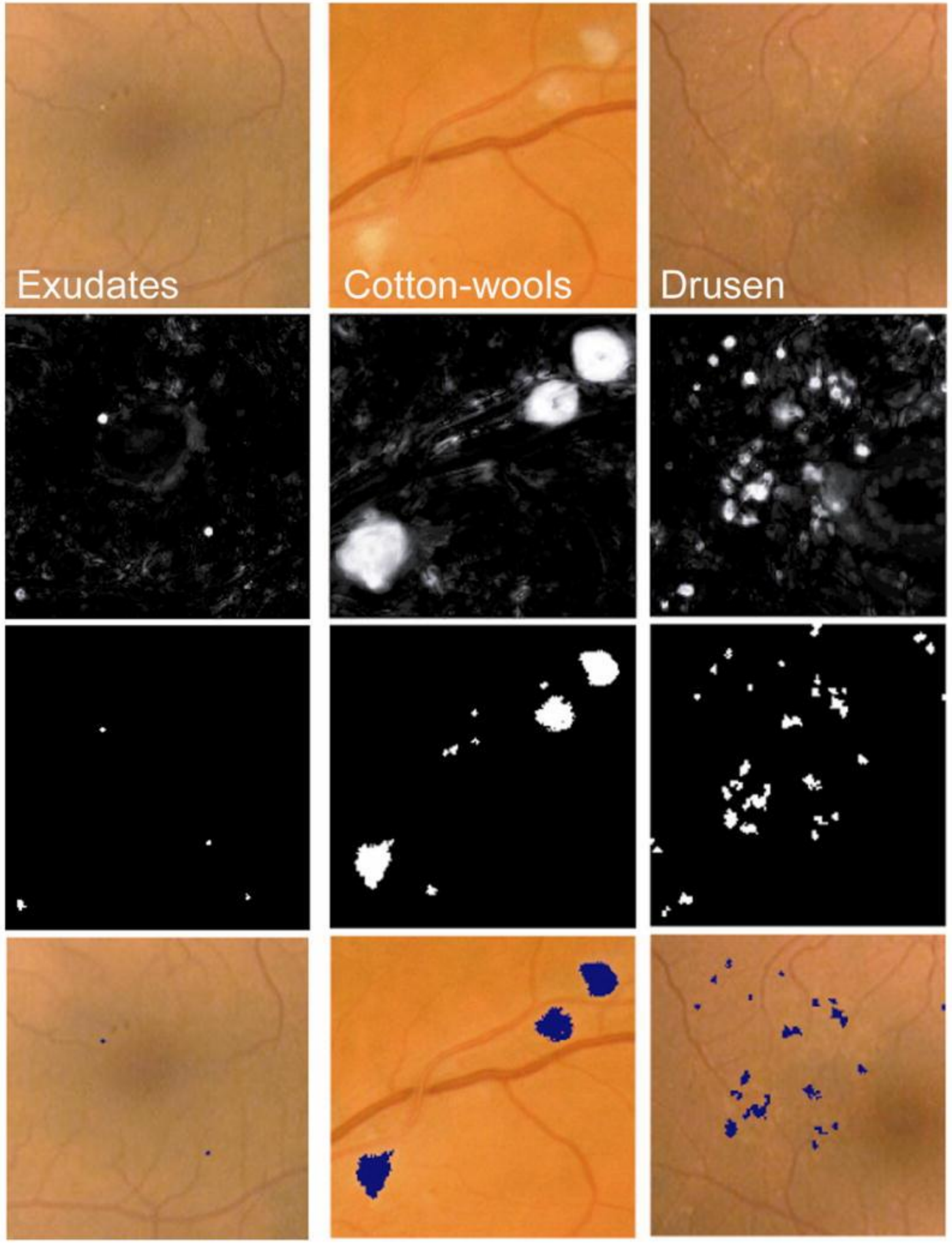
Detection of Retinal Lesions: Exudates

- Cotton wool spots (CWS)
  - Nerve fibre layer infarcts
  - Whitish in appearance
  - Soft exudates
- Hard exudates are visible in NPDR and cotton wool spots in PDR
- Region growing
- Clustering (FCM)
- Thresholding
- Active Contour
- Neural Networks

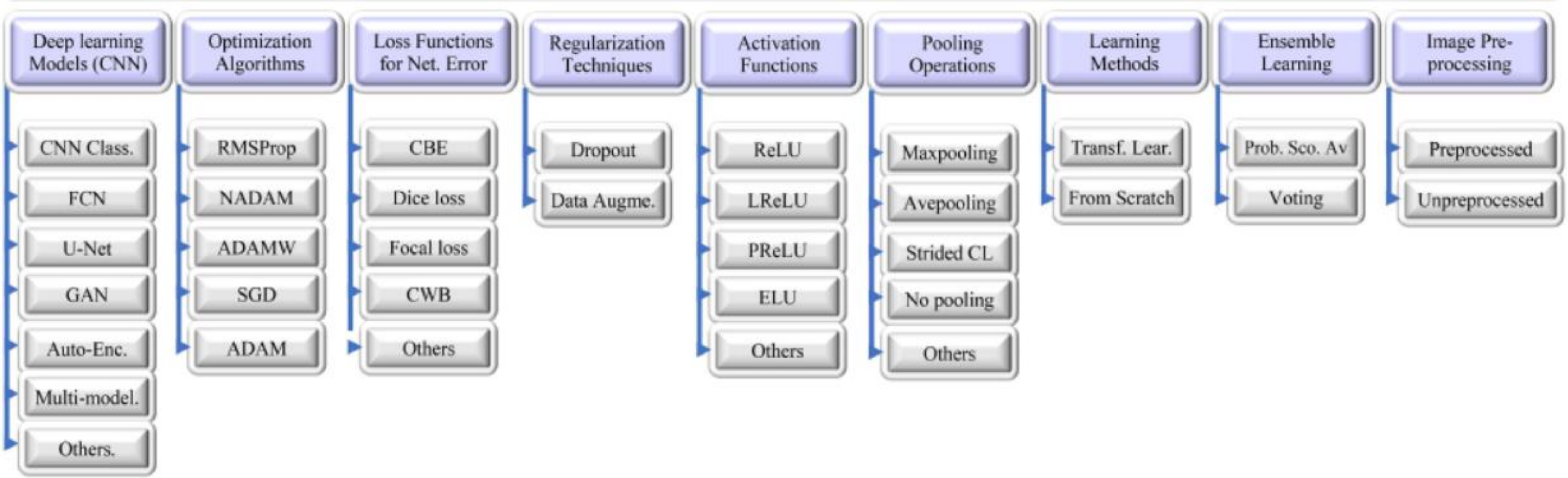
Detection of Retinal Lesions

- Drusen, hard exudates, or cotton wool spots classification
- Each pixel was classified, resulting in a so-called lesion probability map that indicates the probability of each pixel to be part of a bright lesion
- Pixels with high probability were grouped into probable lesion pixel clusters
- Based on cluster characteristics each probable lesion pixel cluster was assigned a probability indicating the likelihood that the pixel cluster was a true bright lesion.
- Each bright lesion cluster likely to be a bright lesion was classified as exudate, cotton-wool spot or drusen.



https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2739583/

Deep Learning Methods for Retinal Blood Vessel Segmentation



A Survey of Deep Learning for Retinal Blood Vessel Segmentation Methods: Taxonomy, Trends, Challenges and Future Directions, IEEE Access

Deep Learning Methods for Retinal Blood Vessel Segmentation

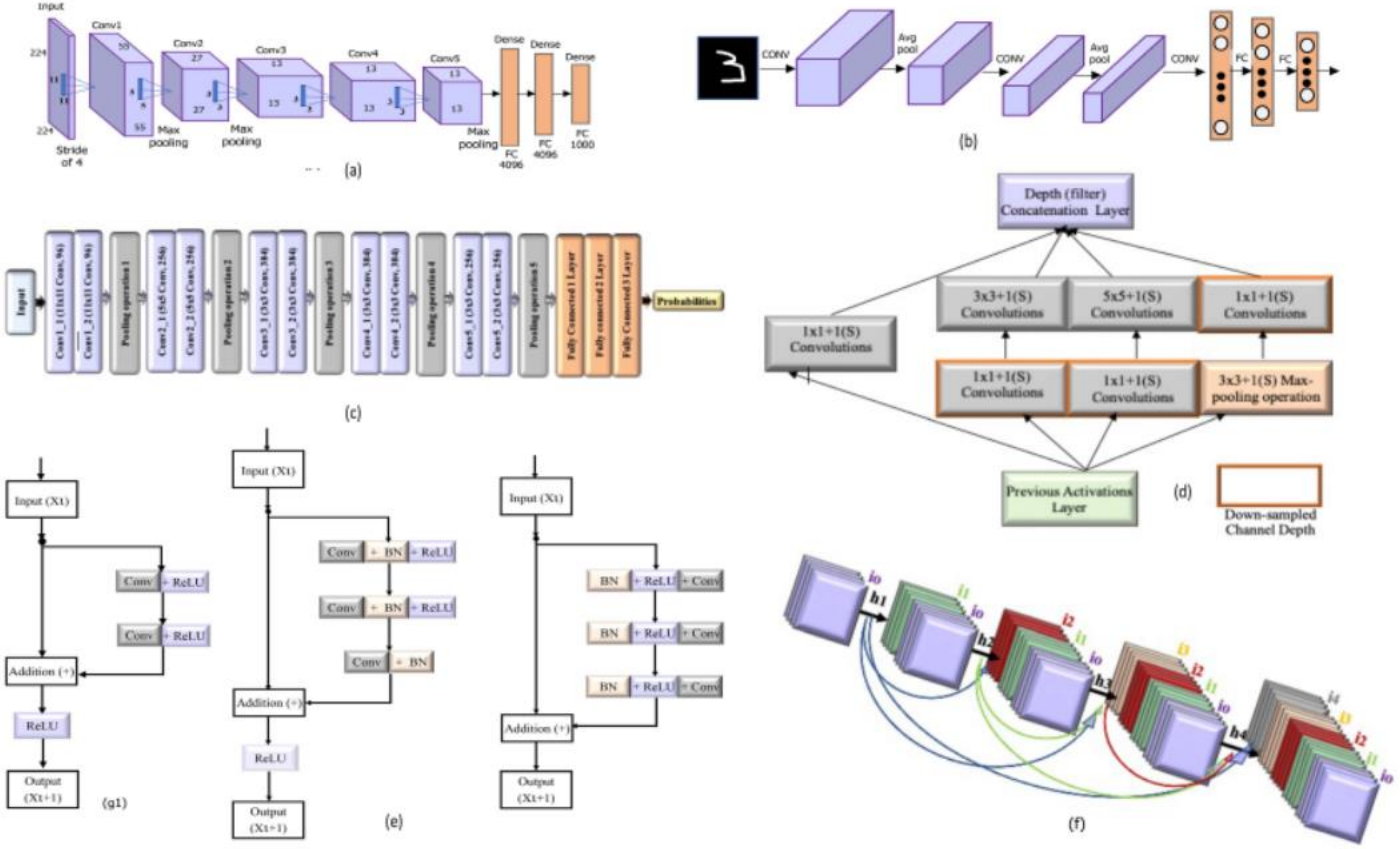


FIGURE 7. The layout diagrams for CNNs classification models (a) LeNet, (b) AlexNet, (c) VGGNet, (d) GoogleNet, (e) ResNet, and (f) DesNet arcitectures.

A Survey of Deep Learning for Retinal Blood Vessel Segmentation Methods: Taxonomy, Trends, Challenges and Future Directions, IEEE Access

Deep Learning Methods for Retinal Blood Vessel Segmentation

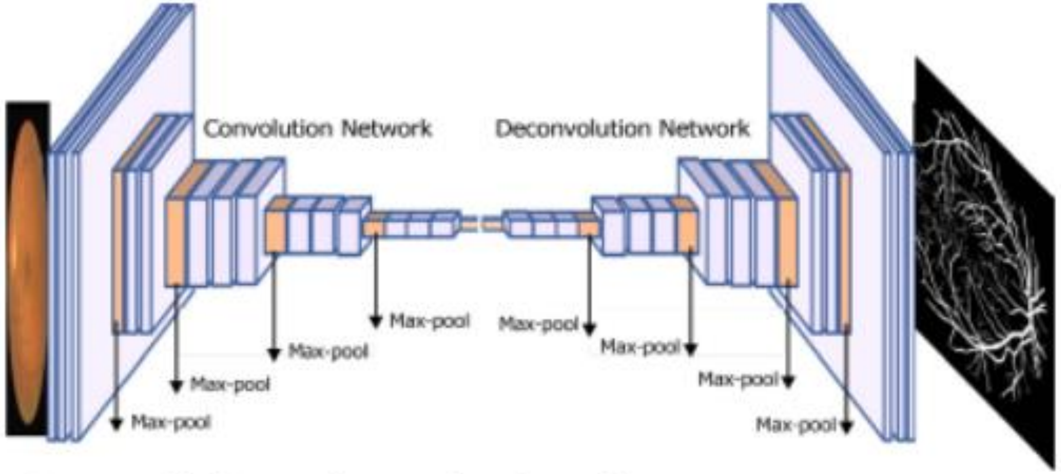


FIGURE 8. The layout diagram for FCN architecture.

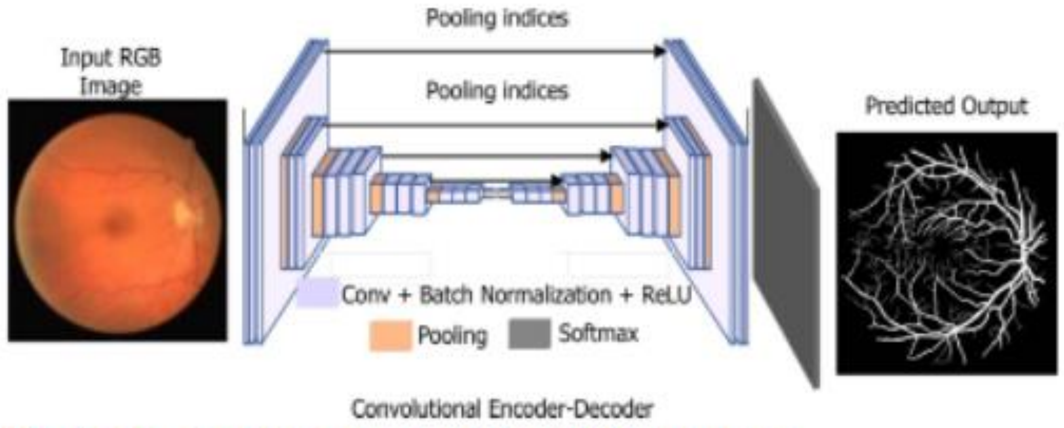


FIGURE 10. The layout diagram for SegNet architecture.

Retinal Image Datasets

- DRIVE
- STARE
- CHASE_DB1
- ROSE-1 SVC
- Other datasets

https://paperswithcode.com/task/retinal-vessel-segmentation