Improved Views in Fundus Imaging: Implications for Diagnostics and Therapeutics

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Outline

- **Imaging of the eye**
  - CSLO imaging
  - polarization imaging
- **Human Imaging and Animal Models**
  - imaging
  - Two photon therapy
- **Wavefront correction via adaptive optics**
- **Clinical applications**

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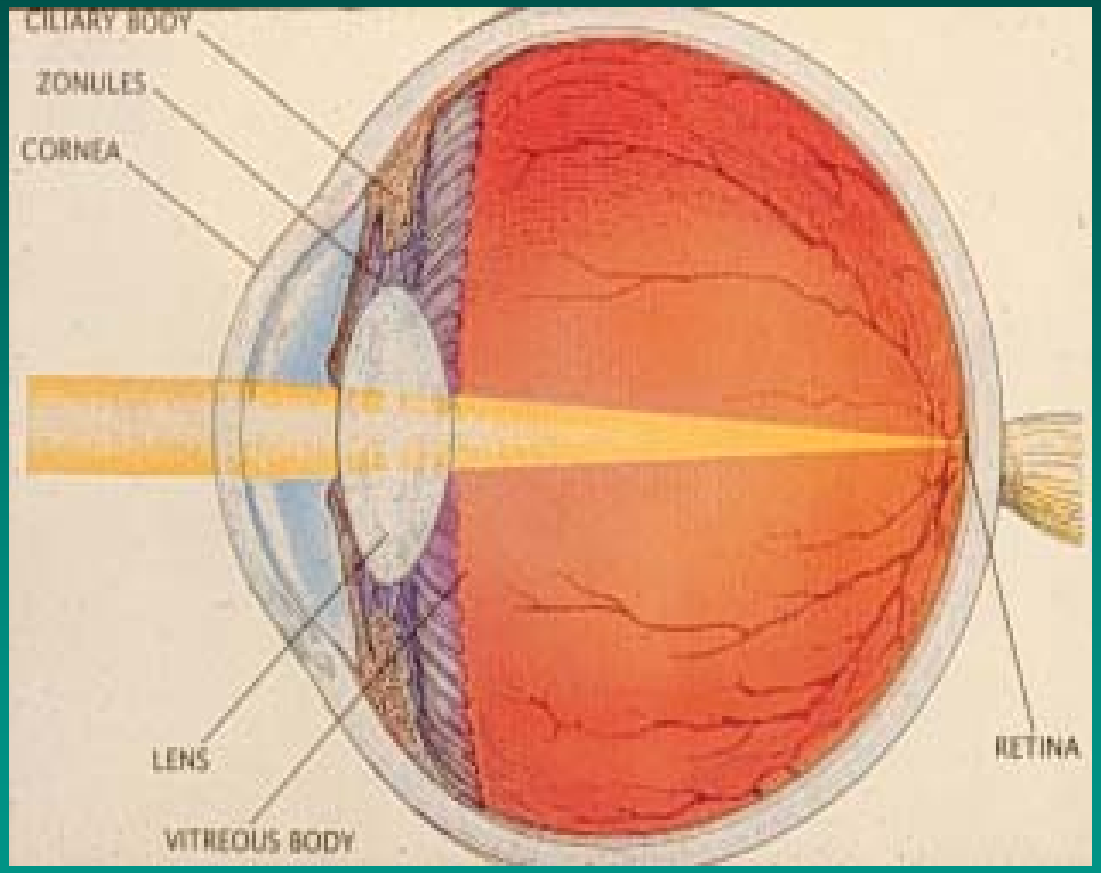
The Eye



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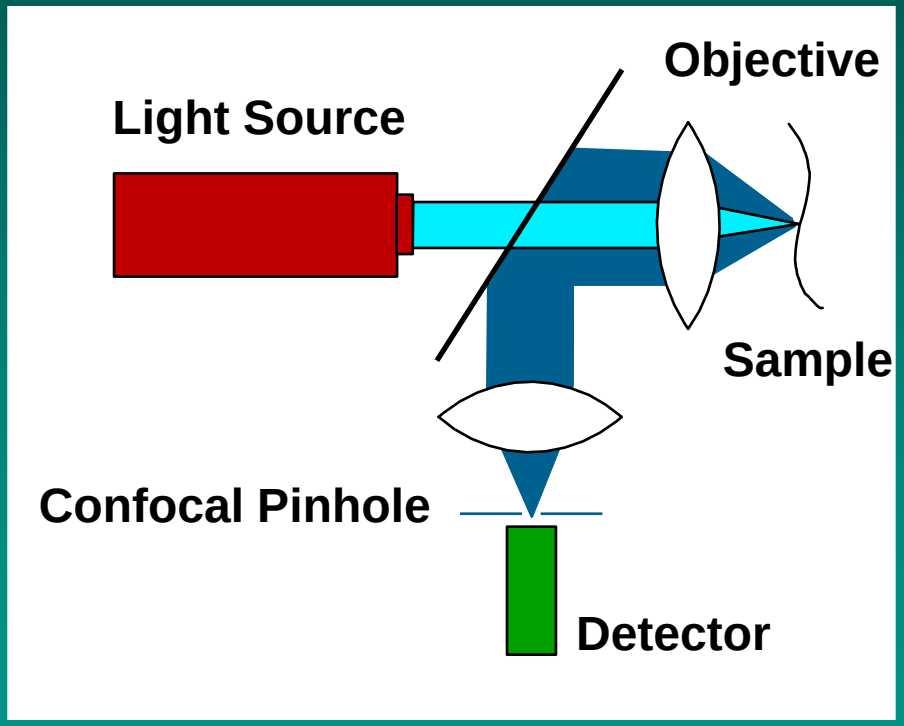
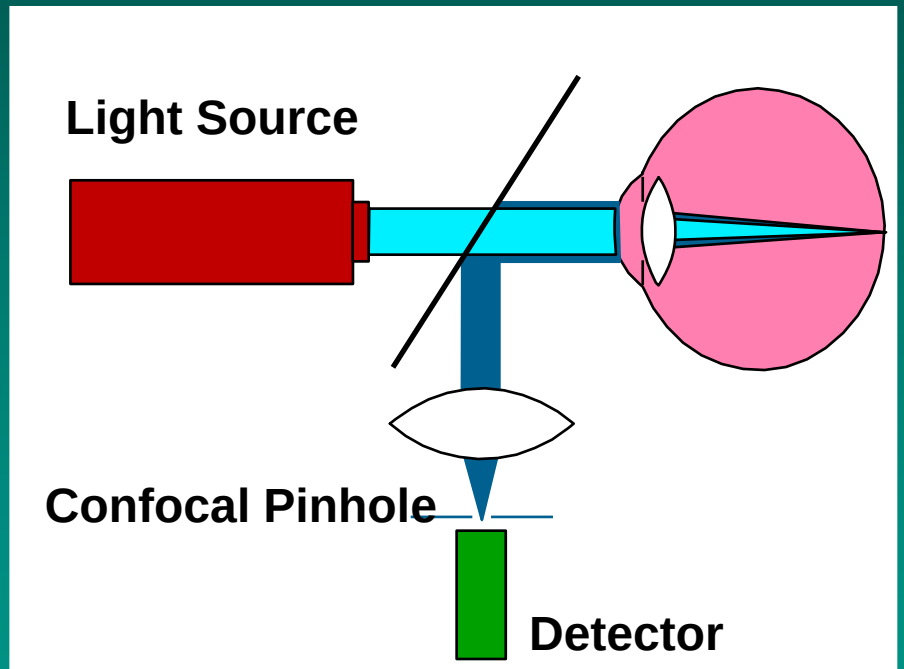
Imaging of the Eye

CSLM



CSLO



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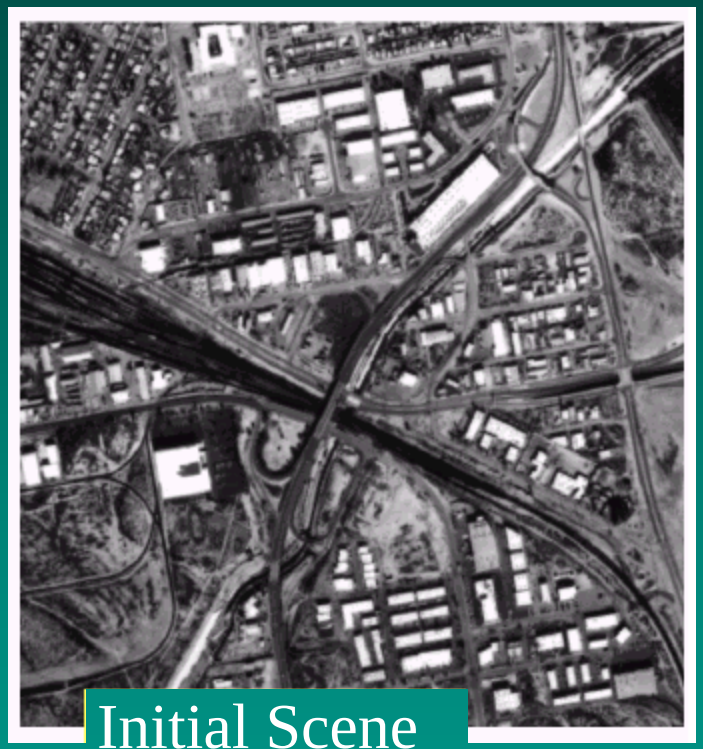
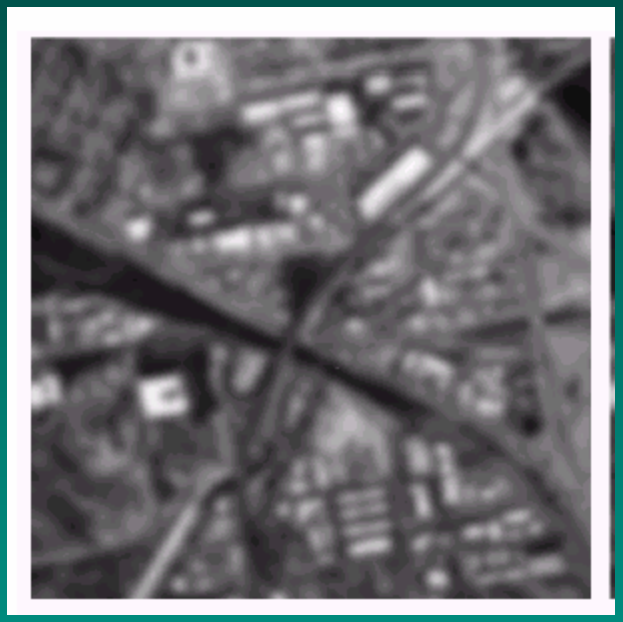
Effect of PSF in Imaging



Initial Scene



Final Scene: Initial Scene is Convolved with the PSF

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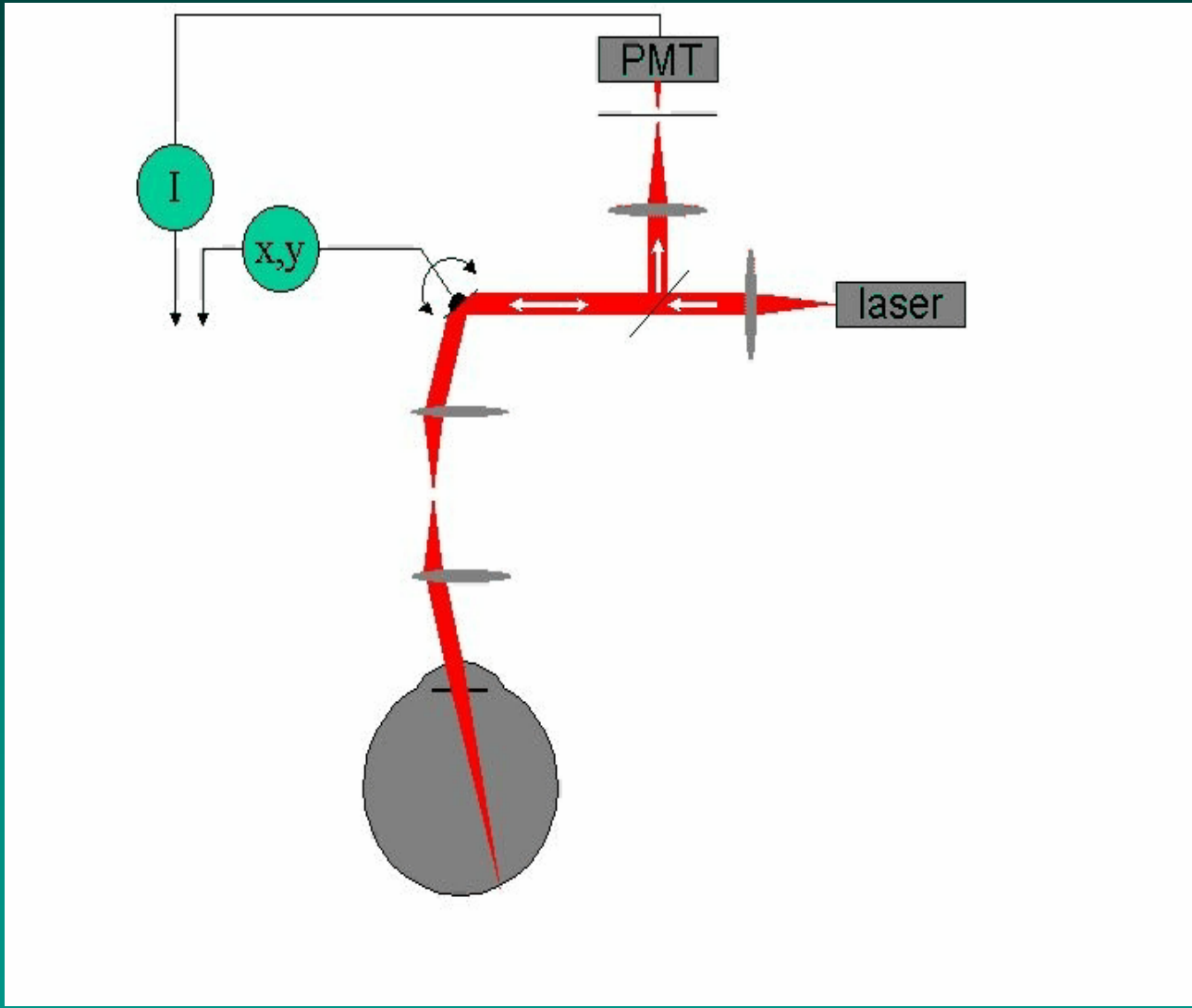
Scanning Laser Ophthalmoscopy



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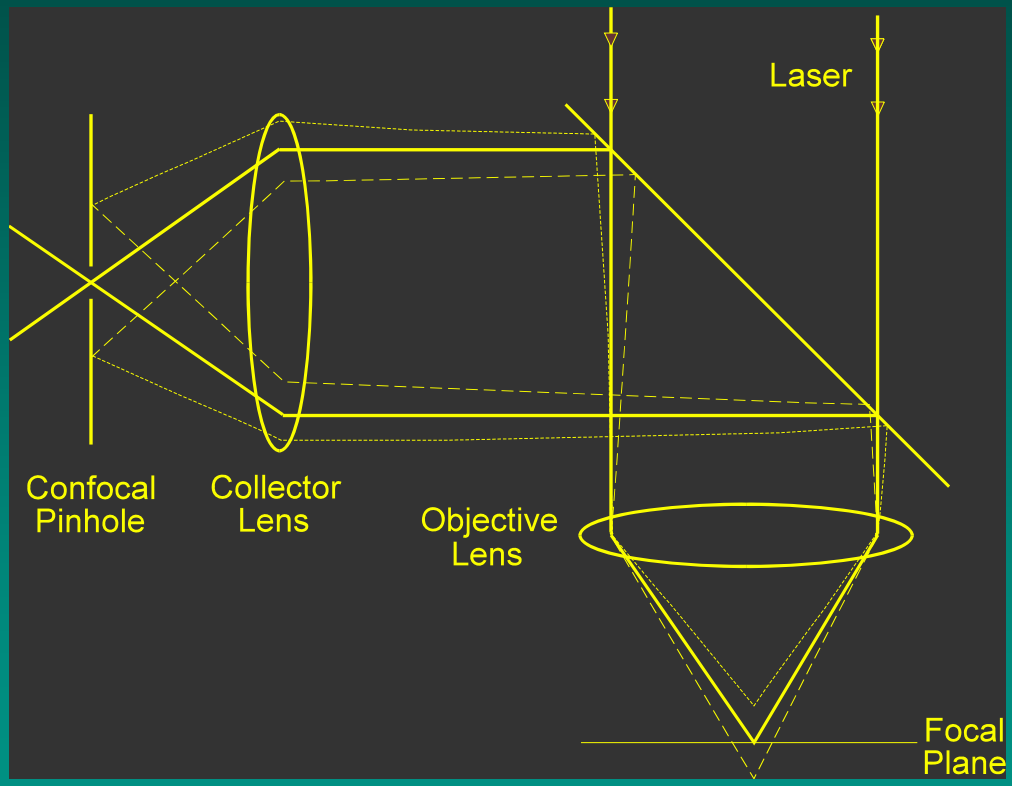
Confocal Imaging

Only light with zero vergence is focused through the confocal pinhole and is detected. This is the source of the instrument's optical sectioning ability.



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CSLO Advantages

- increased illumination allowed in a scanning system
- reduced effect of scattered light
  - ⇨ enhanced contrast and resolution
- enhanced lateral resolution
- enhanced depth resolution

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Fundus photo

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CSLO Image

CSLO image, 10 degree field of view, KM

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Younger Subject

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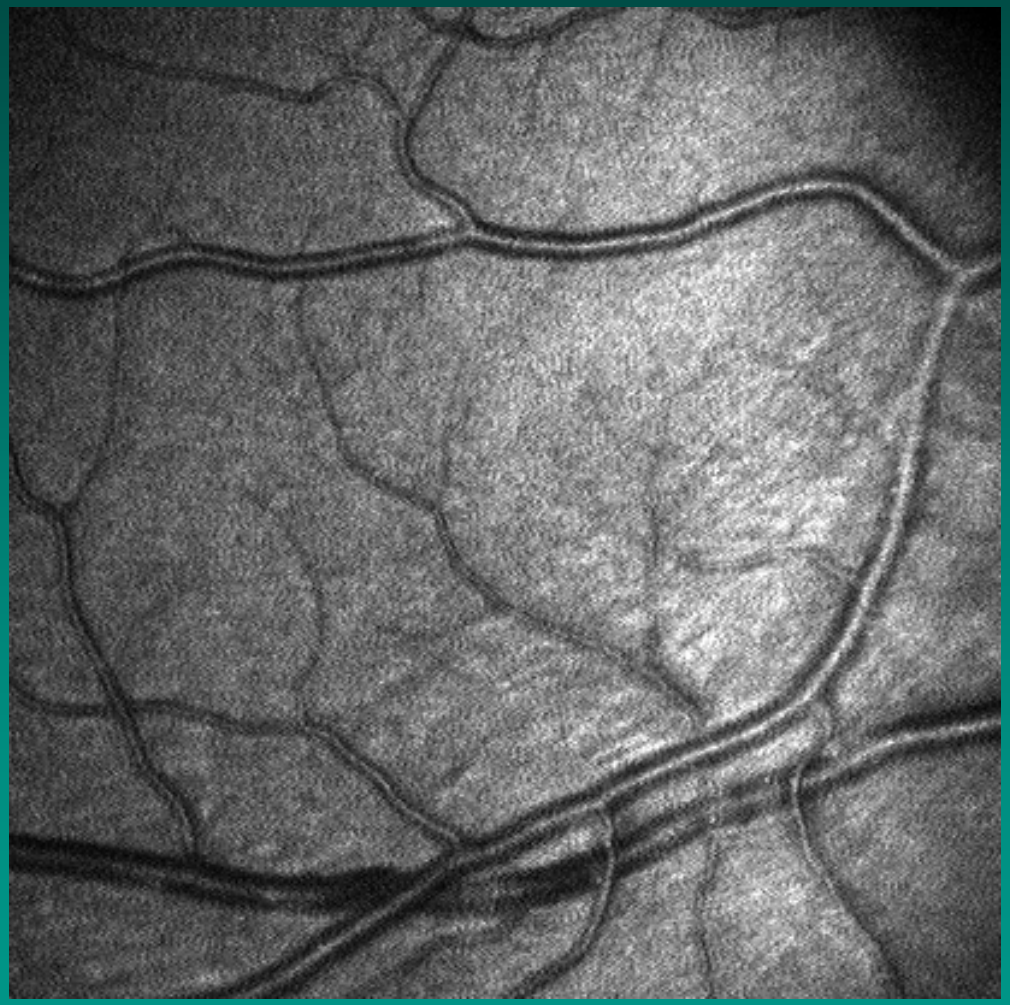
Vessels



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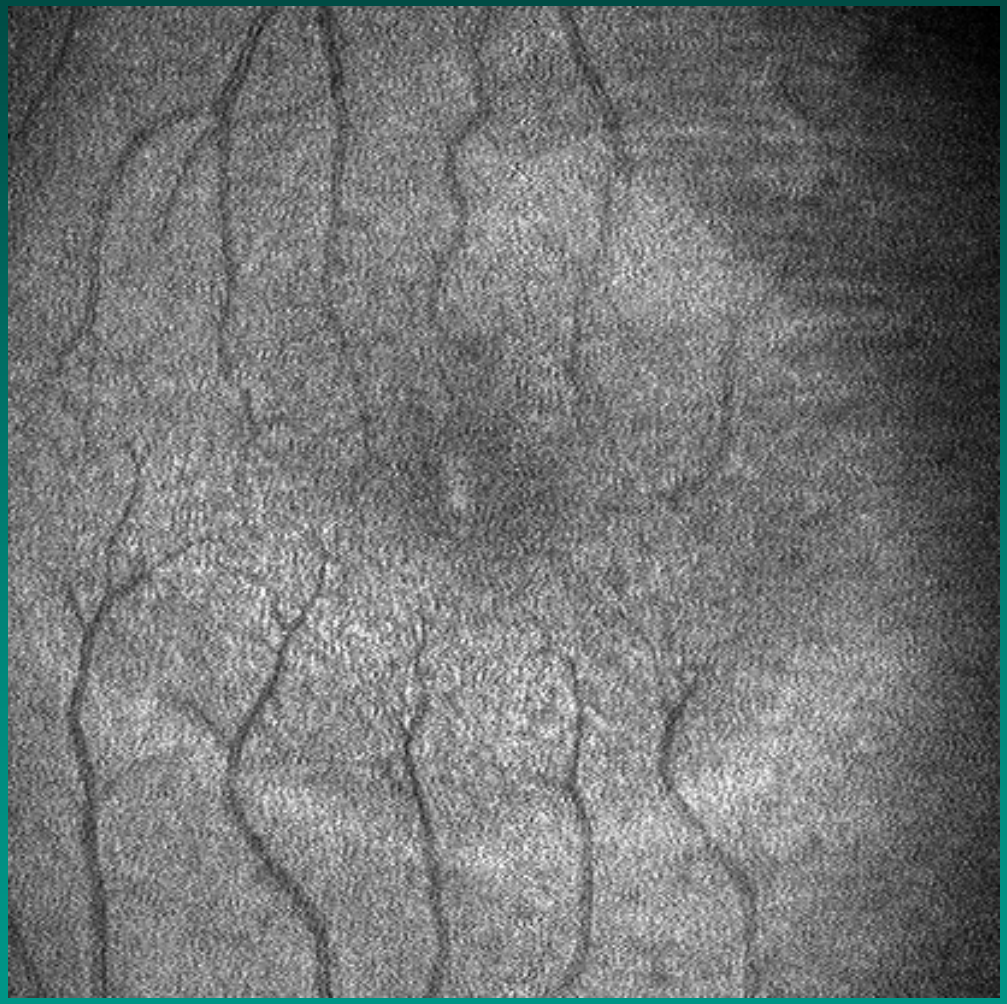
Fovea



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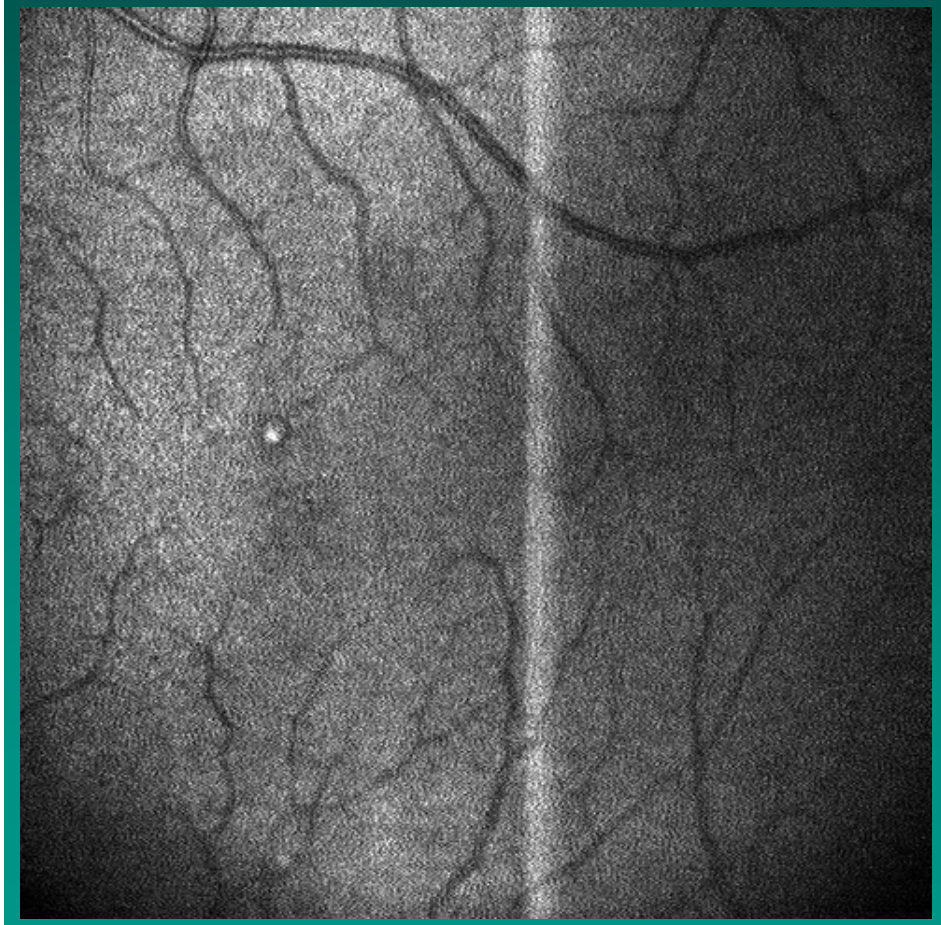
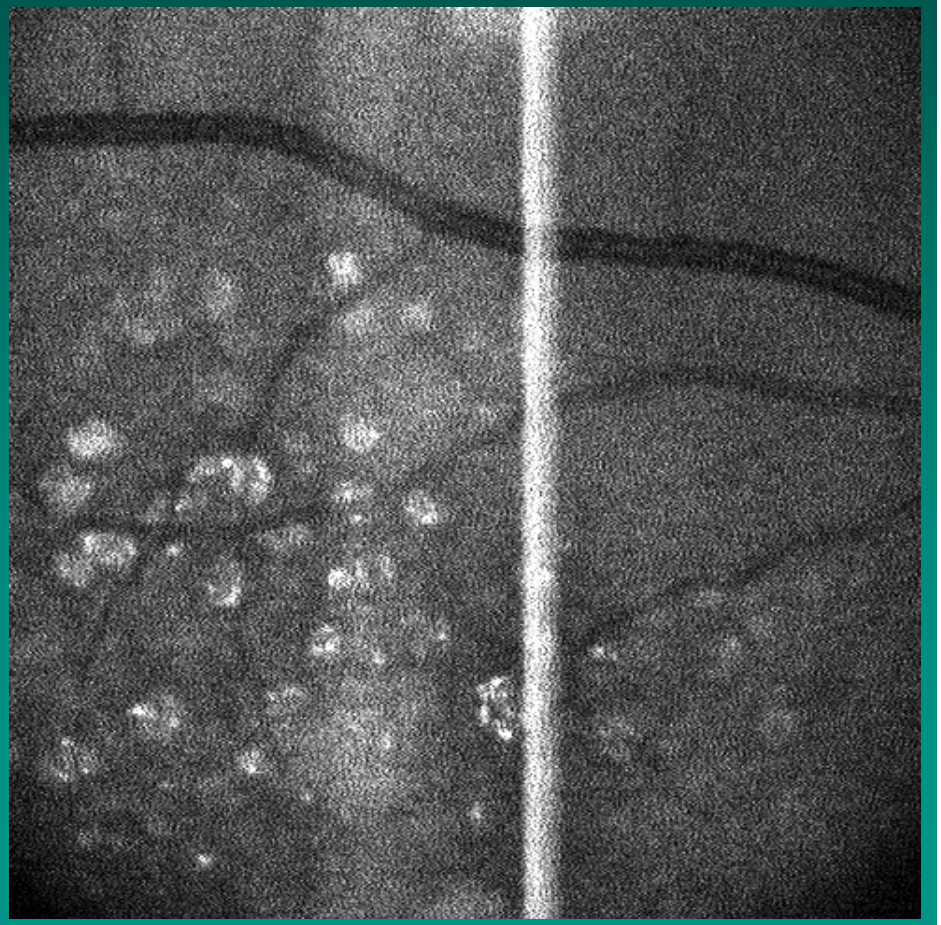
Early ARMD





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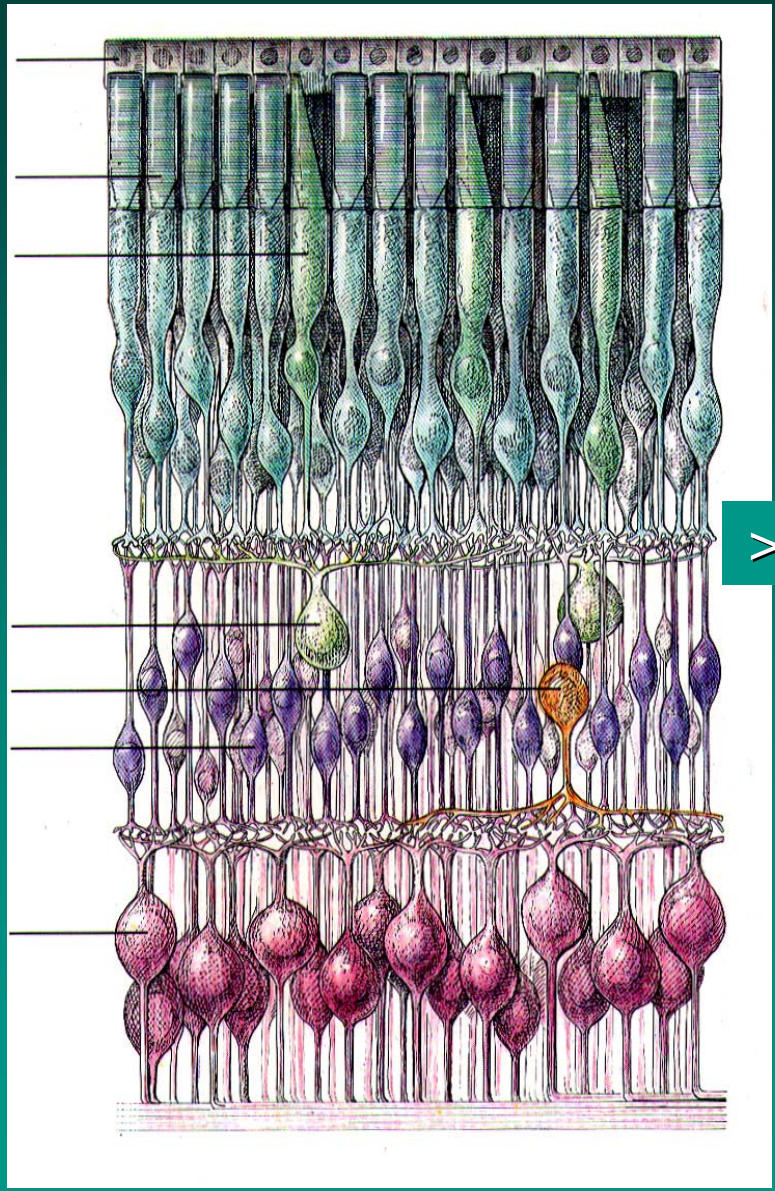
Retina Cross Section



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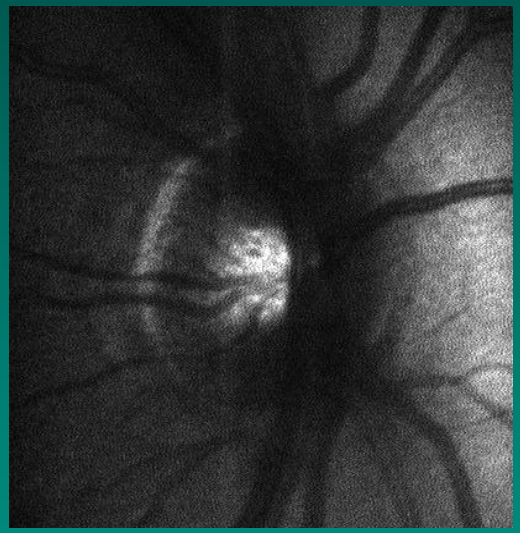
CSLO Depth Resolved



-0.5D focus

0D focus

+0.5D focus

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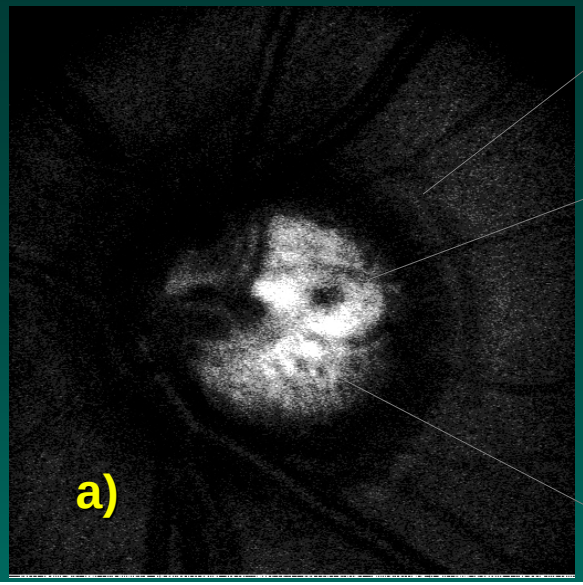
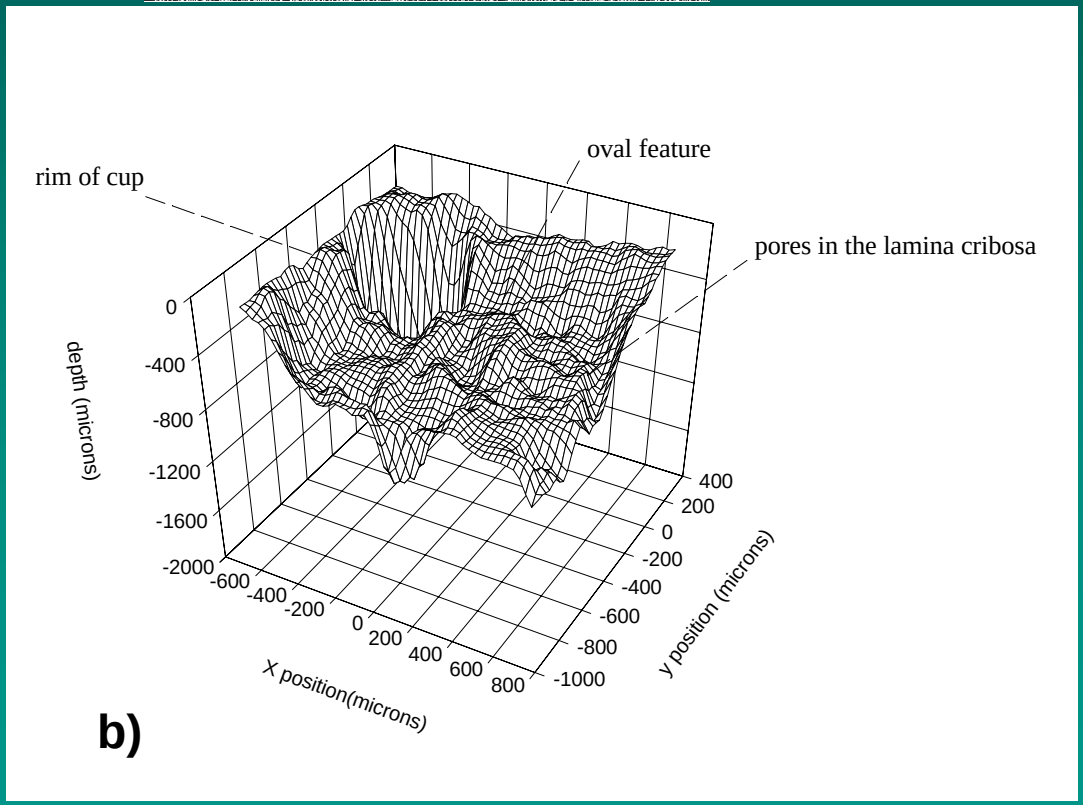


rim of cup

oval feature

pores in the lamina cribosa

Human Optic Nerve Head



b) based on 15 confocal slices.

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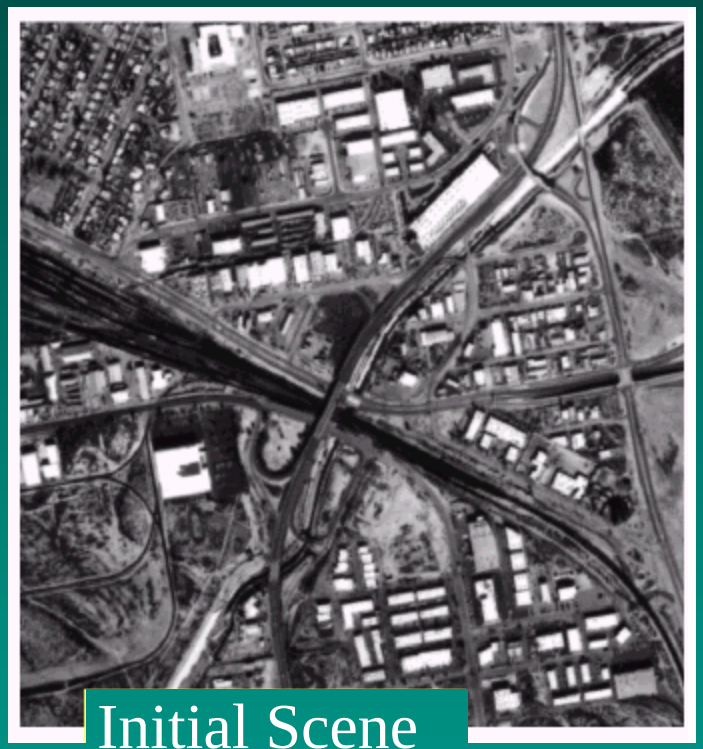
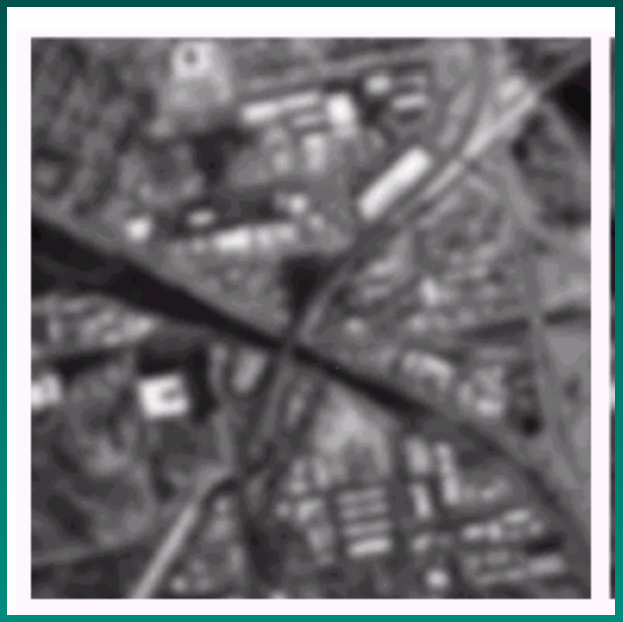
Effect of PSF in Imaging



Initial Scene



Final Scene: Initial Scene is Convolved with the PSF

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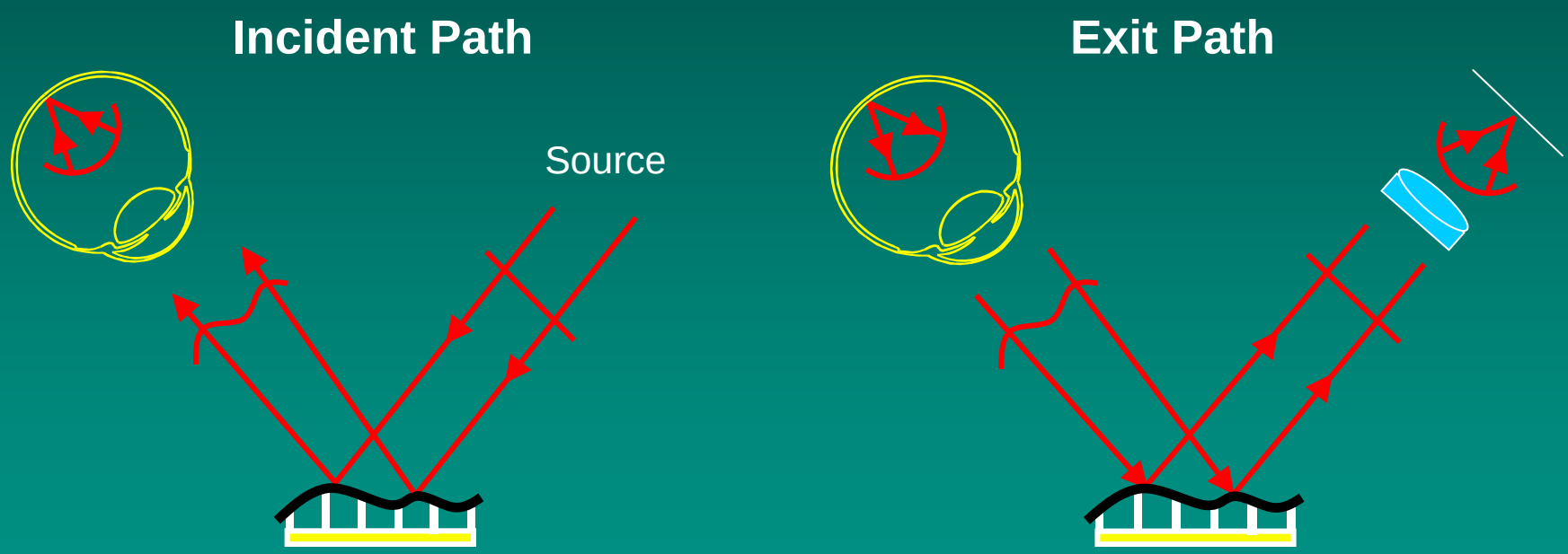
Adaptive Optics in the Eye



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Monochromatic Aberrations

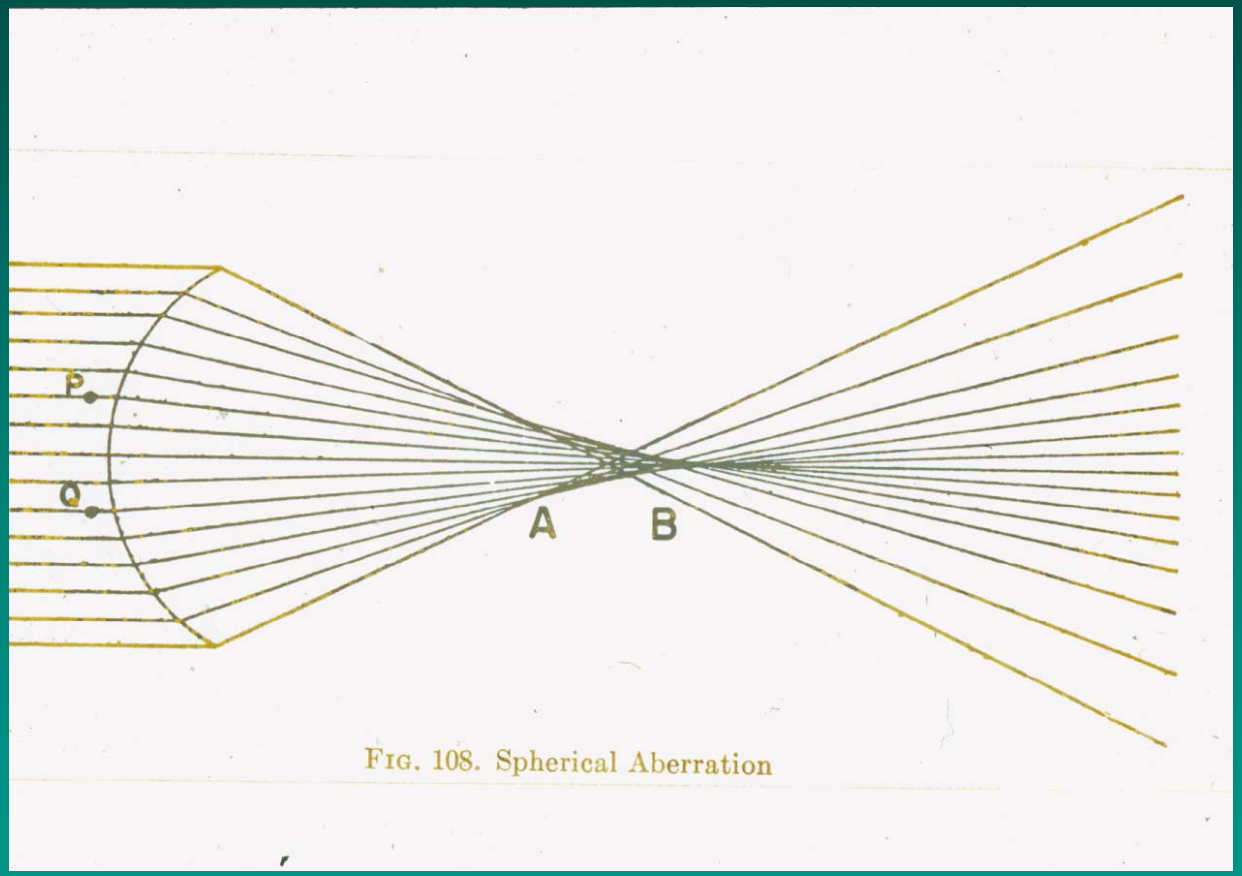

FIG. 108. Spherical Aberration

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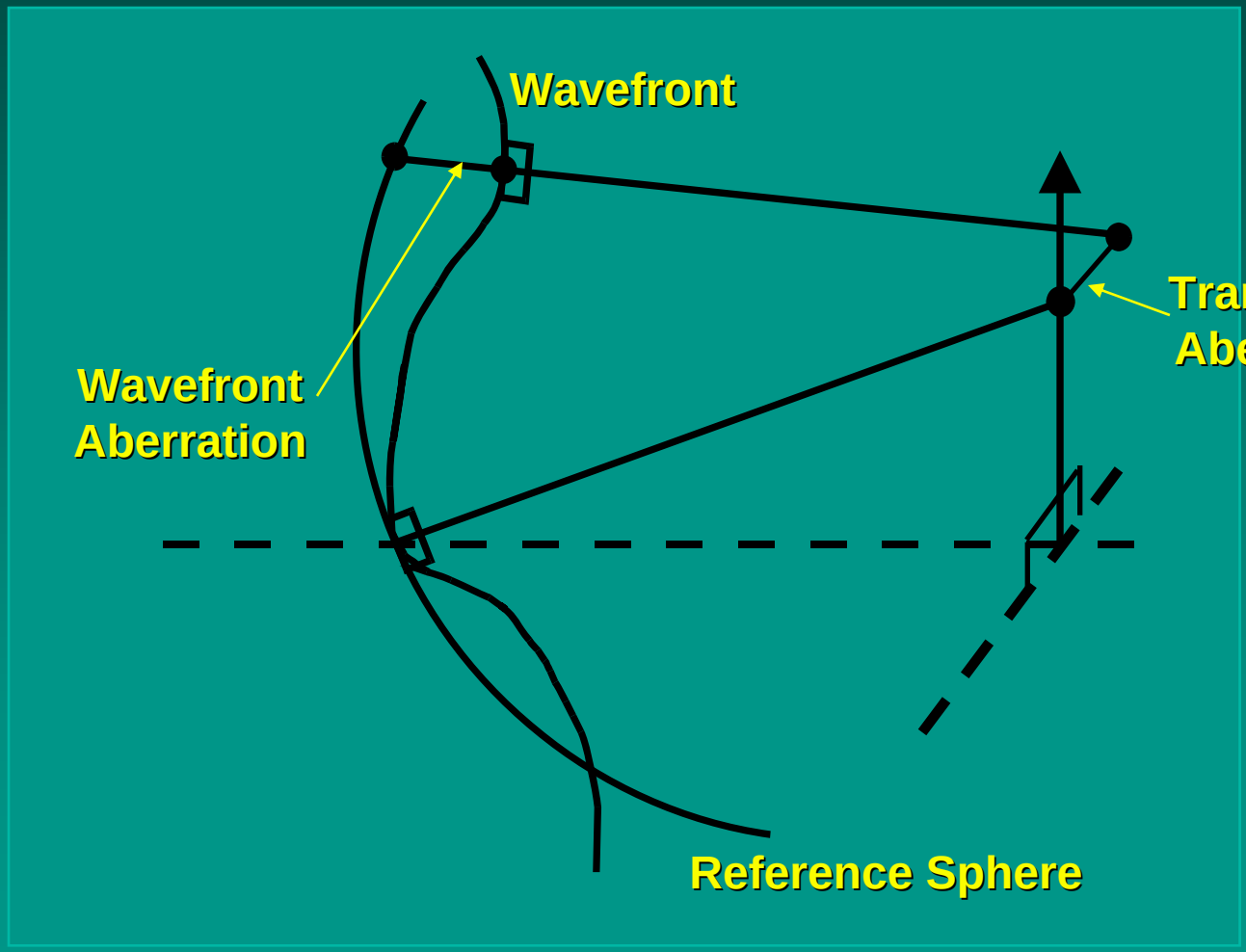
Wavefront Aberration



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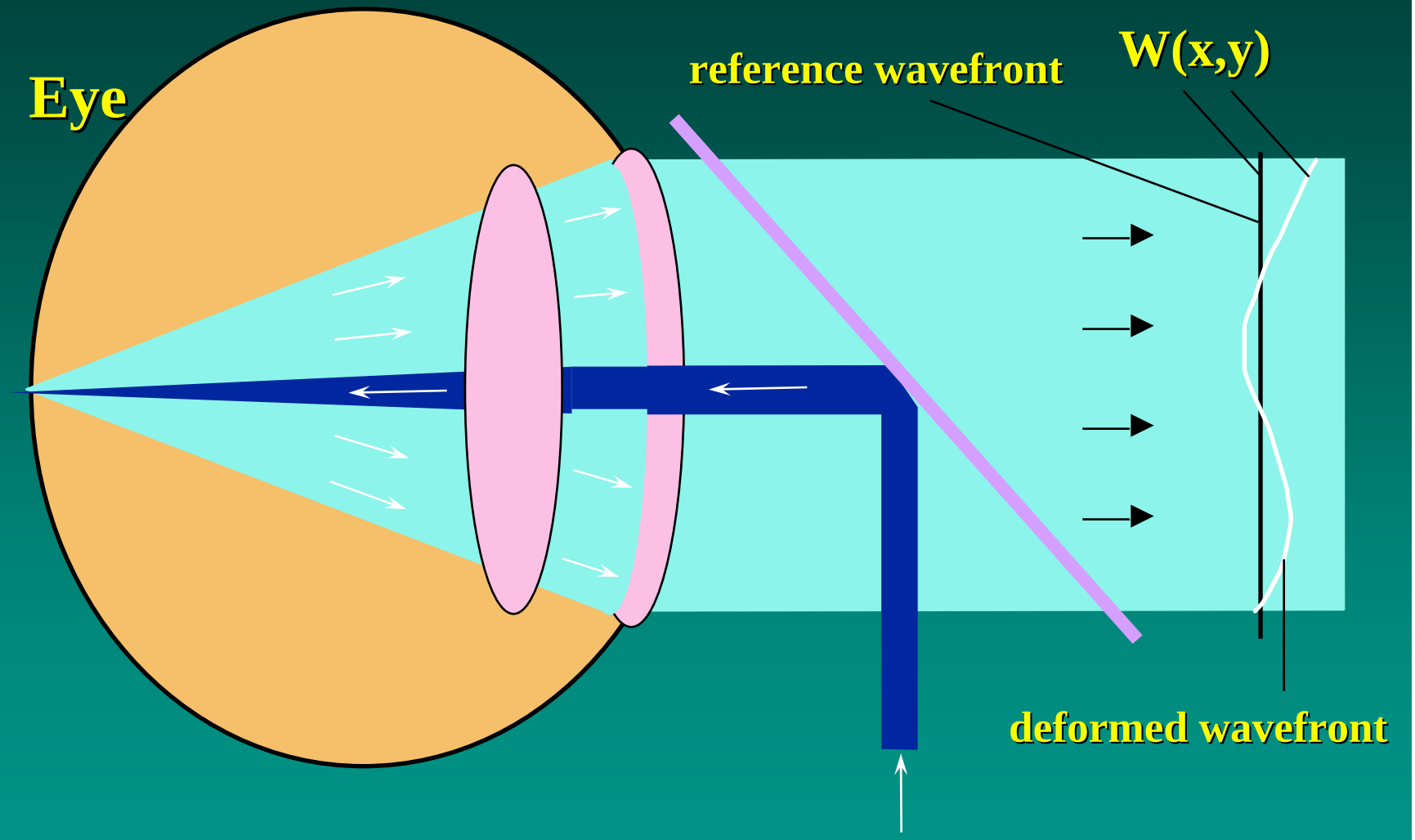
Wavefront Aberration Measurement



Wavefront aberration : W(x,y)

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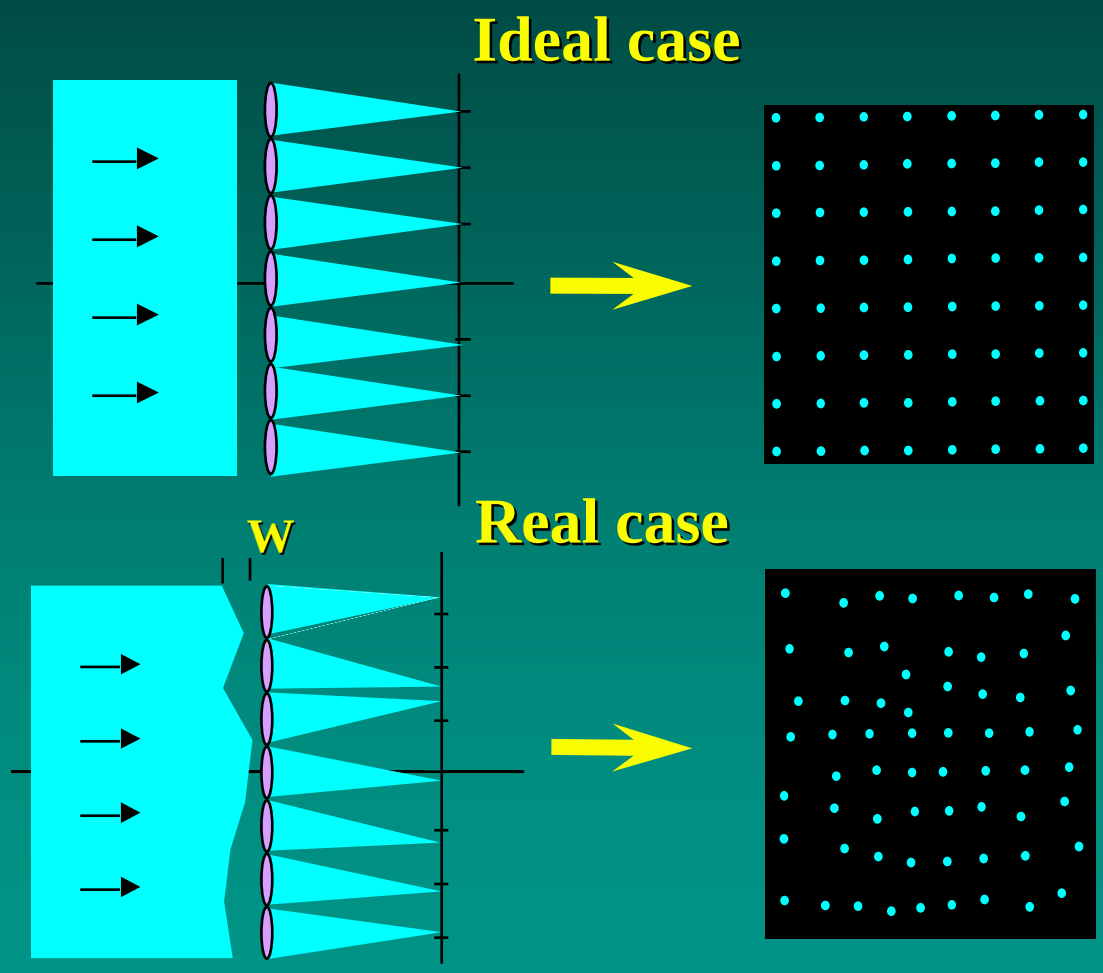
Hartmann-Shack Images



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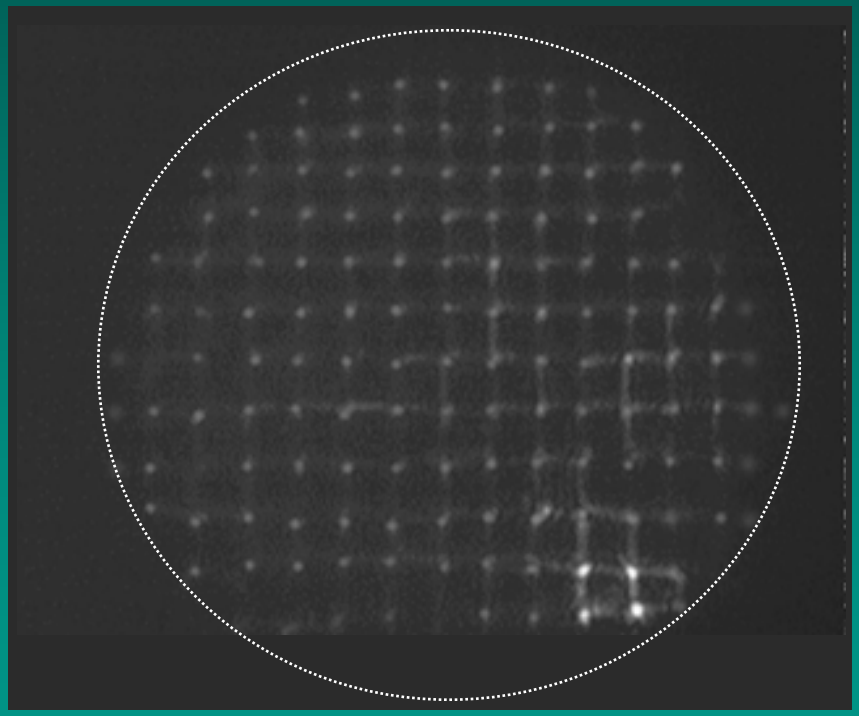
Typical Hartmann-Shack Pattern



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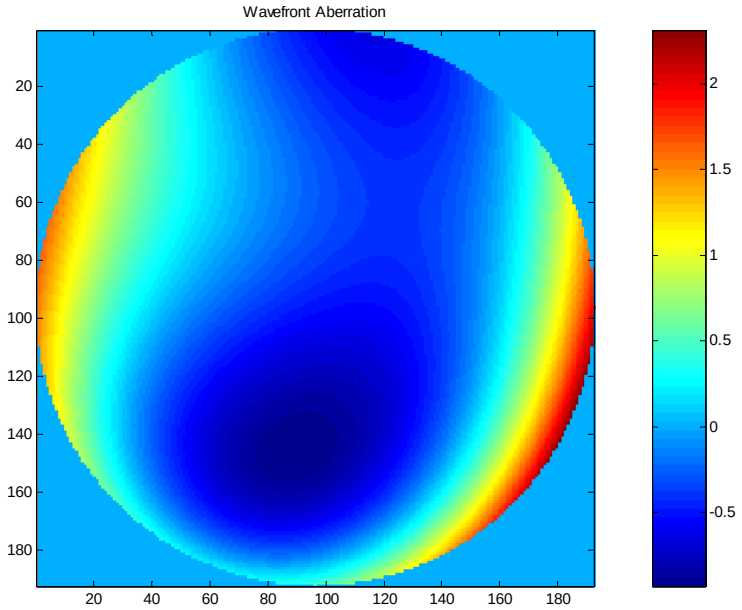
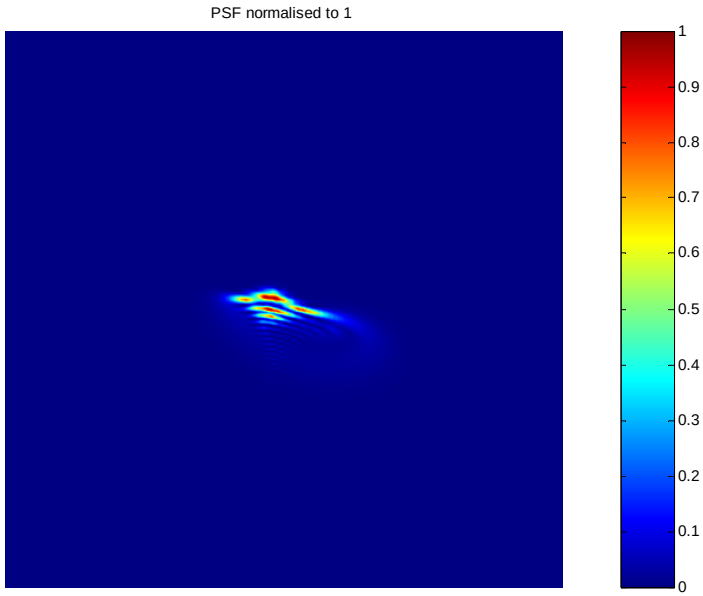
Sample Human Wavefront & PSF

Wavefront



PSF



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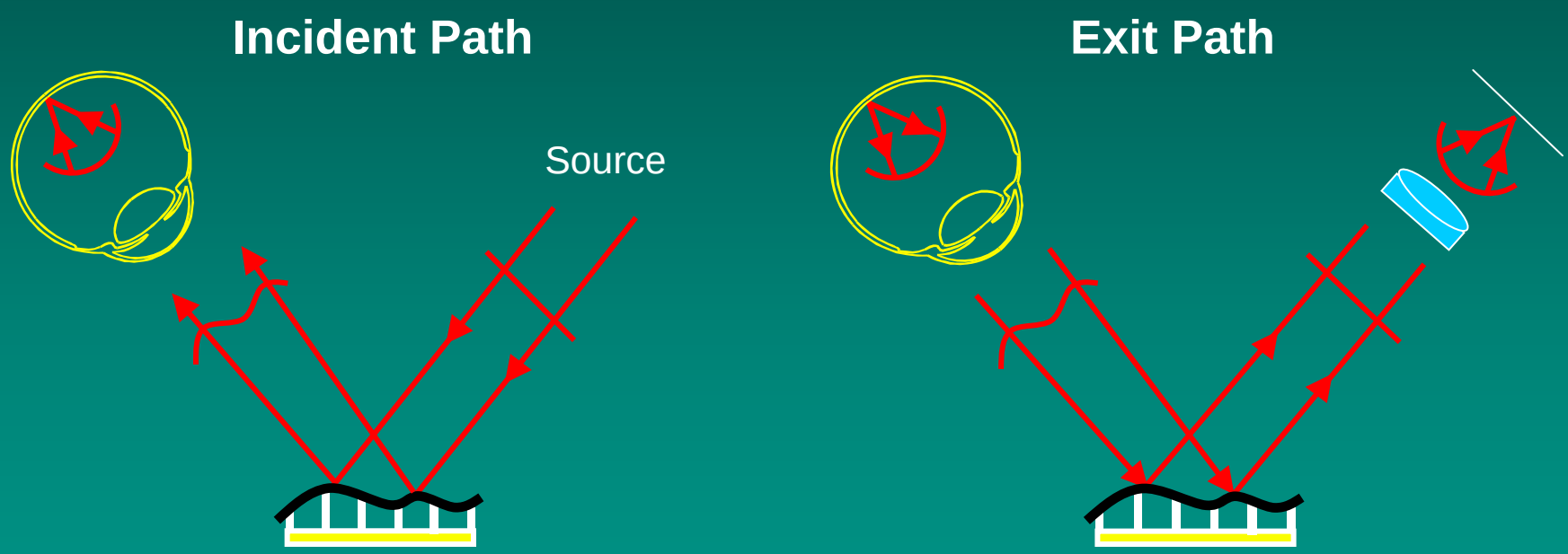
Adaptive Optics in the Eye



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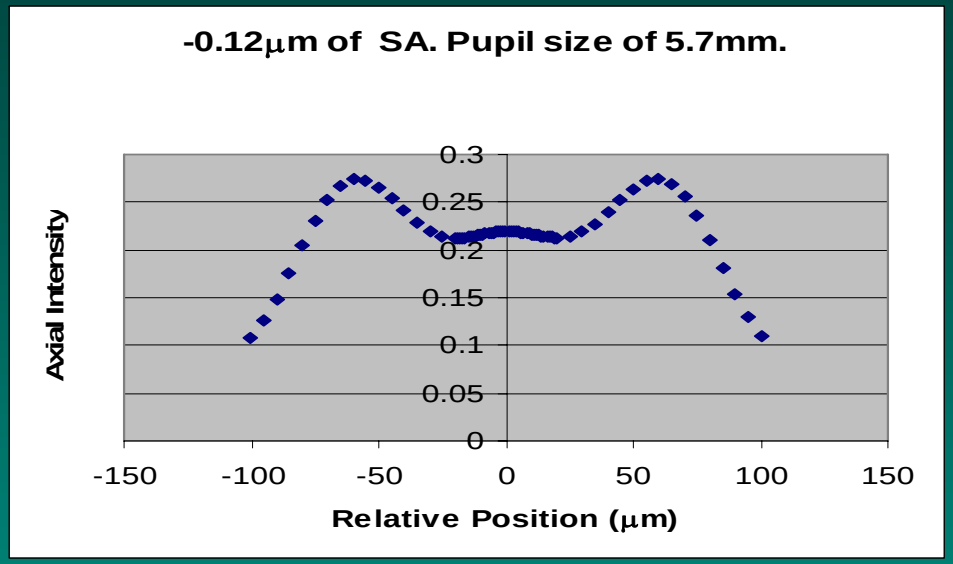
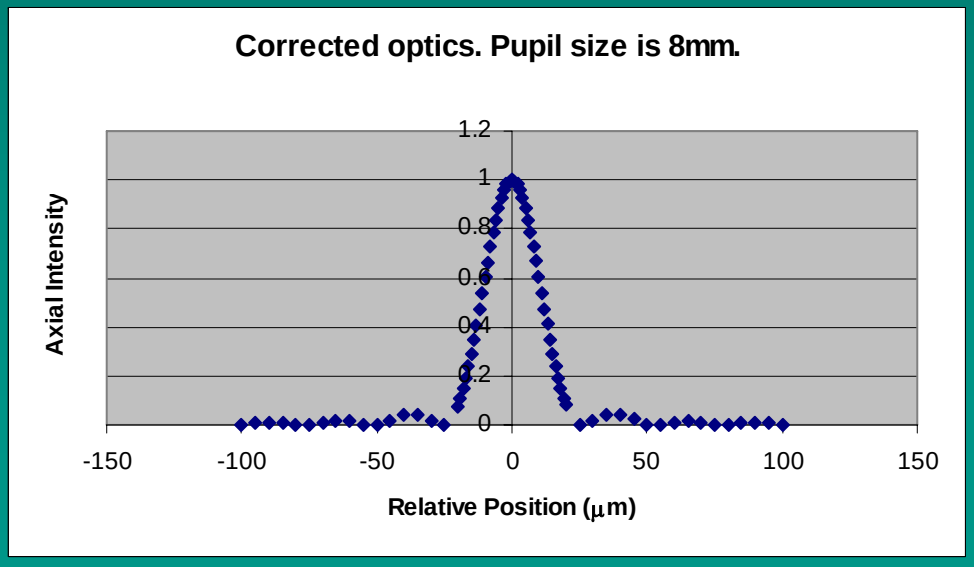
Depth Profile of Blur





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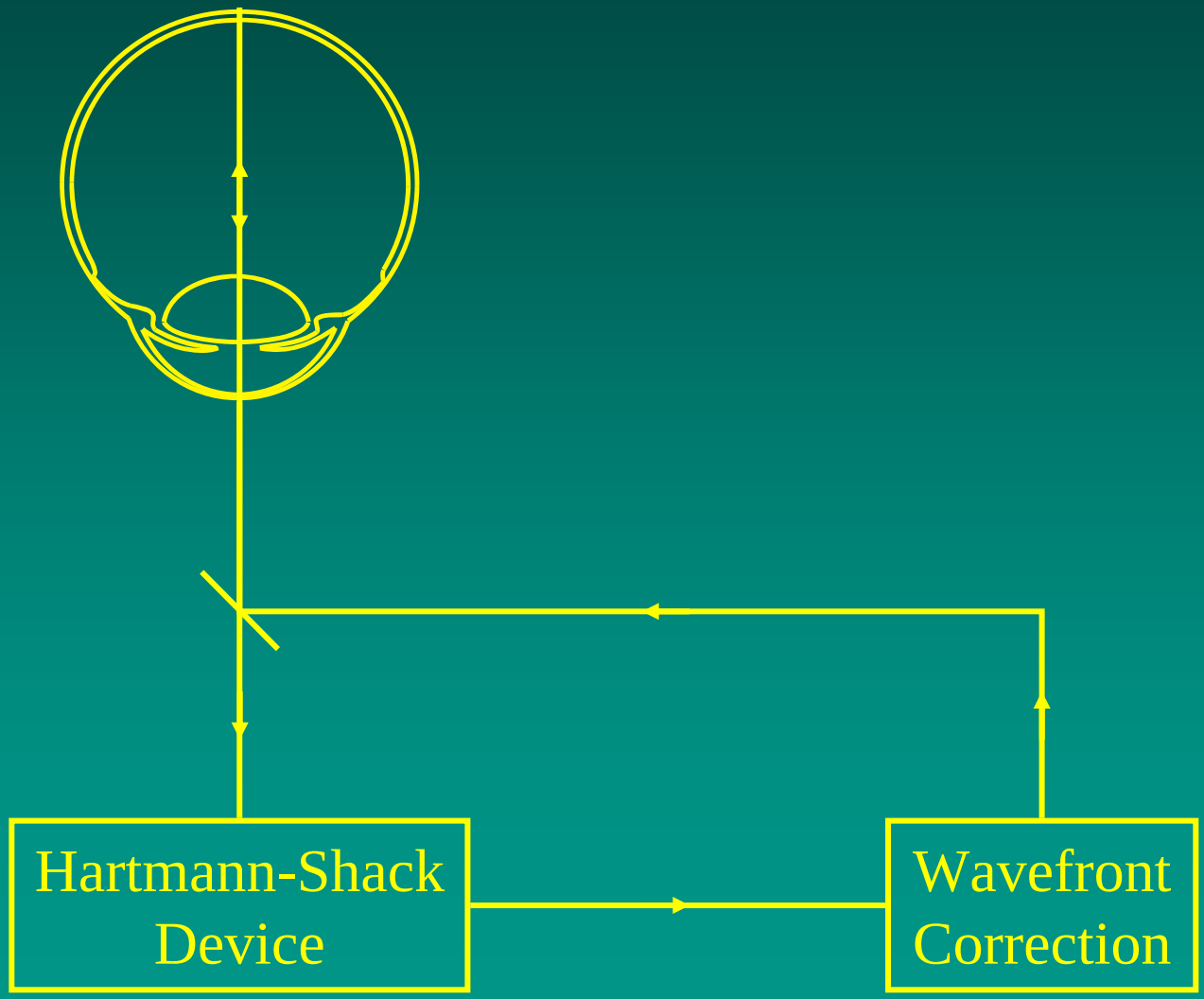
Adaptive Correction of CSLO



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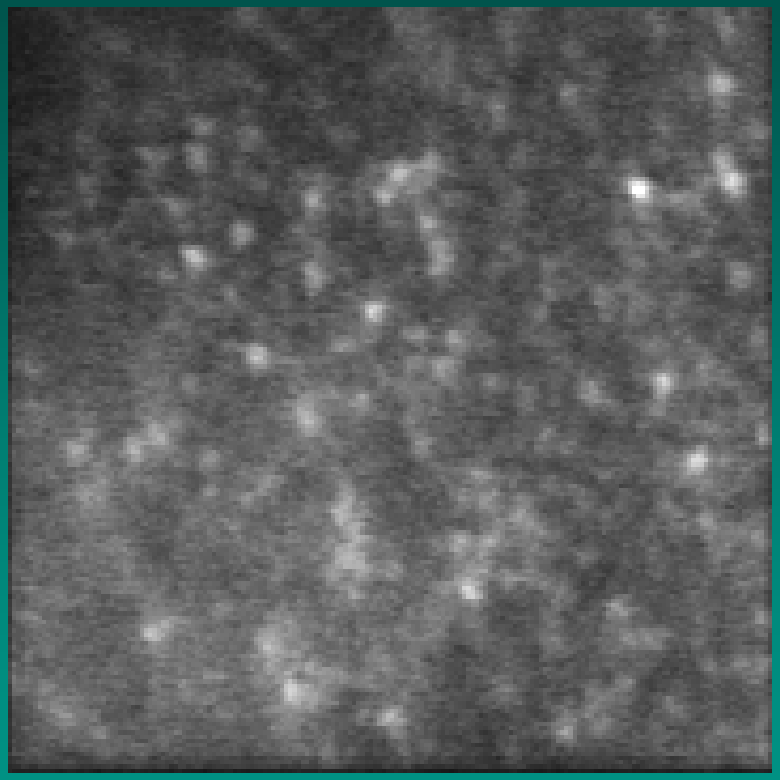
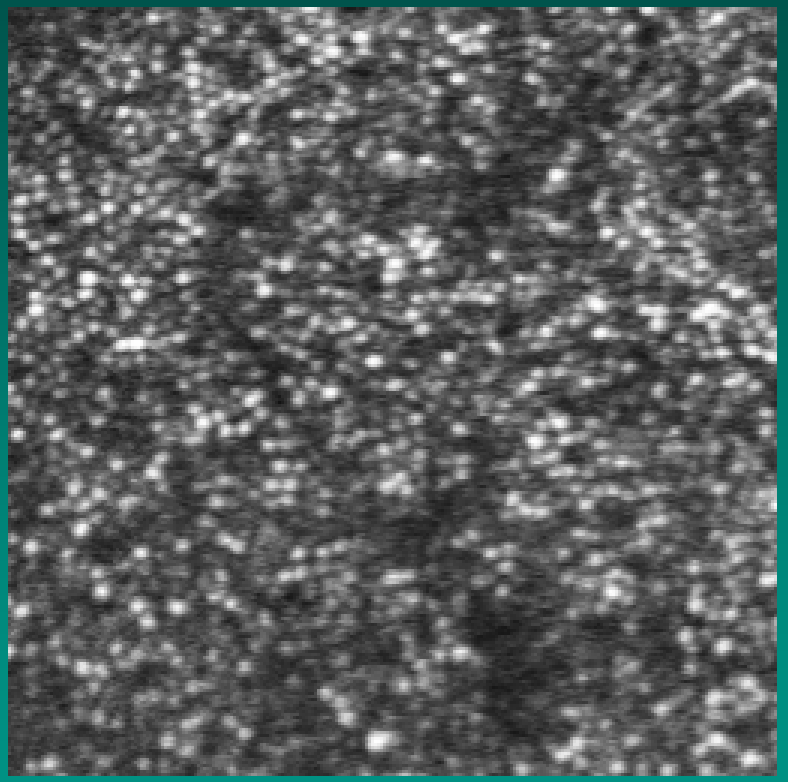
Retinal Imaging with Adaptive Optics



Uncorrected



Corrected

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Deformable Mirrors

Deformable mirrors from Xinetics

From 13 to 900 actuators (degrees of freedom), 3 - 15 inches in diameter

From Julian Cristou

Possible wavefront correcting devices

- membrane mirrors with actuators
- MEMS mirrors
- Ferrofluidic mirrors

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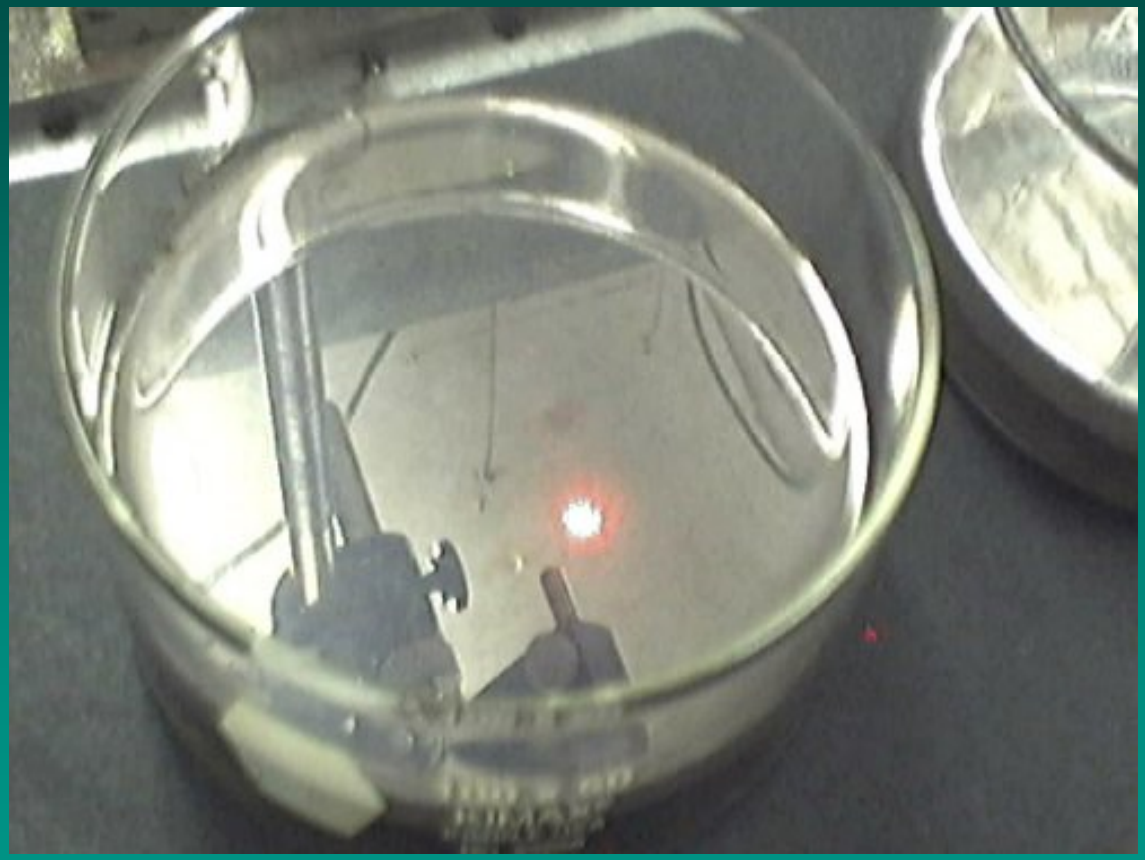
The Ferrofluid / MELLF Combination



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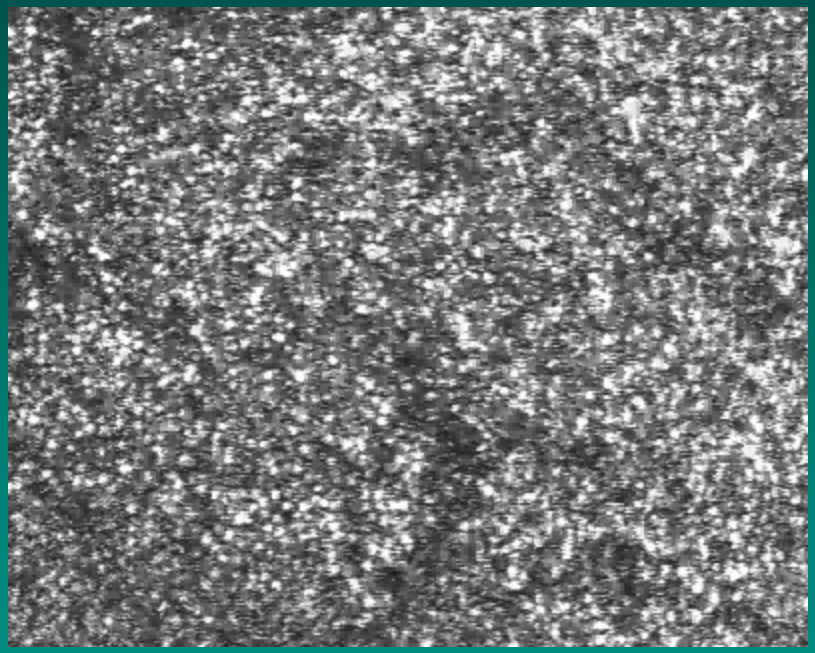
Adaptive Optics SLO



Roorda et al

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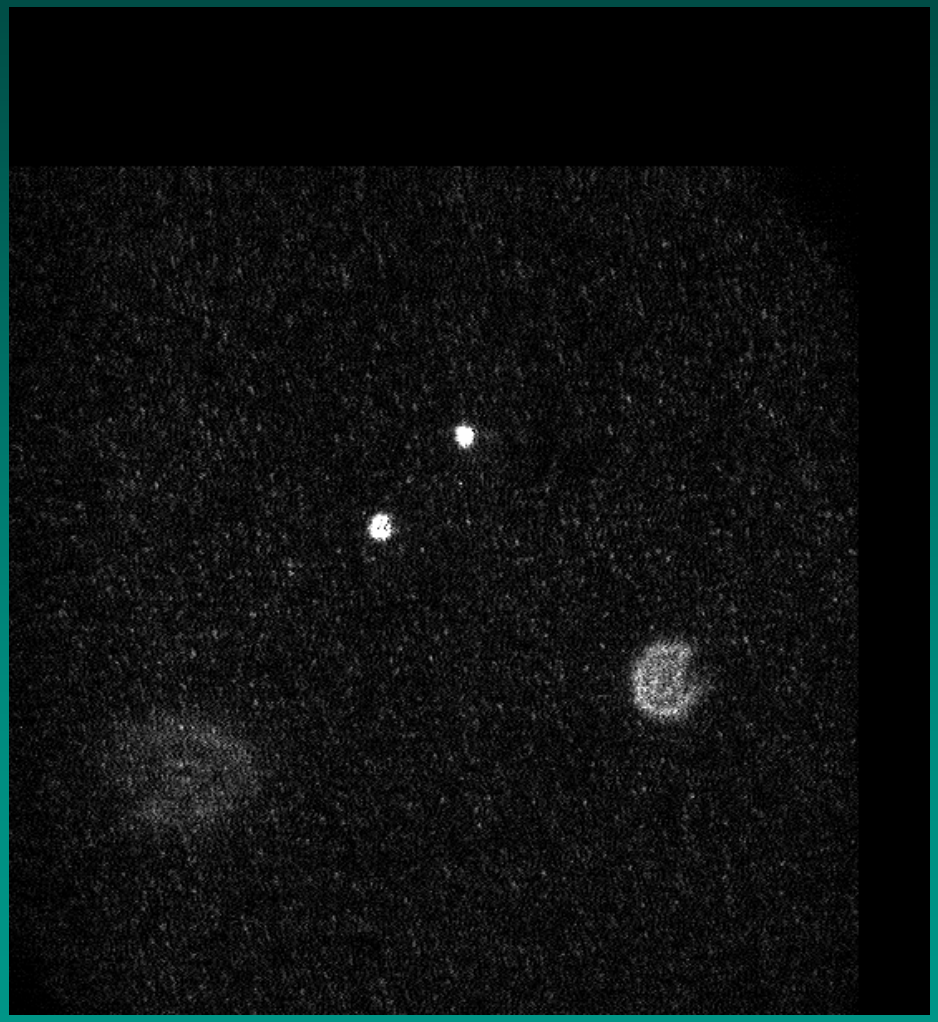
Photoreceptors during growth



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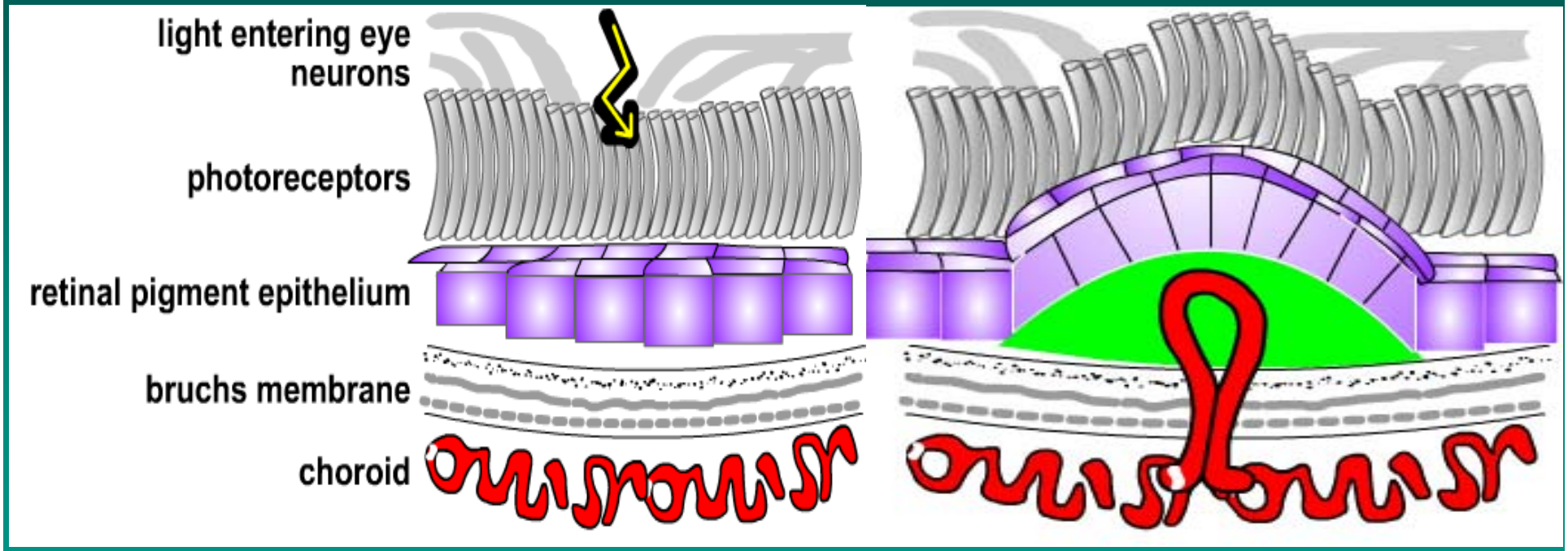
Age Related Macular Degeneration

Normal eye *AMD*



http://www.goodhope.org.uk/departments/eyedept/armd%20pathol.htm

Neovascularization in exudative ARMD

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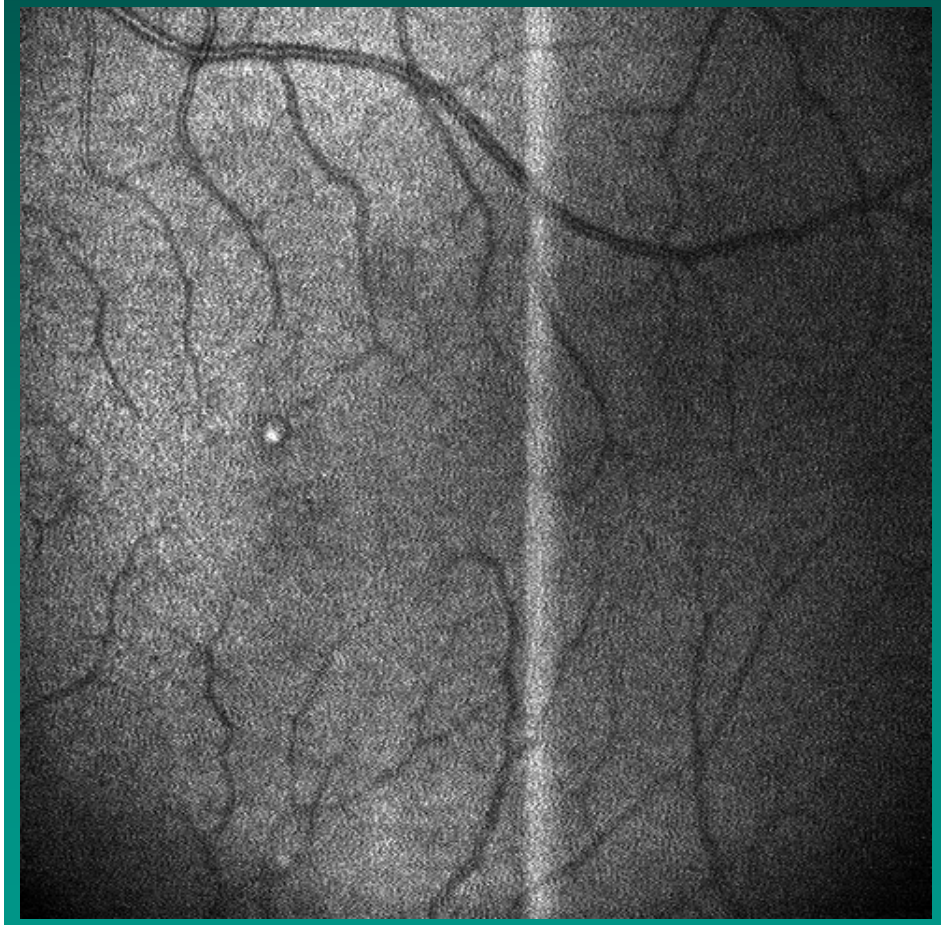
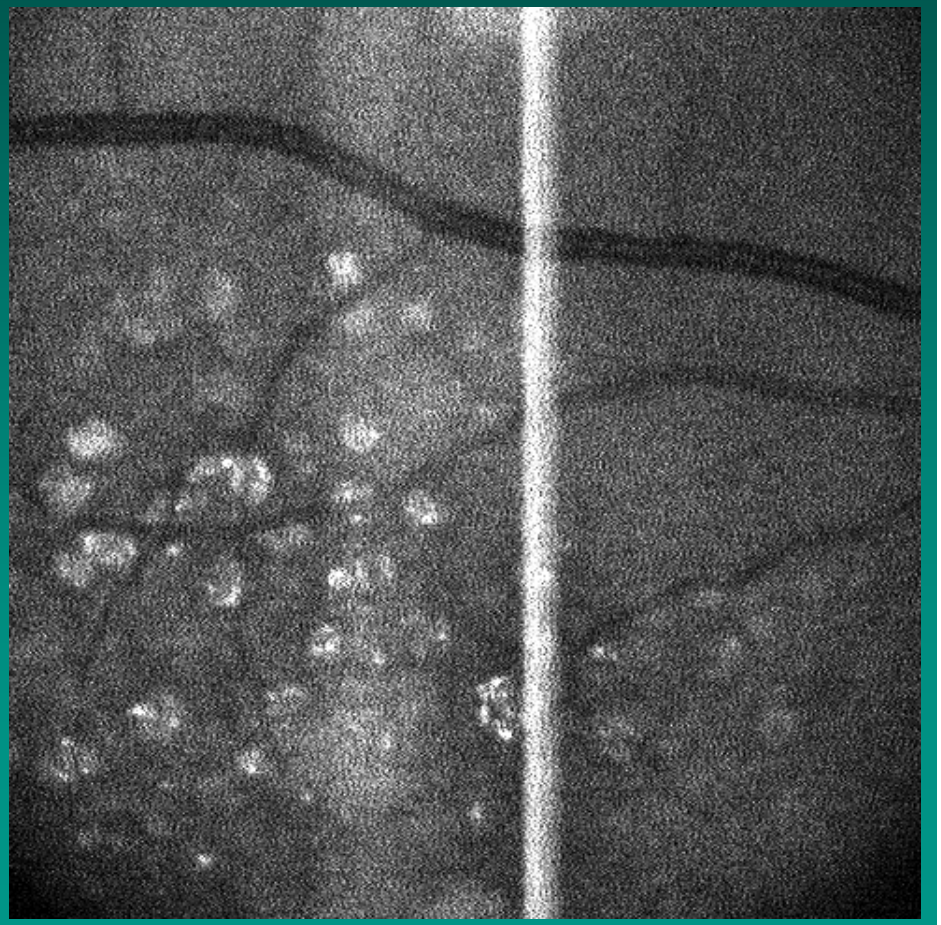
Early ARMD





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TPE-PDT

- **Photodynamic therapy is a proven therapy for AMD**
- **Two photon imaging has advantages which could be extended to therapy**
  - Localization of excitation
  - Penetration of infrared light
  - Less scattering of IR light
  - Higher damage thresholds for adjacent tissue

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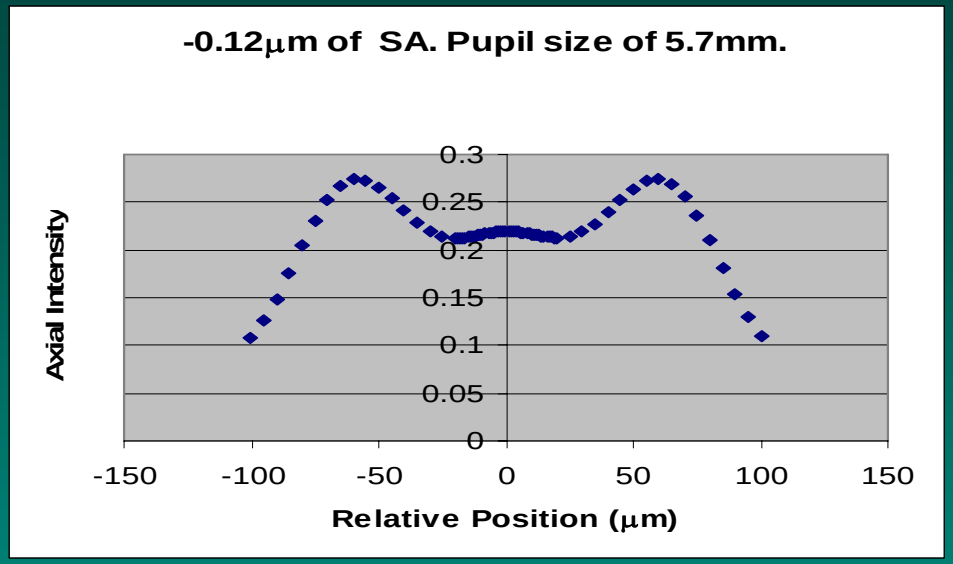
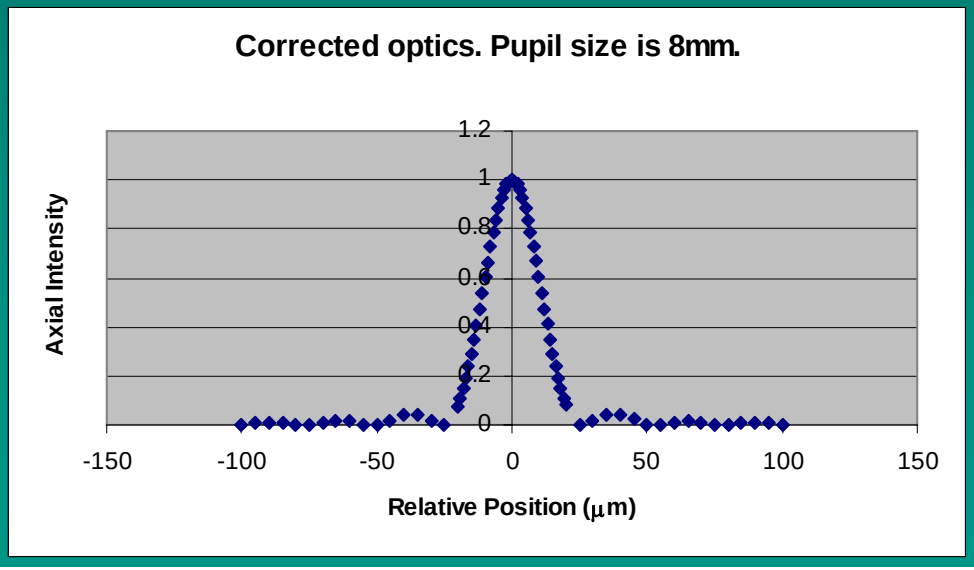
Probability of Drug Excitation

- varies with square of light intensity

uncorrected



AO corrected



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Advantages of Rat Model

Potential resolution in rat fundus images:

- Lateral resolution

$$Res = 1.22\lambda \frac{f}{d}$$

  - varies as f #, which is 3x lower in rat than human, so smaller details potentially resolvable

- Depth resolution

  - varies as square of f#, 10x improvement possible over human

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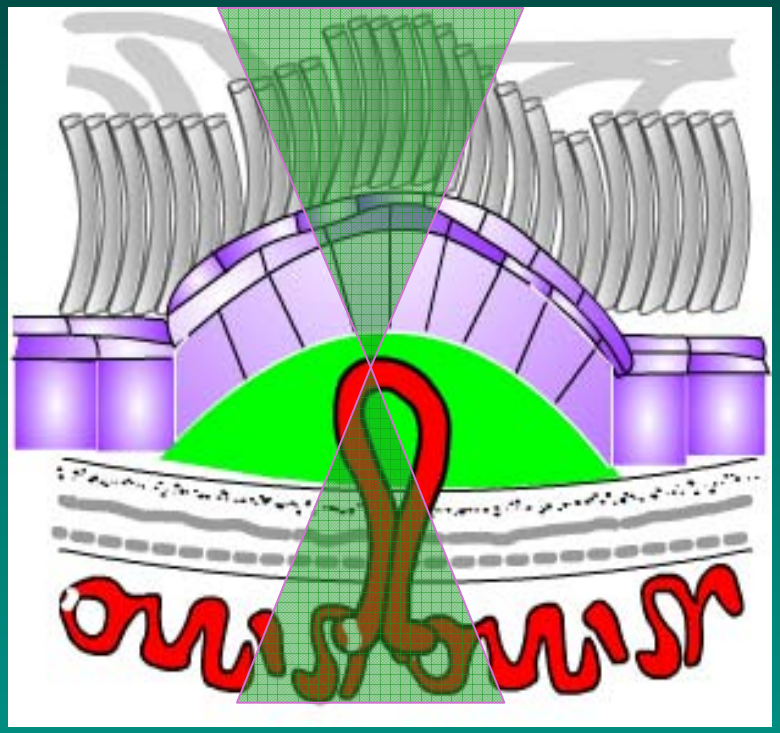
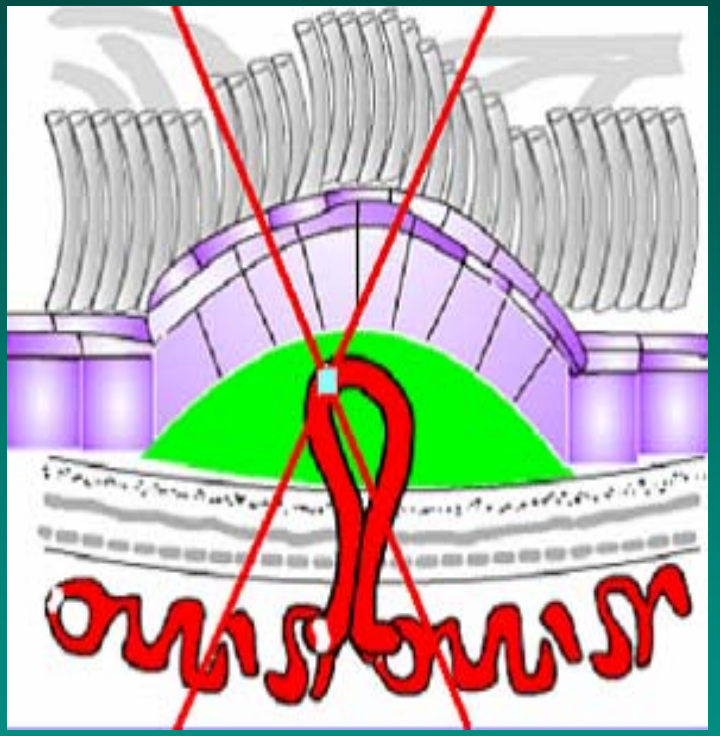
Two Photon Localization





Probability of 1 photon excitation α I

Probability of 2 photon excitation α I^2

Treatment localized to feeder vessels and neovascular membrane leakage

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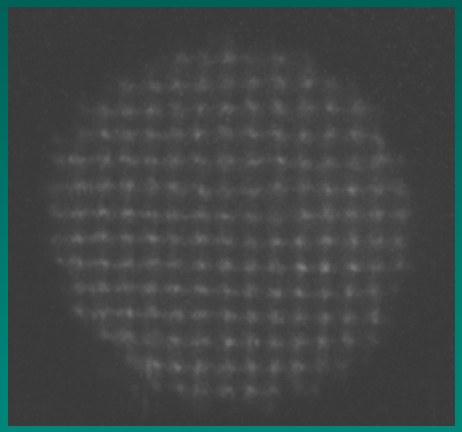
Hartmann Shack Measurements on Small Eyes



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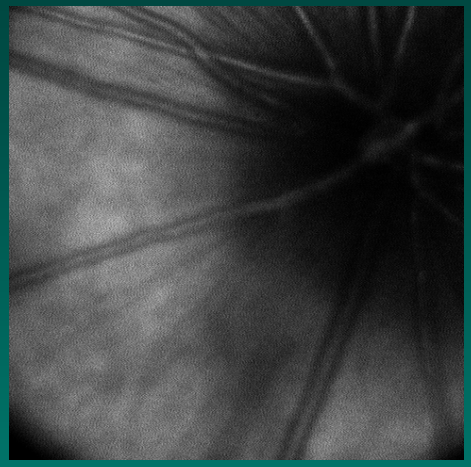
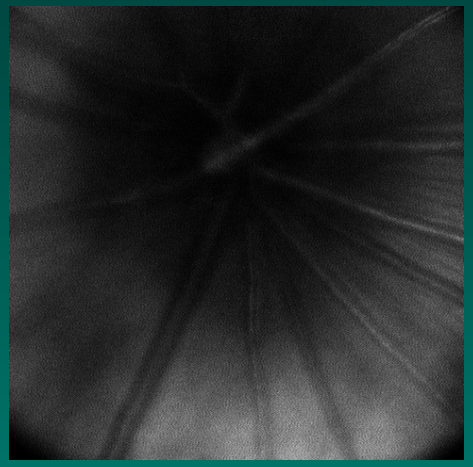
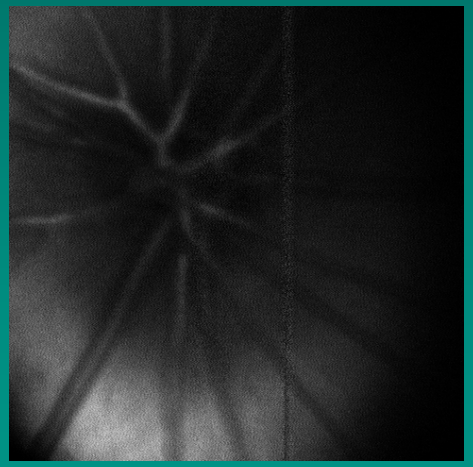
CSLO Images





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Mueller Matrix Polarimetry Methods

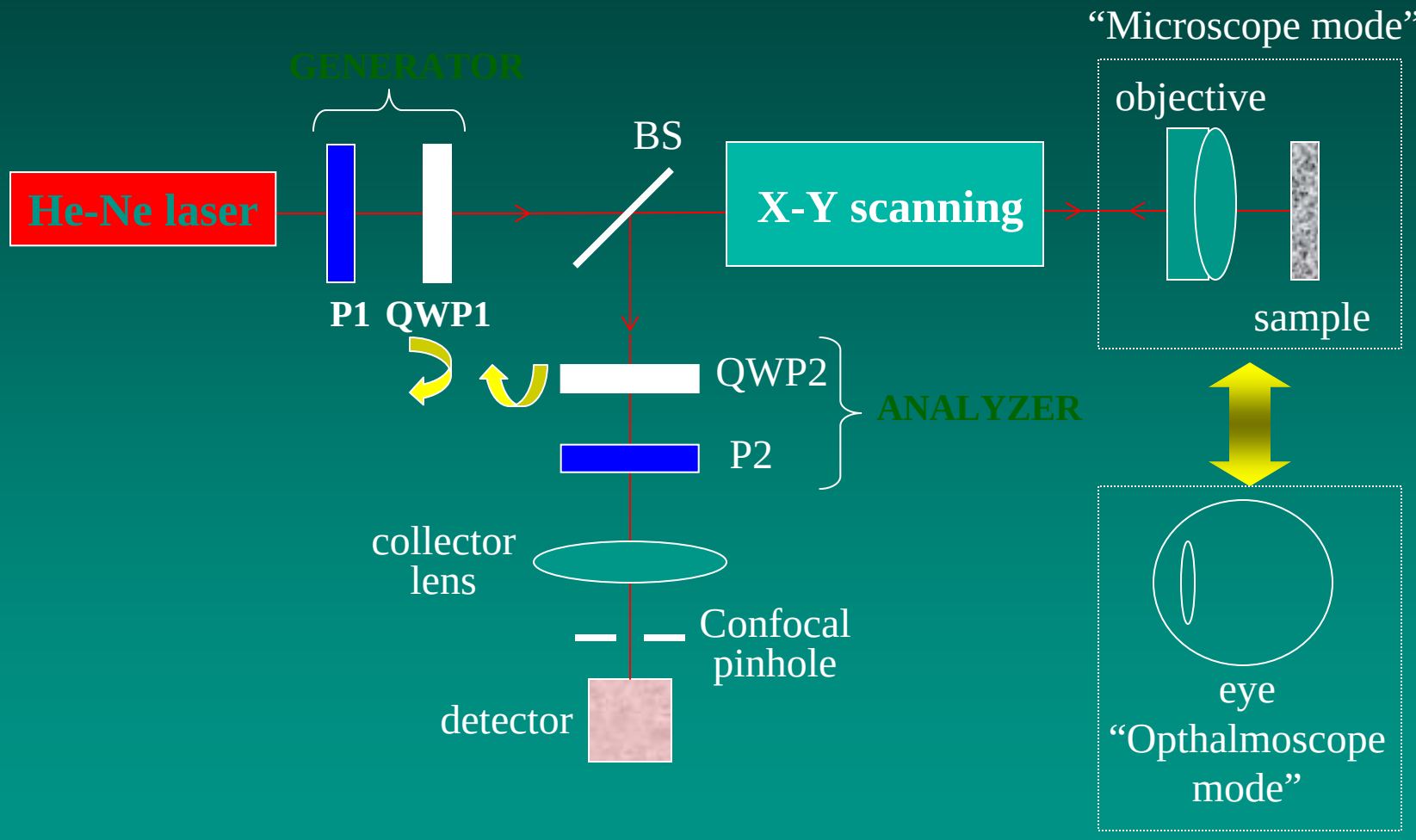

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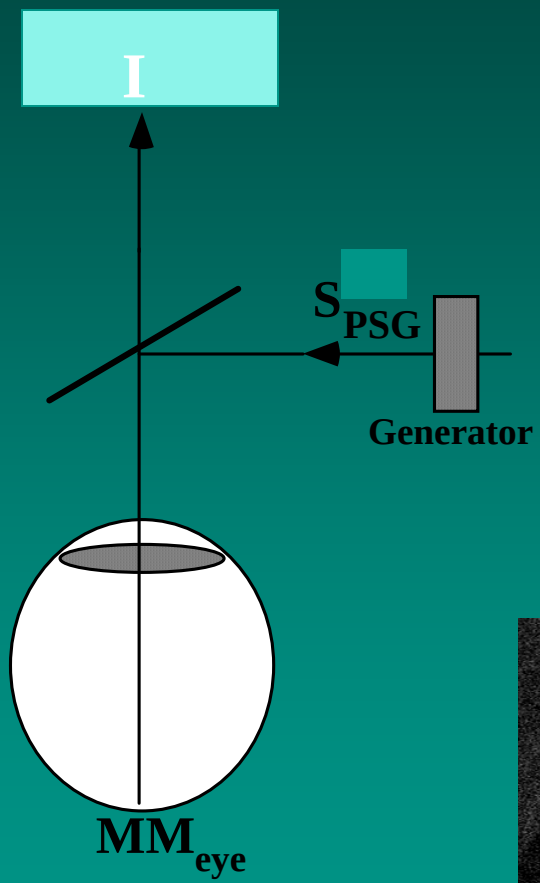
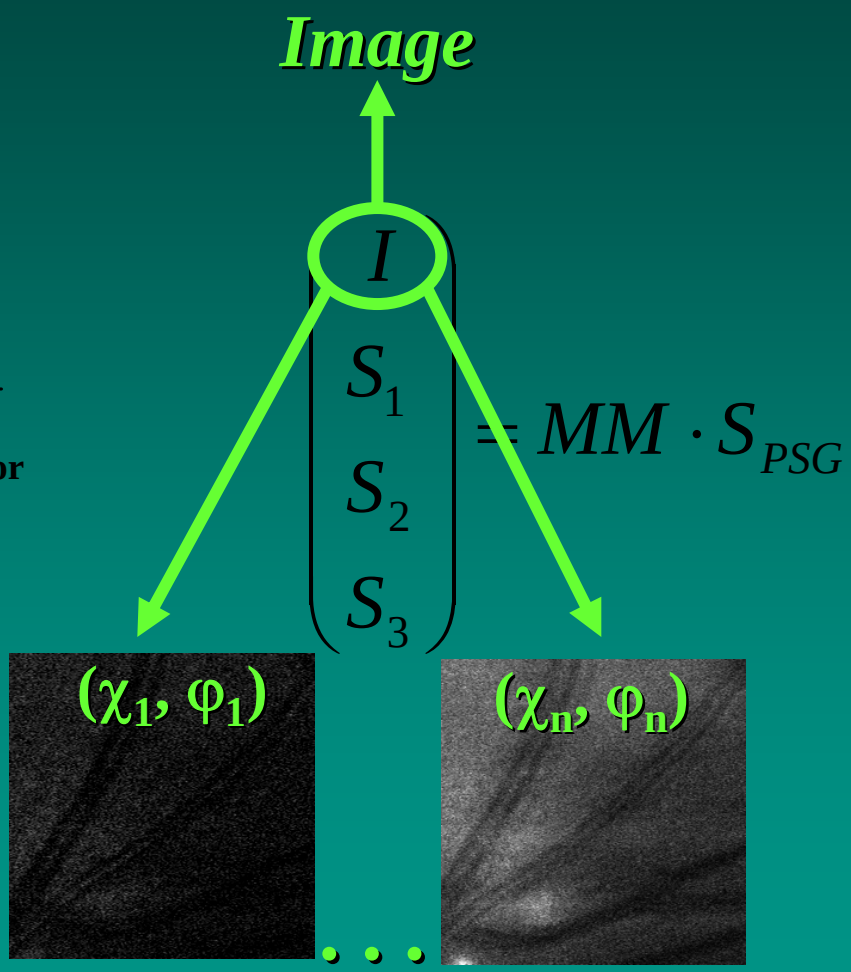
Image Reconstruction





$$SNR = \frac{mean\,(Int)}{stdv}$$

$$C = \frac{(I_{max} - I_{min})}{(I_{max} + I_{min})}$$

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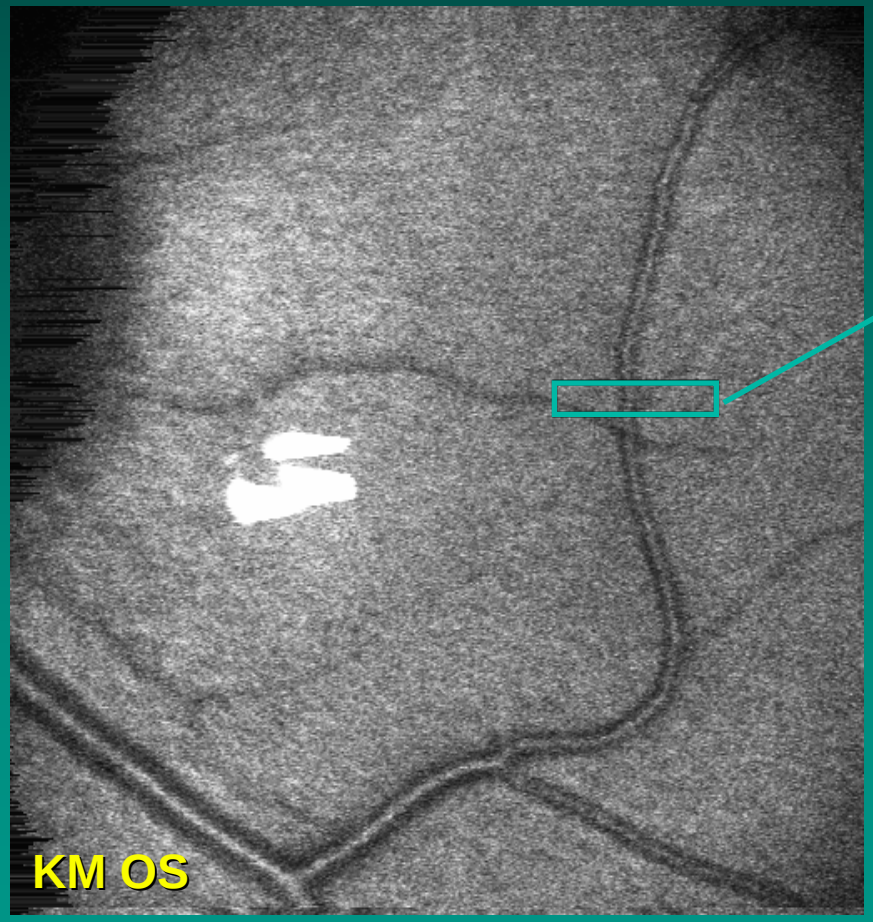
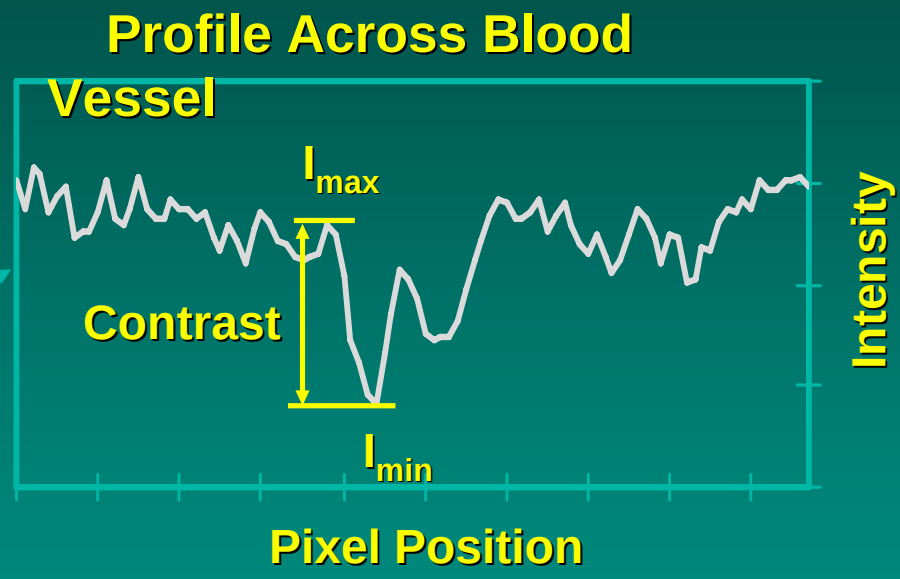
Contrast Measures





$$\text{Contrast} = \frac{I_{max} - I_{min}}{I_{max} + I_{min}}$$

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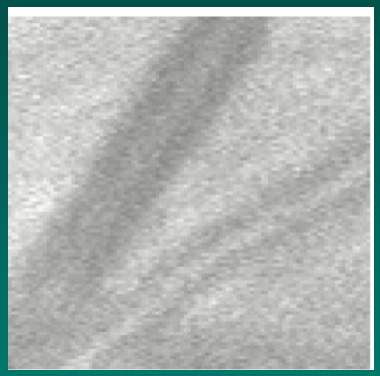
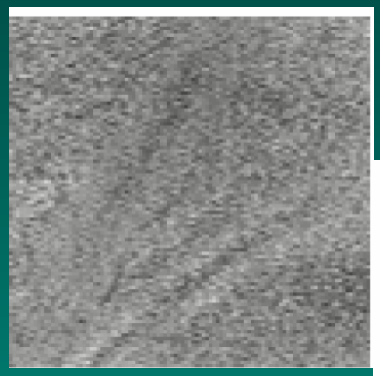
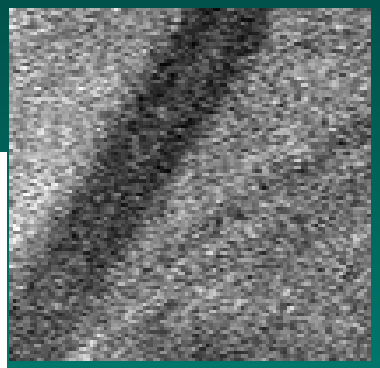
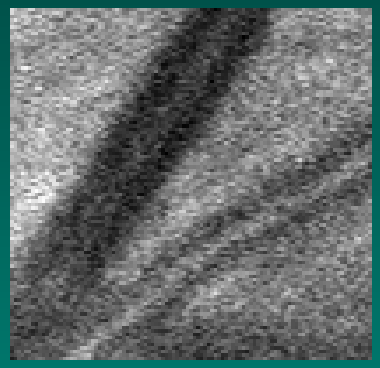
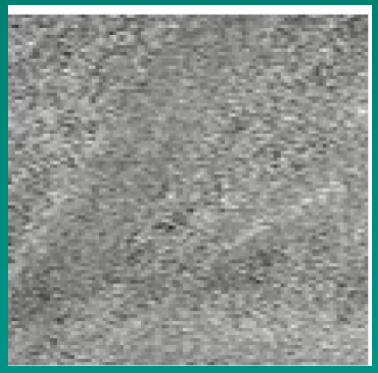
Mueller Matrix Polarimetry & Image Improvement

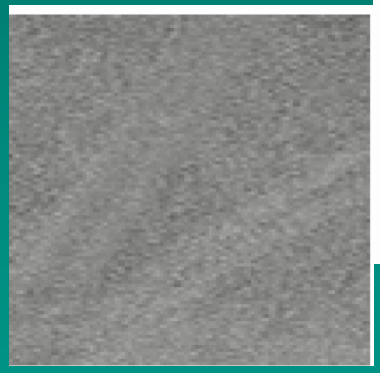


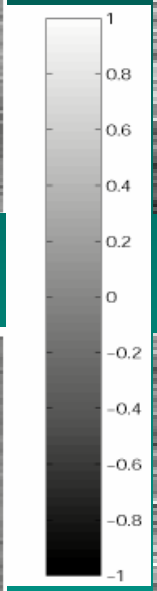


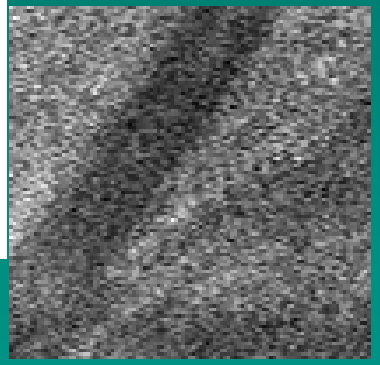


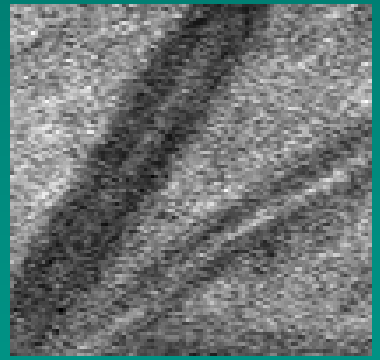












contrast of smaller vessel doubled

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Mueller Matrix Polarimetry (Image Quality Metrics)

M00

Max Acutance

Max Entropy

Max SNR

Min Acutance

Min Entropy

Min SNR

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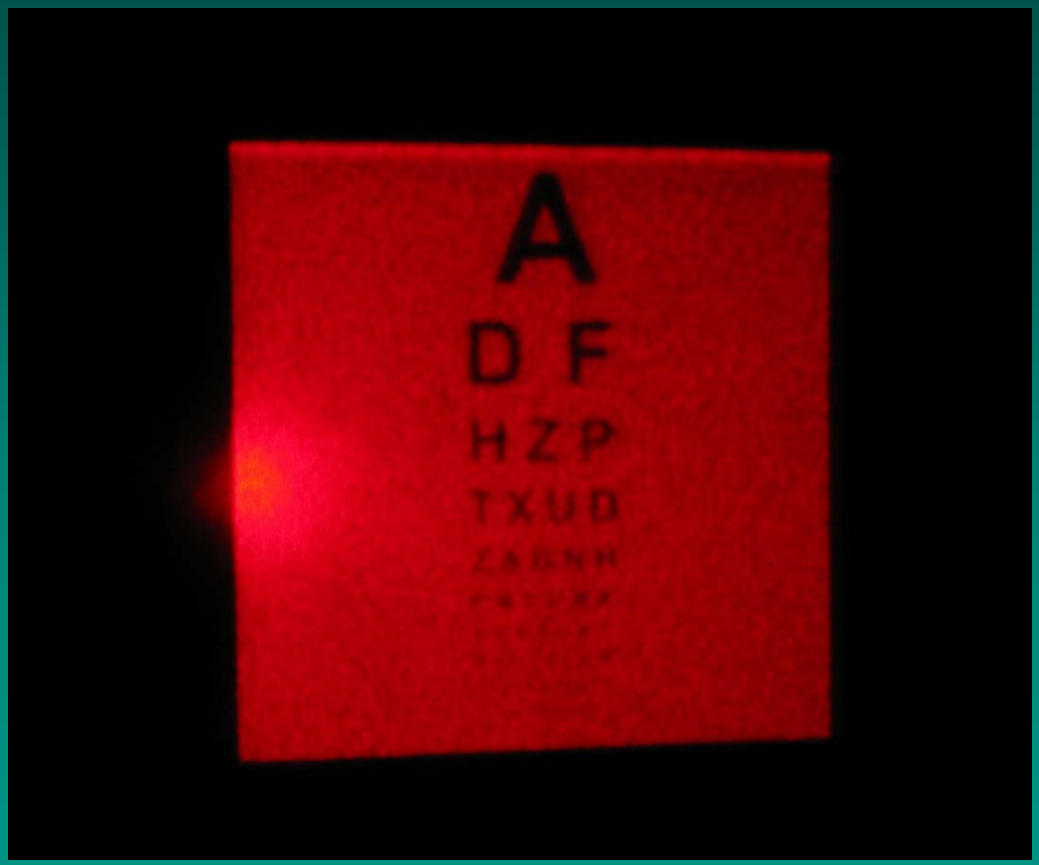
Retinal Writing by Laser Modulation



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Implications to Diagnosis and Treatment of Disease

- **Diagnosis of diabetic retinopathy, glaucoma, retinitis pigmentosa, AMD**
- **Study of normal and abnormal development in humans and animal models**
- **Structure and function in ocular disease**
  - visualization of structural damage
  - study of photodynamic therapy and novel therapies
  - projection of visual targets onto the retina
- **More accurate delivery of light therapy , 2 photon PDT**
- **Testing of therapy in animal models**

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Ongoing Work

- **Delivery of high light flux in a localized volume**
  - Better (and more usable) wavefront correction
  - Novel light sources and delivery
- **High contrast and high resolution imaging**
- **Animal models**
- **AO corrected OCT/CSLO**
- **Structure/Function relationships in diabetic retinopathy**
- **High resolution imaging of myopia development**

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  - Centre for Photonics, OCE, Ontario
  - NSERC Canada
  - Biomedical Photometrics Inc
  - Elcan Optical Technologies
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