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Review on the Applications of Adaptive Optics in Ophthalmology

Muaayed F. AL-Rawi¹, Mhnd Farhan²

¹ Al-Mustansiriyah University, Baghdad, Iraq, email: muaayed@uomustansiriyah.edu.iq

² Baghdad University, Baghdad, Iraq, email: mhndfarhan@yahoo.com

Abstract: *In ophthalmology, adaptive optics (AO) corrects optical aberrations in the eye in real time using deformable mirrors and wavefront sensors. Doctors can now examine individual photoreceptor cells, capillaries, and nerve fibers in the living eye thanks to this innovative technology that makes it possible to view retinal structures under a microscope without invasive surgery. The specific flaws in how light passes through the cornea and lens, two of the eye's natural optics, are measured by wavefront sensing. A sharp, diffraction-limited focus is produced by the deformable mirrors, which employ small, computer-controlled mirrors that precisely cancel out these aberrations. In order to increase their resolution to a cellular or subcellular level, adaptive optics is rarely used as a stand-alone device. Examples of such devices include the Scanning Laser Ophthalmoscope (SLO), which provides quick, high-contrast video streams of the retina, mapping cone mosaics, and observation. Additionally, AO is used in conjunction with Optical Coherence Tomography (OCT) to combine 3D cross-sectional tissue scanning and AO to provide remarkably clear images of the retina's various layers. Furthermore, AO-Microperimetry maps vision loss at the cellular level by connecting the precise physical structure of retinal cells with their localized functional sensitivity. The clinical significance of conventional diagnostic tools frequently identify retinal diseases such as diabetic retinopathy, glaucoma, and Age-related Macular Degeneration (AMD) after irreversible structural damage has already taken place. AO speeds up the development of targeted therapies and allows for real-time monitoring of treatment efficacy by enabling researchers and clinicians to examine the earliest microscopic indications of these conditions. Despite its enormous potential for clinical research, its widespread adoption in typical doctor's offices is constrained by high equipment costs. The aim of this paper is to provide brief explanation about the applications of adaptive optics in ophthalmology.*

Keywords: adaptive optics, imaging ophthalmology, diagnosis and monitoring

1. Introduction

The process of precisely distorting a mirror to correct for light distortion is known as adaptive optics (AO). It is utilized in optical fabrication for microscopy, retinal imaging systems (ophthalmoscopy to lessen optical aberrations), astronomical telescopes, and laser communication systems to eliminate atmospheric distortion. Adaptive optics measures the distortions in a wavefront and uses a device, like a liquid crystal array or a deformable mirror, to compensate for those errors. as displayed in Figure 1. A wavefront sensor (center) can be used to measure the wavefront of an aberrated image (left), which can then be adjusted using a deformable mirror (right). A wavefront sensor (center) can be used to measure the wavefront of an aberrated image (left), which can then be adjusted using a deformable mirror (right).

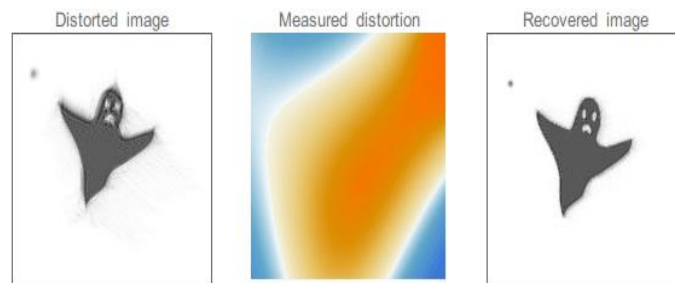


Figure 1. Illustration of removing distortion by AO

Figure 2 displays an illustration of an adaptive optics system that has been simplified. After the light strikes a tip-tilt (TT) mirror, the wavefront is corrected by a deformable mirror (DM). A beamsplitter (BS) taps off a portion of the light to the wavefront sensor and control hardware, which then transmits updated signals to the DM and TT mirrors.

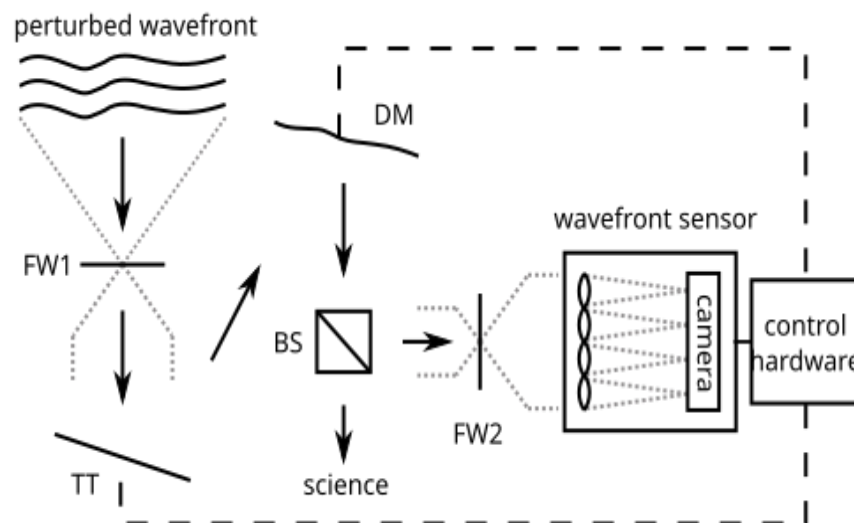


Figure 2. Simplified AO system

2. Applications of AO in Ophthalmology

Ophthalmology is one area where adaptive optics is useful. Ocular aberrations are distortions in the wavefront that travel through the eye's pupil. The quality of the image created on the retina is reduced by these optical aberrations, which occasionally call for the use of contact lenses or glasses. The microscopic structure (cells and capillaries) of the retina cannot be resolved in retinal imaging because light exiting the eye carries similar wavefront distortions. Defocus and astigmatism are examples of "low-order aberrations" that are corrected by spectacles and contact lenses. These abnormalities typically remain stable in people for extended periods of time (months or years). Correction of these is usually insufficient to achieve microscopic resolution, even though it is sufficient for normal visual functioning. To attain microscopic resolution, "high-order aberrations" like coma, spherical aberration, and trefoil must also be fixed. High-order aberrations are distinct from low-order ones.

The cornea, anterior chamber, lens, vitreous body, retina, and other components make up the majority of the human eye. The retina, which lines the inside of the eye, is a light-sensitive layer with an intricate structure. After processing the images that enter the eye through the lens, this layer transmits the signals to the brain via the optic nerve. Human eyes are sensitive to the wavelength and intensity of light and are not perfect refractive systems. Chromatic and monochromatic aberrations are produced when light enters the human eye. A single-wavelength light source can be used to compensate for chromatic aberrations. Monochromatic aberrations, on the other hand, are independent of wavelength and are influenced by a variety of intricate factors, such as changes in the cornea, lens, and tear film shapes. Low-order and high-order aberrations are two common classifications for monochromatic aberrations. Spherical and cylindrical lenses can be used to correct low-order aberrations, but as the human eye's pupil size increases, higher-order aberrations can drastically reduce lateral resolution and deteriorate retinal image quality. Because the human eye can reduce the impact of aberration on vision by altering the size of the pupils, people can see objects clearly in daily life. According to the diffraction limit formula, $r = 0.61\lambda/NA$ (where r is the resolution, λ is the imaging wavelength, and NA is the numerical aperture), these wavefront aberrations typically limit the resolution of human eyes to $\sim 10\text{--}15\ \mu\text{m}$, far from the theoretical lateral resolution of $\sim 2\ \mu\text{m}$. Figure 3 compares the wavefront shape of a normal eye with that of an ideal eye. After traveling through the normal refractive medium, light reflected from the fundus in an ideal eye forms a flat wavefront [1].

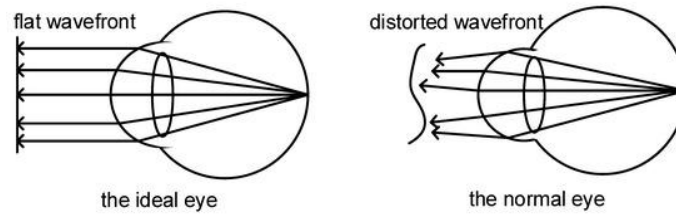


Figure 3. Wavefront shapes of ideal eye and normal eye

2.1. Measurement of ocular aberrations

A wavefront sensor is typically used to measure ocular aberrations, and the Shack-Hartmann is the most popular kind of wavefront sensor. Spatial phase nonuniformities in the wavefront leaving the eye are the cause of ocular aberrations. These are measured in a Shack-Hartmann wavefront sensor by positioning a CCD chip at the back focal plane of a two-dimensional array of tiny lenses (lens lets) in a pupil plane conjugate to the pupil of the eye. A centroiding algorithm is used to determine the locations of the spots that are focused onto the CCD chip by the lens lets. One can numerically reconstruct the wavefront information and estimate the phase nonuniformities causing aberration by comparing the positions of these spots with those of reference spots and using the displacements between the two to determine the local curvature of the wavefront.

In order to create images of individual cones in the living human eye, adaptive optics was initially used in flood-illumination retinal imaging. In addition to single cones, it has also been used in combination with scanning laser ophthalmoscopy to create the first images of retinal microvasculature, related blood flow, and retinal pigment epithelium cells in living human eyes. The first three-dimensional images of living cone photoreceptors have been obtained thanks to adaptive optics and optical coherence tomography [2].

2.2. Correction of ocular aberrations

A phase modulator, such as a deformable mirror, can be positioned at another plane in the system conjugate to the pupil of the eye to correct the local phase errors in the wavefront once they are known. The deformable mirror can be controlled by reconstructing the wavefront using the phase errors. As an alternative, the deformable mirror instructions can be computed directly from the local phase errors.

2.3. Open loop vs. closed loop operation

An operation is referred to as "open loop" if the wavefront error is measured prior to the wavefront corrector's correction. The operation is referred to as "closed loop" if the wavefront error is measured after the wavefront corrector has corrected it. In the latter scenario, the measured wavefront errors will be minimal, and measurement and correction errors are more likely to be eliminated. The standard is closed loop correction.

3. Literature Review

The control problem in adaptive optics systems for retinal imaging is extended to shape control for a flexible membrane that represents a deformable membrane mirror in [3]. The tracking of an unknown and time-varying shape for a distributed membrane is the shape control problem addressed because of the dynamic nature of the aberrations in the eye. Building a Q-parameterized set of stabilizing controllers for the system in question and online Q-parameter tuning to bring the controller closer to the controller required to achieve regulation are the foundations of the suggested controller design method. To enable tuning based on decentralized adaptation algorithms, partial decoupling of the dynamics of the multi-input, multi-output closed loop system is introduced.

A flood-illuminated adaptive optics ophthalmoscope for multilayer imaging of the retina is presented in [4]. The area of the retinal layer that is illuminated can be altered by setting up an adjustable stop in the illumination path. A narrow aperture stop creates a laser beacon for wavefront sensing. The imaging field is expanded and flood illumination is made possible by the large aperture. A movable imaging camera can concentrate on various retinal layers. In the confirming experiment, a 25-year-old Chinese male in good health was imaged. The layers of nerve fibers, blood vessels, and photoreceptors were clearly visible.

The quality of in vivo images of cellular structures in the human retina has improved as a result of recent advancements in retinal image acquisition methods, such as optical coherence tomography (OCT) and scanning laser ophthalmoscopy (SLO), as well as enhanced performance of adaptive optics (AO) equipment as illustrated in [5]. The authors provide a brief overview of the development of AO-OCT instruments in this section. Even though imaging speed and resolution have significantly increased, eye movements that occur during the acquisition of a retinal image with OCT cause motion artifacts in the image, making analysis and registration more difficult. This effect is particularly noticeable in high-resolution datasets obtained using AO-OCT equipment. Retinal motion during data acquisition has been corrected by a number of retinal tracking systems. The authors describe a technique for simultaneously captured adaptive optics-scanning laser op to correct motion artifacts in AO-OCT volume data after acquisition.

A technique for automatically segmenting retinal artery walls in adaptive optics images is presented by the authors in [6]. To the best of our knowledge, this is the first technique to deal with this issue in these kinds of pictures. In order to accomplish this, we suggest modeling these walls as four curves that are roughly parallel to a common reference line that is situated close to the vessel's center. In order to address deformations along vessels, the curves are simultaneously positioned as close to the wall borders as possible using an original tracking procedure once this line has been identified. A deformable model that incorporates a parallelism constraint is then used to fine-tune their placement. By using this method, we can increase the curves' resilience to image noise and regulate how far they are from their reference line. By contrasting the outcomes with

physician segmentations, this model was assessed on healthy individuals. Notably, this model introduces an error that is either very close to or smaller than the inter-physician error.

The authors in [7] suggest a novel technique for retinal vessel segmentation in adaptive optics images. Although it is accurate for vessels with moderate or no alteration, this method is specifically designed for segmenting vessels with significant morphological changes brought on by vasculitis. The robustness and accuracy of the results depend on a pre-segmentation step. This step is based on a particular morphological processing of the original image's isolines, which provide a solid foundation for segmentation due to their placement along the vessel wall borders. The active contour model embedding a parallelism constraint is then used to carry out regularization. This innovative model enables accurate segmentation of the vessel's inner and outer walls. Specifically, compared to current methods, it is more accurate in the case of vasculitis. This approach is the only one that permits quantification. It can be used in clinical settings due to the results and runtime.

Adaptive optics has been used in [8] to resolve the cellular features in retinal imaging. Using the image quality as a guide for the aberration correction, the authors are researching wavefront sensorless adaptive optics (WSAO) for optical coherence tomography and scanning laser ophthalmoscopy. The authors of this report look into open loop performance characterizations.

Retinal pigment epithelial (RPE) cells are crucial for the nourishment of retinal neurosensory photoreceptor cells [9], and RPE defects are linked to a number of blinding disorders. Using adaptive optics (AO) imaging in conjunction with indocyanine green (ICG), their fluorescence signature can now be seen in the living human eye. This encourages us to create an automated RPE detection technique to enhance the quantitative assessment of RPE status in patients. With precision, recall, and F1-Score of 93.6 $\pm$ 4.3 percent, 81.4 $\pm$ 9.5 percent, and 86.7 $\pm$ 5.7 percent, respectively, this paper suggests a spatially-aware, Dense-LinkNet-based regression approach to enhance the detection of in vivo fluorescent cell patterns. These findings show how a deep learning-based regression framework for cell detection can benefit from the addition of spatial inputs.

Early detection is crucial for the successful treatment of retinopathy. In [10], Adaptive optics scanning laser ophthalmoscopy is a promising cellular-level imaging method for early retinopathy detection. The authors suggest combining retinal photoreceptor identification results on ophthalmoscope images using an automated ensemble method. To improve the accuracy of retinal photoreceptor identification, the various identification results are combined with the corresponding ground truth that is produced by simulation. By comparing the generated and ensemble retinal photoreceptor identification results with the ground truths in terms of precision, recall, and F1-score, ensemble method's efficacy is shown. This indicates that the suggested approach can enhance retinal photoreceptor identification.

As a broad category that includes virtual reality (VR), mixed reality (MR), and augmented reality (AR) technology, extended reality (XR) faces a significant default-practice constraint in [11]. The need for users to wear corrective contact lenses or not have vision issues. Many people are unable to wear contact lenses because of discomfort, allergies, dryness, or restrictions following refractive surgery. This paper explores physics-based approaches to resolve this conflict, with a particular emphasis on the creative incorporation of adaptive optics. We envision an XR future where adaptive optics, eye-tracking, and light field displays combine to create an immersive experience free from the limitations of conventional visual corrective aids, drawing inspiration from previous research and current technological developments.

The authors in [12] suggested a two-step process in which specialized active contour models were started from a deep learning-extracted binary mask of the vessels. Since the accuracy of the biomarker heavily depends on the quality of the binary mask, the authors of this paper examine a number of deep neural network architectures. Experiments demonstrate that we can accurately recover the vessel binary mask (mean accuracy of 98.59 percent) using the DeepLabV3+ model in conjunction with the Xception backbone.

The goal of paper in [13] is to quantify biomarkers from retinal artery segmentation in adaptive optics ophthalmoscopy (AOO) images. Methods: To achieve an accurate segmentation of the vessel walls with a focus on bifurcations, deep learning and knowledge-driven deformable models are combined in this method. The resulting segmentation yields biomarkers (junction coefficient, branching coefficient, wall to lumen ratio (wlr)). Findings: dependable and precise measurements and segmentations ($mse = 1.75 \pm 1.24$ pixel) are obtained, with high reproducibility concerning image acquisition and users, and without bias. Significance: An elevated WLR was discovered in a preliminary clinical study of patients with a genetic small vessel disease, some of whom had vascular risk factors, compared to a control group.

A dense residual adversarial network (DRAN) that can restore degraded AO retinal images under various residual aberrations and optical artifacts is the goal of the paper in [14]. In order to improve feature propagation and reduce gradient degradation, our DRAN architecture combines a patch-based discriminator with dense residual blocks in the generator. The authors thoroughly test DRAN on artificially created AO retinal datasets with a range of noise levels, AO correction capabilities, and complex imaging artifacts, such as motion blur, light transmission disturbance, and retinal artifact. DRAN achieves restoration performance with 37.42 dB PSNR and 0.9873 SSIM in imaging conditions with a signal to noise ratio of 38 dB. More significantly, authors's approach maintains strong performance with 29.90 dB PSNR and 0.9506 SSIM when exposed to several complex imaging artifacts. Our DRAN demonstrates greater robustness and generalization under complex clinical artifacts when compared to current learning-based AO restoration techniques, underscoring its potential importance for clinical ophthalmology and diagnostic analysis.

4. Discussion and Conclusions

In an optical system with dynamic aberrations, AO is utilized for real-time aberration compensation to enhance image or beam quality. The cellular and metabolic aspects of the human eye have been profoundly altered by the application of AO-based optical imaging in ophthalmology. AO provides a lateral resolution of about 2 μm , which is not possible with conventional retinal imaging methods (lateral resolution: $\sim 10 - 15 \mu\text{m}$), by correcting the individual optical aberrations. As a result, AO-based retinal imaging technology improves clinical interventions for various eye diseases in addition to helping scientists resolve fine retinal structures.

In conclusion, the use of AO in ophthalmology will unavoidably become one of the key tools for assisting medical professionals in investigating the etiology of different eye conditions, monitoring patients, and encouraging the creation of cutting-edge tools and treatments for refractive surgery and retinal diagnostics.

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