Refractive Adaptive Optics for Ophthalmoscopy

Phaseform develops refractive Adaptive Optics (AO) systems based on innovative hardware and software components. At the heart of our AO approach is a novel optofluidic microsystem technology called Deformable Phase Plates (DPP). These combine the advantages of deformable mirrors and transmissive liquid crystal spatial light modulators in a compact form, paving the way for a new class of ultra-compact, high-efficiency, transmissive AO systems. In this white paper, we discuss how DPP technology can transform the burgeoning field of AO-ophthalmoscopy.

The human visual system is a remarkable and complex organ that has evolved over millions of years. Not only are its intricate inner workings fascinating, but certain structural “quirks” also highlight a seemingly incidental arrangement. One notable example is the retina—a multilayer at the back of the eyeball containing photoreceptor cells (cones and rods) that initiate nerve impulses. These impulses travel through interneurons to the optic nerve and ultimately to the brain, where they are processed to form visual images.

Interestingly, for light to reach the retina, it must first pass through several transparent cell layers before reaching the photoreceptors. This arrangement provides an opportunity for direct observation: with advanced optical instruments, we can look through the pupil and study these intricate structures. Many diseases of the human visual system manifest early on as subtle changes in these retinal layers. Because of its complexity, the eye is not just a window on the world—it can also be a window on our health.

Ophthalmoscopy is the technique of using high-magnification optical imaging to visualize the retina, optic nerve, blood vessels, and macula. Several advanced microscopy-based methods are adapted for ophthalmoscopy, each with advantages and disadvantages: Fundus photography (FP) provides high-quality, single-frame retinal images at a high frame rate but is limited in resolution and contrast [1]. Scanning laser ophthalmoscopy (SLO) improves resolution and contrast and offers some axial sectioning capability, yet sacrifices imaging speed [2]. Optical coherence tomography (OCT) further improves axial sectioning and uniquely provides a cross-sectional view of the entire retina [3].

Unlike microscopy—where maximum resolution is defined by the objective lens and immersion medium—ophthalmoscopy is different. Here, the patient’s eye itself defines both the aperture (the pupil) and the focal length (the lens). A fully dilated pupil (~7–8 mm) offers a theoretical resolution of about 2 µm at visible wavelengths, potentially sufficient to resolve cellular and even subcellular details (e.g., photoreceptors and retinal ganglion cells). However, the human eye is far from a perfect “imaging device”; imperfections cause optical aberrations that worsen as the pupil size increases. Beyond about 2 mm in dilation, conventional ophthalmoscopes often struggle to resolve retinal features at the cellular level. This limitation is significant because many major eye diseases—such as macular degeneration,

diabetic retinopathy, and glaucoma—can be detected early by observing microscopic changes in the retina. The "imperfect eye" thus reduces the effectiveness of standard in vivo ophthalmoscopic diagnostics.

Enter Adaptive Optics

Ocular aberrations vary from patient to patient ("every human eye is different") and are generally static or change only slowly. Nearly three decades ago, correction elements originally developed for astronomical telescopes—where they compensate for atmospheric turbulence—were first introduced into ophthalmoscopy [6]. This "technology transfer" triggered a new era in ophthalmic research, allowing the in vivo visualization of cellular and even subcellular retinal features for the first time. Since then, continued research and development have integrated AO into almost all types of ophthalmoscopes, yielding answers to a wide range of scientific questions about retinal morphology and function. It has also led to the identification of definitive biomarkers for early diagnosis of major eye diseases.

Conventional approach to AO Ophthalmoscopy

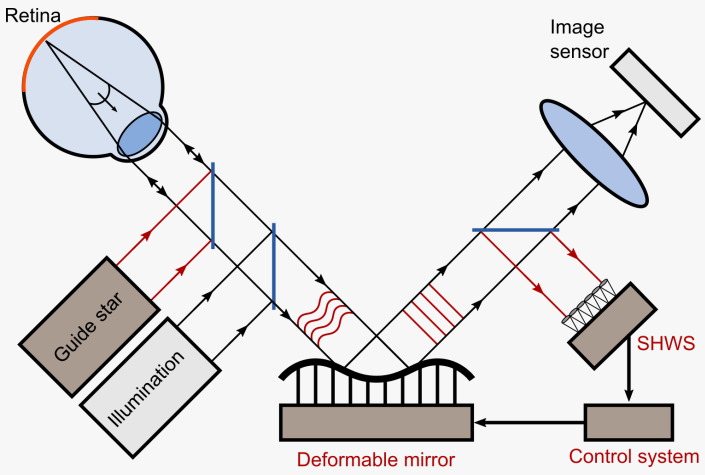

Figure 1: Conventional adaptive optics ophthalmoscope: Eye aberrations are measured with a wavefront sensor, which in closed-loop controls a deformable mirror placed at the conjugate plane of the pupil. This schematic omits the details of the varying illumination and detection optics, as these specifics can change significantly based on the microscopy method used by the instrument.

Figure 1 shows a simplified representation of a standard adaptive optics (AO) design for ophthalmoscopy. To incorporate AO, the system typically includes: 1) a wavefront modulator, usually a reflective deformable mirror (DM), 2) a Shack-Hartmann wavefront sensor (SHWS), and 3) a laser guide star originating from a known point on the retina.

The SHWS measures the distorted wavefront. A control system then computes drive signals that instruct the DM to approximate the inverse of the measured wavefront error. Closed-loop operation continues until the best possible image quality is found after several iterations. Both the DM and SHWS must be conjugated to the pupil plane, often requiring additional relay optics and beam folding. Consequently, the system can become large, complex, and costly, and clinical adoption of AO remains slow. AO ophthalmoscopes therefore often remain confined to large research labs, out of easy reach for clinical applications.

Phaseform's refractive AO solutions provide a new way forward. Their aim is not only to reduce the size and complexity of new systems but also to add AO capability to existing ophthalmoscope infrastructures—opening unprecedented opportunities in ophthalmology.

Phaseform's Approach to AO Ophthalmoscopy

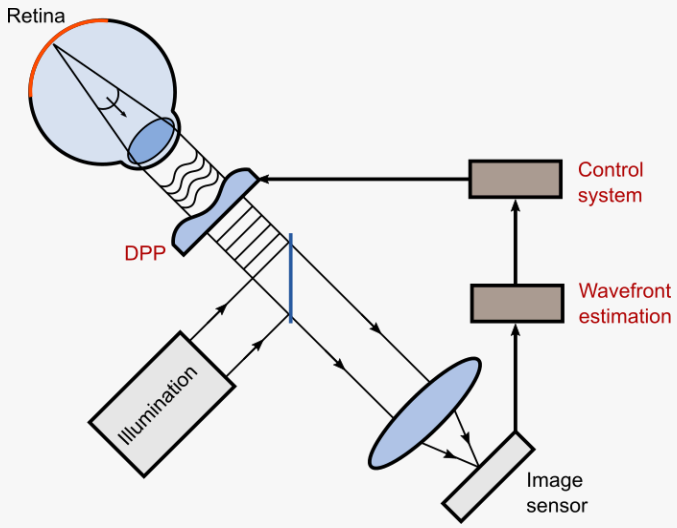

Figure 2: Phaseform's approach to AO ophthalmology. A Deformable Phase Plate (DPP) is placed in close proximity to the eye's pupil. This approach does not require relay or beam folding optics and the SHWS can be omitted by using a wavefront estimation technique.

Figure 2 illustrates Phaseform's AO approach for ophthalmoscopes, enabled by its Deformable Phase Plate (DPP) technology. DPPs are refractive, optofluidic counterparts to conventional continuous-surface deformable mirrors. The clear aperture diameter of ~10 mm covers the maximum human pupil diameter of 7–8 mm. Hence, it can be placed near the pupil without requiring major optical redesign or additional relay optics.

This eliminates much of the alignment complexity and reduces space requirements—problems that typically arise from beam folding in conventional AO ophthalmoscopy. Moreover, the Shack-Hartmann sensor can be omitted by employing sensorless wavefront estimation algorithms, which rely directly on captured images. These algorithms iteratively compute the best control signals for the DPP to optimize image quality. Crucially, such sensorless methods require a hysteresis-free and deterministic adaptive element, which the DPP provides.

By making AO integration more compact and straightforward, this approach enables the retrofit of AO capability into existing ophthalmoscopes—sometimes in just a few hours. It thereby paves the way for new, clinically viable AO-ophthalmoscopy solutions.

A CASE STUDY: Full-field OCT ophthalmoscope with *Truly Plug & Play* AO

In a recent landmark study, in collaboration with vision scientists at the Institut Langevin, Quinze-Vingts National Ophthalmology Hospital, and the Vision Institute (all in Paris), researchers retrofitted a research-grade ophthalmoscope with a DPP-based AO system. Specifically, they used a multimodal full-field OCT ophthalmoscope known for achieving unprecedented imaging speed and field of view in retinal imaging [7,8]. Although state-of-the-art, its optical quality was limited by patient-specific eye aberrations. By adding AO, the instrument could theoretically reach a higher performance level.

Dr. Pedro Mecê and colleagues (Dr. Kate Grieve and Dr. Maxime Bertrand) wanted to enhance the instrument's imaging capabilities cost-effectively and compactly—thus ruling out a conventional DM-based AO system. Instead, they opted for Phaseform's refractive AO approach.

Figure 3: Retrofitting Phaseform's refractive AO system to an existing full-field OCT ophthalmoscope at the Institut Langevin. The only hardware change that was necessary for the AO upgrade was to introduce a DPP after the last lens in the system that is placed in front of the patient's eye (left). By feeding the instrument's image data into Phaseform's AO sensorless wavefront estimation algorithm, the integration was complete. The imaging workflow after AO integration remained mostly intact, the only exception being the aberration estimation step, which took about 3 seconds. The rest of the retinal image acquisition procedure proceeded as usual.

At the Institut Langevin, the AO upgrade involved simply inserting a DPP into the imaging aperture in front of the patient's eye (Figure 3). The existing instrument housing was compatible with standard laboratory components, so the hardware integration took only minutes. Additional software integration allowed sensorless wavefront measurement, using a modal decomposition–based aberration estimation routine. This process relies solely on the imaging modality itself (in this case, spectral domain OCT data) and takes only a few seconds.

During the imaging session, the main workflow stayed largely intact, aside from the extra few seconds needed for aberration estimation before acquisition. After that, the patient simply sat in front of the instrument (Figure 3, right), and the imaging proceeded as usual—but with optical aberrations now actively corrected by the DPP.

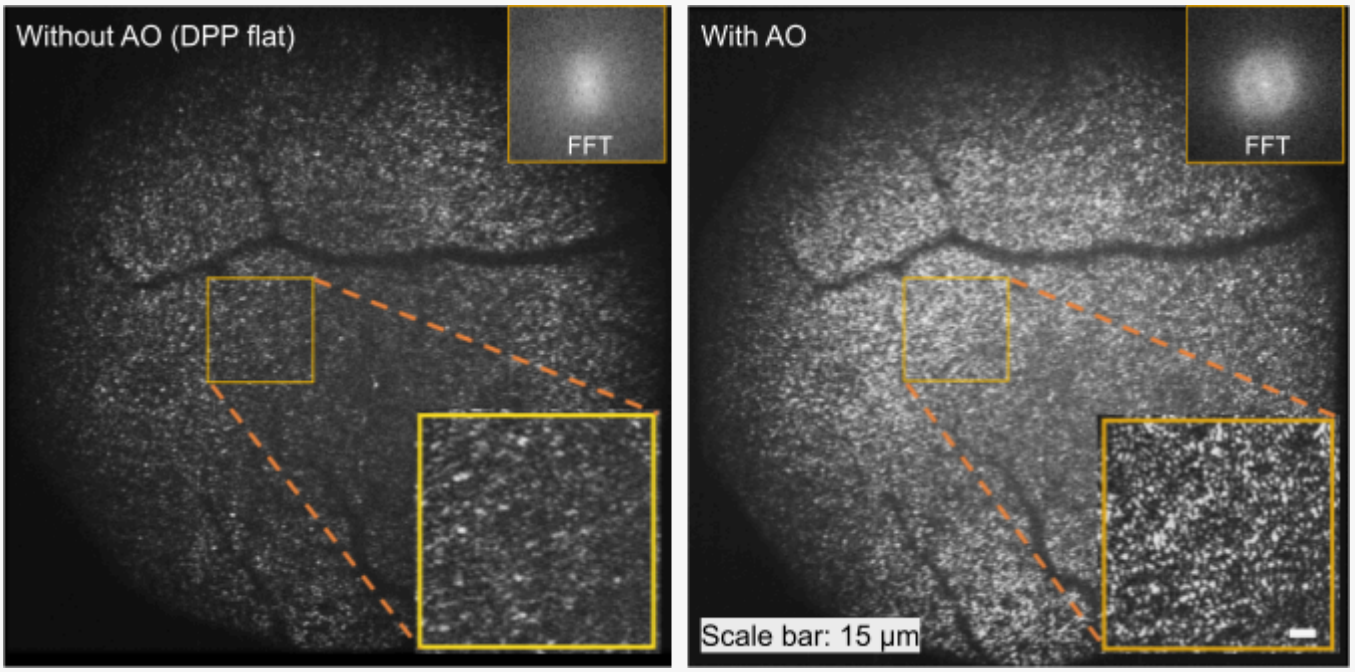

Figure 4: Retinal imaging results acquired by Institut Langevin without (left) and with (right) Phaseform's AO correction. Without AO, even though the pupil of the volunteer was dilated to enable cellular-level resolution, individual cone and rod cells could not be resolved. With AO, image quality has improved substantially across the entire FoV, and the individual photoreceptors could be observed with this instrument after less than one day of full hardware and software integration of Phaseform's AO system. The SNR was also doubled as well. The scale bars on the insets correspond to 15 µm.

Following hardware and software integration—taking less than a day—researchers successfully carried out in vivo experiments on a healthy volunteer. The actual retinal images (Figure 4) show a dense mosaic of photoreceptors near the fovea. Without AO, this region is blurred and subcellular details are not resolved. With AO enabled, a 3 s aberration estimation step was sufficient for full correction, yielding cellular-level resolution of photoreceptors. The signal-to-noise ratio (SNR) also improved by a factor of two, and Fourier-transform analysis of the images showed that the Yellot's ring (the signature frequency of the photoreceptor mosaic) is clearly visible only after AO correction.

Implication

Phaseform's refractive AO technology substantially reduces the cost and complexity barriers for AO ophthalmoscopy. It also allows existing clinical and research instruments to be retrofitted, unlocking the transformative power of advanced wavefront correction. By offering more accurate insights into retinal morphology and function, this technology brings us closer to low-cost, portable, and widely available AO ophthalmoscopes—and therefore to universal, high-quality retinal imaging.

DPP as a General-Use Wavefront Modulator

The first commercial DPP product is the Phaseform Delta 7 Transmissive Wavefront Modulator. This continuous-sheet, refractive, optofluidic device features 63 electrodes and can replicate Zernike modes up to the 7th radial order. Its 10 mm aperture is compatible with 30 mm optical cage systems. The Delta 7 includes dedicated drive electronics, control software, and simulation tools. Applications include: Vision Science and Ophthalmology, Life Science & Microscopy, Material Science & Semiconductor Inspection, 3D Micro and Nano Printing, and AR/VR.

Delta 7 Transmissive Wavefront Modulator

About the company

Phaseform GmbH is a deep-tech spin-off from the Department of Microsystems Engineering (IMTEK) at the University of Freiburg in Germany. Our mission is to make adaptive optics affordable and practical by translating decades of cutting-edge research into innovative products and technologies. Phaseform aspires to lead the adaptive optics market with a vision of continuous innovation in a “New Era of Adaptive Optics.”

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