A diffuser-based computational imaging funduscope

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Abstract: Poor access to eye care is a major global challenge that could be ameliorated by low-cost and portable ocular diagnostic technologies. Diffuser-based imaging enables inexpensive, compact optical systems that could naturally be applied to this need. Here, we present a diffuser-based funduscope capable of reconstructing important clinical features of a model eye. We demonstrate funduscopic image reconstruction over a 33° field of view, and robustness to ±4D refractive error using a constant point-spread-function. Combined with diffuser-based wavefront sensing, this technology could enable combined ocular aberrometry and funduscopic screening through a single, low-costdiffuser sensor.

1. Introduction

An estimated 285 million people worldwide suffer from visual impairment, despite 80% of causes being classified as avoidable [1,2]. Imaging of the back of the eye with a funduscope or ophthalmoscope is a critical step of a comprehensive eye examination to screen for many of these abnormalities. Economic restrictions, a lack of clinical providers, and distance to healthcare settings are some of the largest barriers to delivering effective diagnosis and treatment [3–5]. To overcome these complications, eye care providers such as Aravind Eye Care System and L V Prasad Eye Institute have developed an approach to care that relies heavily on point-of-care screening provided by trained residents at the community level [6–8]. This strategy alleviates issues with transportation and reduces cultural barriers that prevent uptake of services [8]. For these minimally-trained workers to be effective, there is a need for low-cost, portable devices capable of the objective assessment of a wide variety of ophthalmic diseases.

Numerous inexpensive, point-of-care tools for screening and diagnosing ophthalmic conditions have recently been developed. With widespread adoption of mobile phones and rapid advancement of their camera technology, the potential of smartphone-based ophthalmic imaging has been recognized [9–13]. Other portable techniques have been demonstrated with an inexpensive point-and-shoot camera [14] and with a Raspberry Pi [15]. A computational single-pixel ophthalmoscope was recently demonstrated for increased visibility through opacities [16]. Separately, accurate, low-cost ocular aberrometry has been demonstrated with both handheld [17,18] and smartphone-based autorefractors [19]. It is likely that many such devices will be required to tackle the diverse causes of global visual impairment such as age-related macular degeneration, glaucoma, and uncorrected refractive error [20]. A simple, low-cost device that combines funduscopy and aberrometry, two essential parts of a comprehensive eye exam, would simplify distribution and reduce required personnel training time.

Diffuser imaging acquires lightfield data that has been exploited for achieving capabilities beyond traditional lens-based systems. With a thorough characterization of the diffuser, digital refocusing can be achieved [21]. Lens-free, diffuser-based imaging with incoherent light can also enable high-speed volumetric microscopy [22]. Diffuser based phase imaging is made possible by solving the transport-of-intensity equation [23,24]. Extended depth of field photography has been demonstrated by exploiting the invariant point spread function introduced by the
diffuser [25]. Wavefront sensing and ocular aberrometry have also recently been demonstrated with diffusers [26,27]. In each instance, the use of a random diffusing element instead of conventional plenoptic or lens-based imaging system is lower cost and more compact. Taken together, diffuser-based sensing has exciting potential advantages in ocular imaging, and could enable simultaneous funduscopy and ocular aberrometry.

In this paper, we develop and demonstrate funduscopy of a model eye with a diffuser camera. Using an annular ring of LEDs, we flood-illuminate and reconstruct a model eye fundus with a 33° field of view (FOV). We assess image reconstruction quality, and demonstrate robustness of the reconstruction algorithm to refractive error imparted on the object or the point spread function used for reconstruction. This work shows promise for the future development of a low-cost, portable device that could perform funduscopy and aberrometry through a single diffuser camera.

2. Methods

To achieve large field-of-view (FOV) ocular imaging with a diffuser camera, we jointly designed the optical hardware, calibration procedures, acquisition methods, and reconstruction algorithms. Our workflow consists of three stages as shown in Fig. 1, including an initial system point-spread function (PSF) calibration, image acquisition, and computational reconstruction. The PSF is captured by displaying a point source on an OLED screen placed at the front focal plane of a 25-mm focal length simple model eye. During the acquisition stage, the camera captures images of the flood-illuminated fundus blurred by the diffuser. The diffuser PSF is then used to to
deconvolve this blurry image and form a high-quality fundus image. In this section, we first describe our general optical design, then we lay out the specific experimental implementations for optimizing the system performance, and lastly we outline the theoretical principles and formulation of our reconstruction algorithms.

2.1. Optical Design

Existing fundus cameras use lens-based imaging, where high image quality is achieved by optimizing lens design, typically resulting in multi-element, bulky, and expensive systems [15]. We propose the use of a thin diffuser as an alternative for the imaging lens, which would significantly reduce size, weight, and cost of the whole system, in addition to being compatible with diffuser-based aberrometry. As shown in Fig. 2(a) our optical design consists of a wide-field, off-axis illumination module, a relay lens system, and a diffuser camera. In this system, the eye is illuminated with an LED ring through a beam splitter (BS). The reflected light from the fundus first passes through a 4F relay lens system. The diffuser is placed at the conjugate plane of the eye lens, which is illuminated by parallel beams for an emmetropic eye. The image sensor is placed at a small distance away from the diffuser to capture a sharp caustic pattern.

![Ray-tracing models of the (a) imaging, and (b) illumination paths. (a) The diffuser is conjugate to the cornea so that each point on the retina produces an approximately-shifted caustic PSF. (b) The LEDs are also imaged to the cornea and use a ring geometry to reduce specular reflection. The FOV of the system is currently limited by the numerical aperture of the illumination optics. All focal lengths and distances are in units of mm.](image)

To achieve large FOV imaging and illumination, a carefully designed optical system is required. Our system can be split into two parts: one to illuminate the eye, and another to image the reflected light from the fundus, as shown in Fig. 2. To simulate the eye, a curved retinal surface ($r = 14$ mm), a bi-convex lens ($f = 25$ mm), and an iris ($d = 7.7$ mm) are used in the Zemax model (Fig. 2(a)). This results in collimated light exiting the pupil from any spot on the fundus. A relay lens system is used to image the iris to the diffuser plane. To avoid large angle distortion, two lens groups (Lens 1 and Lens 2) each containing two doublets are inserted. Lens 1 has a
short focal lens and can collect a large angle of reflected light leaving the eye. The light is relayed by Lens 2 through the beam splitter and onto the diffuser. To avoid the beam splitter blocking the large field angle, Lens 2 should also have a short focal length to achieve small magnification. However, the volume of the beam splitter limits the minimum length of $d_4 + d_5$ to larger than 40mm. The relay lens system was designed by taking all of these limitations into consideration. Lens 1 consists of two $f = 75$mm doublets and Lens 2 consists of two $f = 100$mm doublets. The Zemax simulation, in which we modeled the system with the actual lenses used, shows that the reflected angle within $\pm 15^\circ$ can be well imaged to the diffuser plane. For the large field angle ($30^\circ$), the reflected light relayed on the diffuser has a noticeable shift. As shown in Fig. 2(b), the off-axis LED ring is conjugate to eye lens. The diameter of the LED ring is designed to be 8mm for matching the size of the eye pupil after being demagnified by the relay system. By adjusting the distance to Lens 2, the illumination FOV can be fine tuned.

2.2. Hardware design & implementation

An overview of the diffuser-based funduscope is shown in Fig. 3(a). The setup is compact, especially for the illumination and diffuser-cam parts, as shown in Fig. 3(b). To increase the contrast and reduce the stray-light background, a pair of crossed polarizers are placed in front of the LED and the diffuser-cam. The LED ring is implemented with an off-the-shelf LED matrix (Spacing = 2 mm, SparkFun LuMini LED Matrix - 8 x 8 (64 x APA102-2020)). Due to the discrete grid of the array, the actual diameter of the ring is 9.5 mm in our prototype (Fig. 3(c)). In addition, the LED array is covered by a 3D-printed cap to limit the divergence angle of the illumination, and (d) diffuser camera components including a 3D printed iris placed in front of the diffuser to limit the size of the PSF.
angle as in Fig. 3(c). For the diffuser-cam, a 0.5Å† holographic diffuser (Edmunds Optics 47-989) and a 3D-printed iris with 3.2 mm diameter are placed adjacent to one another and ~6 mm before a monochromatic sCMOS image sensor (Thorlabs Quantalux). The distance between the image sensor and the diffuser does not need to be precise because diffuser caustic patterns are intrinsically more robust to defocus than point spread functions from large lenses. Intuitively, this is because each diffuser feature can be treated as a low numerical aperture (NA) lens that provides a large depth-of-focus.

2.3. Algorithm

The final fundus images are reconstructed following a general framework that incorporates a pre-calibrated PSF to deconvolve raw measurements. To enable high-quality reconstruction of the retinal images, we use a deconvolution algorithm based on a 2D linear shift-invariant (LSI) model.

The LSI model assumes that raw measurements are the convolution of the object and a single invariant PSF that is pre-captured with an on-axis point source as the imaging object. With this LSI deconvolution model, our preliminary experiments showed high-resolution reconstruction in the central FOV region of a diffuser image of the retinal object. However, the direct deconvolution algorithm is inevitably sensitive to noise due to the poor conditioning of the inverse problem using the non-conjugate imaging geometry.

We mitigated this poor-conditioning by incorporating priors in the deconvolution algorithm. The prior we used for the inverse solution is carried out by L-2 norm regularizer. We formulated the regularized inverse problem through the minimization of:

$$\mathbf{x} = \arg\min_{\mathbf{x}} ||\mathbf{y} - \mathbf{h} * \mathbf{x}||_2^2 + \mu||\mathbf{x}||_2^2,$$

where $\mathbf{y}$ denotes the measurement, $\mathbf{x}$ the object, $\mathbf{h}$ is the PSF, and $\mu||\mathbf{x}||_2^2$ is the L-2 regularization function with weight $\mu$. This commonly called Tikhonov regularized solution and is conveniently calculated by first performing the Fourier transform, then Fourier domain filtering, and lastly inverse Fourier transforming. The optimal regularization parameter $\mu$ is found by picking the visually optimal reconstruction when varying $\mu$ in a predefined small range.

3. Results

Our imaging system is capable of generating high contrast reconstructions in a number different scenarios. In this section, we demonstrate our experimental results in three conditions. First, we conducted PSF calibration and FOV analysis of the imaging system using a simple model eye with a self-illuminated OLED screen for its retina. Then, we replaced the self-illuminated OLED screen with various objects printed on paper, and projected the system’s off-axis, ring illumination to the simple model eye for reconstruction. The first two experiments show the effect of the system’s illumination on FOV. Last, we use a commercial model eye to assess the ability of the diffuser funduscope to perform high-quality reconstructions in a physiologically realistic object.

3.1. Simple model eye with self-illuminating object

For analyzing the FOV of the imaging system in the absence of illumination limitations, we measured a self-illuminated simple model eye (Fig. 4(a)). The simple model eye is composed of an object placed at the focal plane of a biconvex lens ($f = 25$ mm), which provides a crude simplification of the human eye. We use an OLED screen as a self-illuminated object, placed at the focal plane. The PSF is measured first by displaying an on-axis point source (diameter 275 $\mu$m) on the screen, which produces the caustic pattern, shown in Fig. 4(a). Next, the screen displayed an array of equally spaced point sources for calibrating the FOV as shown in Fig. 4(b).
Here, the green outlined insert is our raw measurement and the right-hand-side is our regularized reconstruction. We observe in this setting that the system is able to reconstruct over a 50° angular FOV. Figure 4(c) shows our reconstruction from displaying a retinal image on the screen and demonstrated a relatively wide FOV of 48.3°.

3.2. Simple model eye with external illumination

Next, we tested our external illumination system. In this experiment, the simple model eye is also used, however we substituted the OLED screen with a printed paper object, as shown in Fig. 5 (a). We first analyzed the FOV by imaging a printed ruler with both positive and negative contrast (Fig. 5 (b)). The imaging system reconstructed an image of a 15 mm length of the ruler, equivalent to a 33.4° angular FOV. We then printed and imaged the same retinal image displayed in Fig. 4 (c) on the paper, as illustrated in Fig. 5 (c). A 33° angular FOV was reconstructed, and vessels and other small features can clearly be resolved.

3.3. Commercial model eye with external illumination

To investigate the performance of our combined imaging and illumination system in a physiologically-realistic scenario, we next imaged a commercial model eye (HEINE Ophthalmoscope Trainer),
which has realistic retinal structures and allows varying amounts of refractive error. Figure 6 (a) shows the overall procedure of this experiment. First, raw data is acquired (green insert) without refractive error (0D), and reconstructed using the same PSF used in previous experiments (Fig. 4 (a)). Next, to test the robustness of the system to refractive error, we further experimented with two commonly-seen scenarios: (1) reconstruction with different refractive error and a single PSF acquired at 0D, and (2) reconstruction of an emmetropic model eye diffuser image using PSFs acquired at a range different retinal positions. These two experiments are analogous to imaging through near-sighted or far-sighted human eyes. Figure 6 (b) shows that when the refractive error is within a range of -4D to 4D, no significant degradation of image quality occurs. In Fig. 6 (c), the distance at which the PSF was acquired was varied, simulating refractive error in eyes that are too short or too long. The reconstruction results indicate that when the refractive error reached as high as -5.5D/+7.6D, we do observed slight degradation of image quality in both contrast and resolution.

4. Discussion

4.1. Self-illuminated object

The initial set of experiments with a self-illuminated OLED screen used as the retina in a simple model eye provided insight into the fundamental operation and ability of the diffuser-based funduscope in the absence of illumination constraints. For initial calibration and subsequent deconvolution, the system PSF was measured by illuminating an on-axis point source on the
OLED screen. As seen in Fig. 4 (a), the PSF is a highly structured caustic pattern, which is the fundamental signal used in both DiffuserCam [22] and diffuser-based ocular aberrometry [27].

Next, a point source array was illuminated on the screen (Fig. 4 (b)), and the acquired image (green inset) is deconvolved with the system PSF to reveal the initial object. From this reconstruction result, we can determine that our detection path is able to resolve a 51° angular FOV. Interestingly, when looking at the acquired signal before reconstruction (Fig. 4 (b), green insert), the expected appearance of the PSF convolved with a point source array can be observed.

When the image of a retina with diabetic retinopathy is displayed on the OLED screen (Fig. 4 (c)), a similar 48.3° FOV is reconstructed. Many important features of the retina are visible, including the optic disk and healthy vasculature, as well as retinal scarring and hemorrhage. The detection FOV is similar to the 45° FOV typically achieved by non-mydriatic fundus photography [28]. The reconstructed structures at large field angles are more blurred and have lower contrast, due to distortion of a flat screen. When exiting the simple model eye lens, these rays are not parallel, which changes their PSF, making it no longer spatially invariant. When applying our deconvolution algorithm with a fixed PSF, the reconstruction performance of structure at high field angle decreases.

4.2. External illumination with a simple model eye

In the next set of experiments, we turned on the system’s ring LED illumination, and demonstrated simple model eye reconstructions with different objects printed on paper as the retina (Fig. 5). We first used printed rulings of known size for calibration (Fig. 5 (b)). From these objects, we observed a high contrast reconstruction over a 33.4° FOV. Comparing these results with the 51° FOV demonstrated with the OLED retina (Fig. 4 (b)), we acknowledge that the current system FOV is limited by the extent of the LED illumination. This can be mitigated by designing a wider
illumination range. Using the same two printed ruler patterns in Fig. 5 (b) with opposite contrast demonstrate the impact of signal sparsity on reconstruction quality. The sparse-printed rulings (white rulings and black background, left) is reconstructed with higher contrast, as compared to its counterpart, the dense-printed rulings (black rulings on white background, right).

Lastly, we printed the same retina pattern used on the OLED screen (Fig. 4 (c)) for detection and reconstruction using the ring LED illumination (Fig. 5 (c)). Again we observe a similar FOV as observed with the ruler, less than when we used the displayed retina on the OLED screen, further indicating our FOV is limited by the illumination extent. However, despite a more limited FOV, we still observe the same key retinal features as different regions of interest are imaged and reconstructed (yellow, orange, and blue dashed circles).

4.3. Commercial Model Eye Reconstruction

In the last set of experiments, we replaced the simple model eye with a commercial model eye to test a more physiologically realistic object, and to accurately introduce refractive error (Fig. 6). Reconstructions of the commercial model eye fundus were performed with LED illumination, using the same PSF acquired from the on-axis point source in the calibration step (Fig. 4 (a)), and with 0D refractive error. The initial result of the commercial model eye fundus reconstruction is shown in Fig. 6 (a), where the optic disk and blood vessels are clearly visible. A similar angular FOV was observed here with the commercial model eye as was previously demonstrated with the simple model eye. The FOV, though limited by the extent of illumination provided by the ring LED, still reveals a greater FOV than conventional direct ophthalmoscopy [28].

After reconstructing an initial image of the commercial model eye fundus with emmetropia, refractive error was introduced between -4D and 4D (Fig. 6 (b)). Despite the introduction of refractive error, the diffuser funduscope is still able to produce reconstructions of similar quality to when there was no refractive error. Importantly, fundus images were reconstructed using the same PSF as applied in the 0D case and in the reconstructions of Fig. 5, and no re-calibration was required.

Finally, we evaluated the image reconstruction quality produced if the PSF were acquired from locations other than the focal point of the model eye lens (Fig. 6 (c)). PSFs were acquired as the OLED screen was translated from -4mm to +4mm, to simulate the PSF acquired from eyes that are too long (myopia), and too short (hyperopia), respectively. Using a thin-lens approximation, this spans refractive error from -5.5D to +7.6D, respectively. Next, the raw data acquired from the 0D refractive error case was reconstructed with these varied PSFs. Again the fundus was reconstructed successfully over a similar 33° FOV, though some degradation of contrast and resolution begin to appear at the extreme refractive errors.

Together, these results demonstrate that the diffuser funduscope is robust to refractive error over a range of myopia and hyperopia severe enough to cover a substantial range of clinical cases [29]. This is because the 0.5° holographic diffuser used in this study can be thought of being composed a random array of dysmorphic lenslets, each with a very large f/# and large depth-of-focus [22]. Further, the reconstruction quality we achieve is similar to that achieved by other computational ophthalmoscope techniques [16]. Overall, we believe our imaging system is robust and stable to refractive error within a reasonable range, and shows promise for improving medical diagnosis of retinal disease.

5. Conclusion

Visual impairment is a pressing global health concern, and many of its causes are considered avoidable. This problem can in part be solved by the development and distribution of robust, low-cost diagnostic devices that require minimal training to operate. In this paper we develop and demonstrate one such approach for retinal imaging by developing and characterizing a compact, low-cost diffuser funduscope. We demonstrate high quality funduscopy of a model
eye that is robust to a large range of refractive error. Further, the point spread function used for deconvolution is a caustic pattern produced by the same holographic diffuser from which ocular aberrometry has been previously demonstrated. In future work, we envision these two techniques working synergistically, allowing simultaneous measurement of refractive error and funduscopy in one compact, inexpensive device.

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Disclosures

GNM and NJD are listed as co-inventors on a provisional patent application assigned to Johns Hopkins University that is related to the technologies described in this article. They may be entitled to future royalties from this intellectual property.

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