Advanced Fundus Camera with Innovative NIR Multispectral Color Imaging System

-Application Field Development of Dynamic Intelligent Systems Using High-Speed Vision-

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Abstract

We developed a fundus camera using multispectral imaging with six different wavelengths, i.e., R, G, B, NIR1 (800 nm), NIR2 (870 nm), and NIR3 (940 nm), in an image sensor. A band pass filter was created in the near-infrared (NIR) range using two kinds of inorganic multilayer films. We can freely design any band pass filter using such interference films based on the Fabry–Perot principle. The total thickness of the band pass filter was approximately 1.1 μ m. Therefore, the band pass filter could be applied in an image sensor with a fine pixel size of approximately less than 2.25 μ m·(1.5 μ m pixel size). Moreover, we developed a process technology that could create a checkered pattern on an etching film as thin as several tens of nm. In the developed fundus camera, images were reproduced in full color despite using three NIR wavelengths. In addition, there was no dazzling. Individuals could capture the fundus of their eye themselves and diagnose it simultaneously. The developed fundus camera could accumulate several frame images and follow the inherent movement of the eye because of its high frame rate. Fundus images with high signal-to-noise ratios were reproduced.

1 Introduction

This paper describes the development of the next-generation of fundus cameras with a high frame rate based on intelligent imaging technologies [1]. Even though the quality of photos or videos is frequently evaluated based on the aesthetic appeal of associated images, our primary goal is to improve acquisition speed and processing. In this work, we aim to eliminate the bottlenecks that limit image processing speed to develop high-speed imaging, transfer, and processing systems in several different forms for the realization of real-time image processing. The specific objective of this study is to advance intelligent systems that utilize visual modalities far beyond human capability by integrating sophisticated processing with real-world applications to acquire previously inaccessible information (Fig. 1). We are developing a solution system that can be implemented in the form of a compact camera for multiple applications including physiological monitoring and pathological diagnosis. For example, the characteristics of eye movement are potentially an indicator of neuropathology. Involuntary eye movement occurs at a rate of approximately 100 Hz. This type of rapid motion can be accurately tracked by the system, which operates at approximately 1000 fps. Furthermore, it is possible for an individual to observe and acquire images of the fundus of the eye without assistance by utilizing the fundus camera developed in this study.

In one of the several proof of concepts for dynamic intelligent systems using high-speed vision, we aim to develop a solution system that can be used as a camera to facilitate the tracking of the rapid movement of the eye. Another potential application of this compact camera is to capture diagnostic health information, which will allow for the active control and management of health by individuals (Fig. 2). Further, this camera can acquire images in multiband spectral ranges based on near-infrared (NIR) spectral imaging technology. In this regard, advanced NIR multispectral technology has been developed. The following NIR wavelengths

have been acquired for target images using this technique: NIR1: 780–800 nm; NIR2: 870 nm; NIR3: 940 nm. A color image can be reproduced using only multi-NIR signals in the absence of visible light (0 lux) by employing interpolation and color correction processing. NIR multi-spectral filters, which are inorganic multilayers, have been developed to distinguish and obtain signals at NIR1, NIR2, and NIR3. For this purpose, these filters use the Fabry-Perot optical principle. Two kinds of films with different refractive indexes are alternately formed. It is possible to transmit specific NIR wavelengths by forming the same upper and lower film structures and controlling the film thickness of the high refractive index film at its center. We have also developed a Fabry-Perot multilayer fabrication process on a CMOS image sensor as a Bayer array. Advanced multispectral imaging is performed, where we control only the thickness at the center to distinguish between signals at NIR1, NIR2, and NIR3. In the fundus camera, an NIR color image is reproduced with a high signal-to-noise ratio using a high frame rate.

The fundus of the eye is the only site in the human body where arteries and capillaries can be directly observed noninvasively. By examining the fundus oculi, it is possible to observe the state of blood vessels and the retina/optic papilla and thus diagnose various diseases ranging from glaucoma and retinal detachment to diabetes and arteriosclerosis. The next-generation of fundus cameras with a high frame rate has been developed based on intelligent imaging technologies.

2 NIR color imaging

The wavelength range of a photo signal obtained using Si material is from approximately 350 nm to approximately 1000 nm. Si can perform photoelectric conversion from the ultraviolet to the NIR region in this wavelength range. Conventional digital cameras with common CIS can acquire color images only in the visible light range (wave length: 450 nm to 700 nm) [2] using an NIR cut filter

and do not utilize the NIR wavelength region [3]. However, NIR wavelength can be included in RGB images using a camera without an NIR cut filter. Target images were acquired at the following wavelengths using multispectral technology: NIR1: 780–800 nm; NIR2: 870 nm; NIR3: 940 nm (Fig. 3). Using this image sensor and imaging system, color images were reproduced using only multi-NIR signals without visible light (0 lux) by utilizing interpolation and color correction processing (Fig. 4) [4].

3 Fabry-Perot multispectral technology

A spectroscopic technique with NIR reflected light with a sharp peak is developed using a band pass filter (BPF) with multilayer interference in the NIR region. There is a specific transmitted wavelength in the BPF, and other wavelengths are reflected by the Fabry-Perot filter. This phenomenon is similar to a mirror. Mirrors are fabricated for incident light with a peripheral wavelength of λ by alternately stacking thin films of two kinds of refractive indexes with a thickness of $\lambda/4$. When a spacer film with a thickness of $\lambda/2$ is inserted between the two mirrors thus produced, the phase of a light wave is reversed and only the light in the vicinity of λ_0 is transmitted (Fabry-Perot resonator) (Fig. 5). Further, it is possible to shift transmission wavelength by adjusting the thickness of the spacer film. Figure 6 shows the configuration of the multilayer interference BPF designed in this study. The transmittance peak wavelength can be shifted by adjusting the thickness of the high refractive index film layer, "2H", which is shown at the center of the figure. The transmittance peak wavelength shifts to the short wavelength side when film thickness is decreased and to the long wavelength side when film thickness is increased. An actual multilayer interference BPF is fabricated through the simulation of filter transmittance and the corresponding film thickness to obtain a BPF with transmittance peaks at the three wavelengths in the NIR region. Furthermore, NIR imaging is performed using the designed multilayer film interference BPF, and a color image is obtained (Fig. 7). Fig. 8 shows the semiconductor process that is utilized to manufacture the filter.

Figure 9 shows the top view of a filter film formed with a checkered pattern with a thickness of approximately 1.1 μ m. The total thickness of the BPFs can be adopted in an image sensor with fine pixel sizes ($<2.25 \mu m^2 (1.5 \mu m \text{ pixel size})$, which is cost effective). Two kinds of films with different refractive indexes are alternately formed. It is possible to transmit specific NIR wavelengths by forming the same upper and lower film structures and controlling the film thickness of the high refractive index film at its center. Advanced multispectral imaging is performed, where we control only the thickness at the center to distinguish the wavelength of the photons that reach a photodiode. In fabricating BPFs at three wavelengths in the NIR region on one image sensor, the same substrate layer as that shown in Fig. 8a is formed on a photodiode. As it is necessary to change the film thickness at the center of the three BPFs, the film at the center is formed and patterned for three different thicknesses. Then, by forming the same upper layer structure as that shown in Fig. 8c, it is possible to form the film structure of the three filters on one chip.

4 NIR multispectral fundus camera

Valuable information can be obtained using multispectral imaging, e.g., human vitals such as blood pressure. The fundus of the eye is the only site in the human body where arteries and capillaries can be directly observed noninvasively [5].

In fundus observation, particularly NIR observation, it is reported that an NIR wavelength of 940 nm, which is used in spectroscopy, can be utilized to capture the image of the choroidal condition of

the posterior uvea. Furthermore, the abnormalities of choroidal vessels that cannot be observed with visible light can be confirmed [6]. Therefore, NIR observation using the fundus camera can provide valuable information such as blood pressure. However, the fundus camera currently experiences certain issues. Only a skillful operator (medical doctor) can obtain fundus images, and it is almost impossible for individuals to obtain fundus images themselves. In a conventional fundus camera, a strong flashlight is necessary to obtain clear images using a high-speed shutter because there is involuntary eye movement (approximately 100 Hz). Furthermore, continuous shooting is difficult. In developing countries, only few hospitals have installed fundus cameras. Even the diagnosis of the fundus is difficult. We have developed a fundus camera system that enables individuals to photograph the fundus themselves at NIR1, NIR2, and NIR3 without dazzling. Hence, individuals can obtain the images of the fundus and check them simultaneously (Fig. 10). The location of the NIR light source is designed to focus light on a pupil through the fundus lens to achieve Maxwellian illumination (Fig. 11).

An optical system focused on the fundus is used. Light of three wavelengths is irradiated to the fundus. Reflected light is imaged by the camera through a beam splitter. The optical images captured at NIR1, NIR2, and NIR3 are shown (Fig. 12).

Typically, there is fixational eye movement, and this type of rapid motion can be accurately tracked by the system, which operates at a high frame rate. It is possible for an individual to observe and acquire the images of the fundus of the eye without assistance by utilizing the fundus camera. In addition, the color images of the fundus are obtained by the multispectral imaging system with interpolation and color correction processing using the high frame rate camera module at NIR1, NIR2, and NIR3. We use the efficient second-order minimization method, which performs template matching through planar projective transformation (8 degrees of freedom) by nonlinear minimization. Even though this method cannot reduce the number of calculations per iteration, it has been reported that ultra-high-speed tracking can be achieved for planar images by effectively using parallelization in recent CPU hardware [7]. We have confirmed that this algorithm adaptation can provide a blur-free fundus image. (Fig. 13). Concurrently, we have achieved the denoising of the obtained fundus images through image integration with high frame rate images. A captured image is accumulated by several frame images, and the inherent movement of the eye is followed by employing a high frame rate camera (Fig. 14). A low noise fundus image is reproduced (Fig. 15). We can observe different conditions of the fundus image using NIR multispectral imaging. In the near future, the NIR multispectral camera can provide data about human vitals, and these data can be analyzed for understanding personal health as a form of preventive medicine.

5 Conclusion

An advanced fundus camera with an NIR multispectral imaging system and a CMOS image sensor was developed.

In the near future, this system can be utilized for diagnosing multiple retinal diseases and disorders, thereby enabling health care professionals to detect and identify pathology earlier in the disease process to prevent debilitating vision loss and the worsening of disease conditions.

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References

- 1. Sumi, H., et al.: Contribution title. In: Symposium on VLSI Technology Digest of Technical Papers, pp.163–164, Publisher, Location (2018).
- 2. Rosenberger, M., et al.: Contribution title. In: IEEE imaging Systems and Techniques (IST), pp. 7–12, Publisher, Location (2016).
- 3. Hertel, D., et al.: Contribution title. In: IEEE Intelligent Vehicles Symposium, pp. 273–278, Publisher, Location (2009).
- 4. Sumi, H., et al.: IEICE Technical Report OPE2017-114 (2017-12), pp. 125-130.
- 5. Ferreira, L. F. F.: Article Title. Experimental Physiology 90(5), 715–726 (2005).
- 6. Zimmer, C., et al.: Article title. Retina Today vol(issue) 94–99 (2014).
- 7. Kagami, S., et al.: IEICE Technical Report OPE2017-114 (2017-12), pp. 125-130.

Applications of High-speed Vision

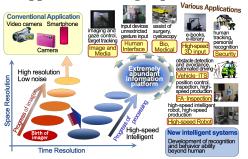


Fig. 1. Various application fields of dynamic intelligent systems using high-speed vision.



Fig. 2. Fundus of the eye is the only site in the human body where arteries and capillaries can be directly observed noninvasively.

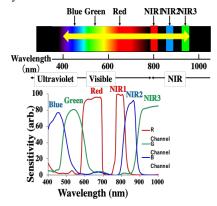


Fig. 3. Multispectral RGB + NIR1, NIR2, NIR3. There are relationships between red and NIR1, blue and NIR2, and green and NIR3 signals.



Fig. 4. In a 0 lx no-visible-light environment, a color image has been reproduced with only NIR illumination using the camera.

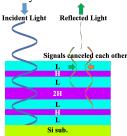


Fig. 5. Transmission of light close to reference wavelength λ . The wavelength of transmit-ted light can be controlled by changing the film thickness at the center.

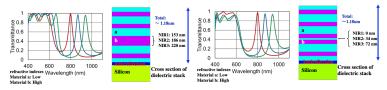


Fig. 6. Inorganic multilayer filter, which uses the Fabry–Perot optical principle. Two kinds of films with different refractive indexes are alternately stacked. It is possible to transmit specific NIR wavelengths by forming the same upper and lower film structures and controlling the film thickness at the center. Total thickness is approximately 1.18 μ m for use in a fine pixel image sensor.

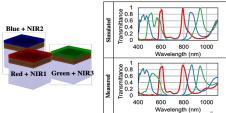


Fig.7. Advanced multispectral imaging is achieved, where we control only the thickness at the center to distinguish the wavelengths of photons.

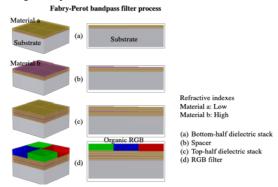
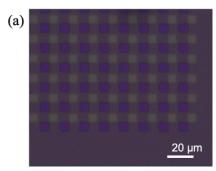
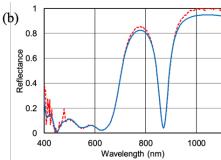


Fig. 8. Multispectral graphs of NIR 1,2,3 and visible RGB imaging technologies to demonstrate process sequence.



Checkered pattern for $7.5 \times 7.5 \mu m$ pixel array; color differences are due to the difference in spectral reflectance, even though the tri-BPF has low visible light reflectance.



Measured thickness is 1.18 µm for 870 nm BPF. Refractive index data use the actual measurements from spectroscopic ellipsometry

Fig. 9. (a) Optical microphotograph of fabricated Fabry–Perot BPF array reflectance. (b) Fabricated film thickness is derived by fitting curves to measured spectral reflectance data. Refractive indexes of the dielectric materials were measured via spectroscopic ellipsometry. The plot shows measured spectral reflectance (dashed red) and fitted (solid blue) data.

- ✓ No dazzling
- ✓ Eye iris is opened easily.
- ✓ Video can be captured while viewing the fundus image
- ✓ Alignment possible (self-viewable)

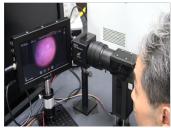
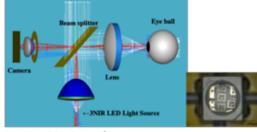


Fig. 10. Developed camera system that enables individuals to capture images of the fundus themselves while checking it.



White line: from Light Source / Light source: 3NIR wave length (800, Blue · Red Line: Refracted Light from fundus 870, 940 nm) NIR LED 3NIR + RGB

Fig. 11. Location of the NIR light source was designed to focus light on a pupil through the fundus lens to achieve Maxwellian illumination.

Selfie Multi-spectral NIR fundus image

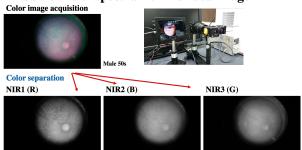
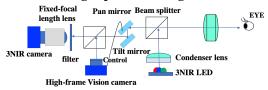


Fig. 12. Optical images captured at NIR1, NIR2, and NIR3. Color images of the fundus obtained by the multispectral imaging system with interpolation and color correction processing using camera module at NIR1, NIR2, and NIR3.

Full automatically observation of the fundus: High-speed vision algorism



 $(J^T J)dx = -J^T e_0, \ J = (J_1 + J_2)/2$

J₁: Derivative of template, J₂: Derivative of the current candidate region (Coordinate transformation is parameterized via exponential mapping)

Fig. 13. Involuntary eye movement at approximately 100 Hz can be followed. Stable images are captured by image algorithm.

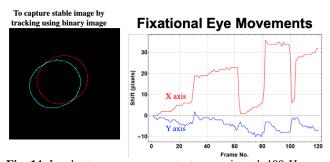


Fig. 14. Involuntary eye movement at approximately 100 Hz can be followed. Stable image captured by image algorithm.

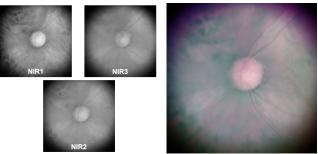


Fig. 15. Fundus camera can accumulate several frames of images and follow the movements of the eye with high frame rate to reproduce fundus images with high signal-to-noise ratio.