High-resolution imaging of the living human fovea: measurement of the intercenter cone distance by speckle interferometry

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A high-resolution method that allows direct measurements of the intercenter cone distance in the living human fovea is proposed. The experimental technique is similar to that used in stellar speckle interferometry. It is based on the recording and posterior processing of coherent short-exposure images of a small area of the central fovea. By using this optical–digital procedure, we have obtained what are to our knowledge the first objective measurements *in vivo* of the cone spacing in the human fovea. The reconstruction of the whole spatial information of the cone mosaic would also be possible by further improvements of the technique by subsequent application of image-reconstruction algorithms.

The sampling of the retinal images by the photoreceptor mosaic plays an important role in the spatial information processing performed by the human visual system. After the low-pass filtering carried out by the optics of the eye, the imaging properties of the mosaic depend directly on the spatial distribution of photoreceptors. However, actual topographic data from the cone mosaic of the living eye, by objective methods, are not yet available. Traditional measurements of the structural parameters of the photoreceptor mosaic in the human fovea and the periphery were obtained by means of histological studies.[1–3] Histological measurements could differ from measurements made in the living human eye owing to tissue distortions during processing, because of the fragility of the photoreceptor mosaic. Williams has proposed an indirect psychophysical method that allows for the estimation of the cone spacing and the packing geometry in the living human retina.[4–6] However, to our knowledge, objective physical measurements on the distribution of cones in the living human fovea have not yet been reported. Such results would clarify important questions, mainly those related to the actual intercenter cone distance and the regularity of the mosaic in the fovea. These are important structural data for evaluating the physical limits of visual resolution and the possible aliasing artifacts that could occur in the sampling of retinal images.

Direct observations of the cone mosaic have been carried out in lower vertebrates,[7] but the application of that method of the living human eye presents many problems. The main reason is that the optical image quality of the eye[8–10] is not good enough to resolve the close separation between cones. Therefore, resolving the human cone mosaic through the optical system of the eye is similar to a high-resolution imaging problem in astronomy. Here we present an objective method to measure directly the spatial distribution of the foveal cone mosaic of the human eye *in vivo*. The method is based on stellar speckle interferometry[11,12] similar to that used in astronomy to resolve binary stars through atmospheric turbulence. We obtain short-exposure speckle images of a small area of the fovea. Then, after selecting the best specklegrams, we compute the averaged power spectrum, which contains spatial frequency information as far as the diffraction limit of the eye.

In our case, for a normal eye with a 7-mm pupil diameter and incident light with a wavelength of 632 nm, the minimum separable size on the retina by diffraction will be approximately 1.8 μm. On the other hand, according to histological studies, the center-to-center spacing between cones in the central fovea is thought to range from 2.1 μm (Ref. 3) to 2.8 μm.[1] Under these conditions, in principle, we will be able to resolve foveal cone details by using this high-resolution technique.

The procedure involves recording a large number of short-exposure images of the central fovea formed with coherent light using the experimental setup shown in Fig. 1. A He–Ne laser beam is expanded by lens L_1 and filtered by a 400-μm pinhole (D) that acts simultaneously as the object and fixation test. The beam collimated by lens L_2 enters the eye after reflection in a pellicle beam splitter (BS) and forms an image of approximately 55-μm diameter on the central foveal mosaic (M). The light reflected from the retina contains information on the spatial distribution of the cone array. It leaves the eye, and after the light is transmitted through the BS and a polarizer (P), lens L_3 forms the aerial foveal image on high-sensitivity photographic film (Kodak Recording 1000 ASA). After development, the aerial foveal images are digitized by using a microdensitometer and stored in a computer. Two examples of typical short-term exposure aerial foveal images are shown in Fig. 2. The exposure time for each image was 4 msec. The corneal irradiance was of the order of 0.3 mW/cm^2, which is more than 1 order below U.S. security standards.

Since the whole imaging process is carried out in

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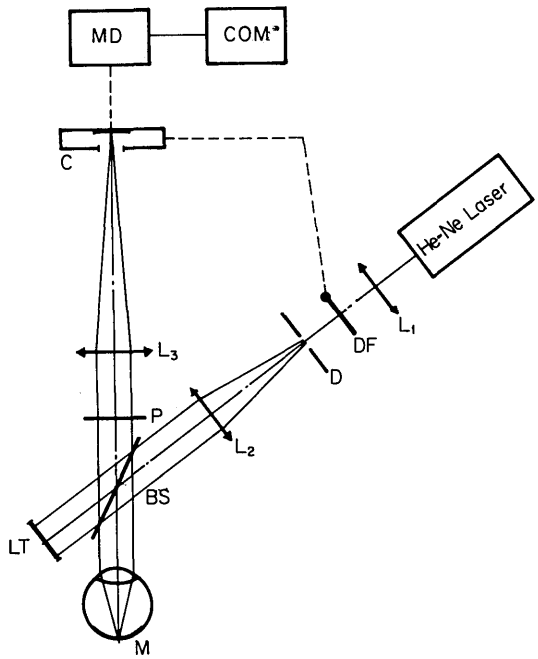


Fig. 1. Experimental setup for the recording of the short-term-exposure foveal images. DF, density filter; LT, light trap; C, camera; MD, digital microdensitometer; COM, computer.

coherent light, the short-exposure aerial images of the central part of the fovea $[i_k(x'', y'')]$ can be expressed by

$$i_k(x'', y'') = |r(x', y') \otimes a_k(x', y')|^2, \quad (1)$$

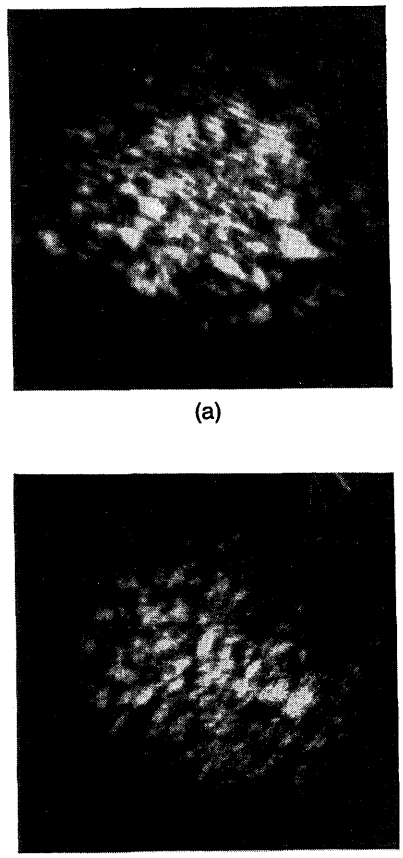
where $\otimes$ denotes convolution, $r(x', y')$ is the complex reflection factor of the cone mosaic, and $a_k(x', y')$ is the amplitude spread function of the human eye.[8] After the aerial images have been digitized, the power spectrum of each instantaneous image is computed. Since the signal-to-noise ratio is low for a single power spectrum, we have averaged many individual power spectra, as expressed by

$$\langle |\bar{I}|^2 \rangle = \frac{1}{N} \sum_{k=1}^{N} |FT[i_k(x'', y'')]|^2, \quad (2)$$

where FT denotes a Fourier transformation.

A plot of the power spectrum corresponding to the instantaneous image of Fig. 2(a) is presented in Fig. 3. Figure 4 shows the average of 10 two-dimensional power spectra from a normal subject. The mean center-to-center cone distance in the human fovea is directly obtained from the result presented in Fig. 4. The value $1/s$ in the spatial frequency domain is correlated to the local average spacing between rows of cones in the foveola. The ring that appears in this experimental result has the same shape as those obtained by computer simulation and optical transform, using digitized patterns corresponding to excised foveas.[13,14] The cone spacing in the foveola for the same normal subject as above was $0.51' \pm 0.02'$ of arc. This corresponds to 2.45 ± 0.1 μm on the retina using as a conversion factor the focal length of a schematic eye.[15] This result is in the middle of a wide range of data (2–3 μm) obtained from histological studies.[1–3] We have obtained local mean cone spacing for three different normal young subjects. Variations of these results were always lower than the standard deviation of the experimental error. This numerical result can be directly applied to more precise evaluations of the physical limits of visual resolution and to aliasing caused by foveal undersampling. By a method of analysis similar to that used in Ref. 16, we would be able to study the problem of foveal aliasing using our objective data of both the image quality of the eye and cone spacing.

Another important point concerns the regularity of the foveal cone mosaic.[13] To obtain actual high-resolution imaging of the fundus (cone mosaic topogra-



(a)

(b)

Fig. 2. Typical examples of short-exposure (4-msec) coherent images from the foveal cone mosaic.

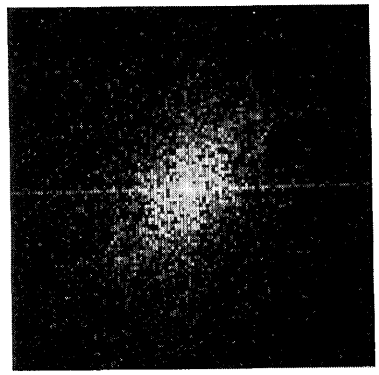


Fig. 3. Two-dimensional power spectrum of the instantaneous image shown in Fig. 2(a).

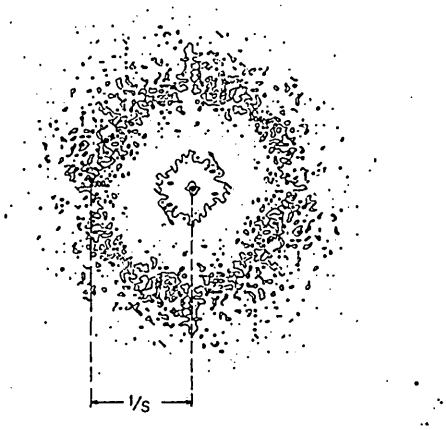


Fig. 4. Average of two-dimensional power spectrum of 10 instantaneous images of the central fovea. $1/s$ is the spatial frequency value corresponding to the mean interdistance between rows of cones.

phy), using the stellar speckle interferometry method presented here, would require the use of algorithms to recover the lost phase information. This is because high resolution is obtained by averaging individual power spectra, with the accompanying loss of phase information and then the ability to reconstruct the image itself. Unfortunately, since the performance of phase-retrieval algorithms on noisy data is poor, further research and higher signal-to-noise ratios will be necessary to obtain high-resolution images of the human retina. Despite this, from the analysis of instantaneous foveal images (Fig. 2) and their two-dimensional power spectra (Fig. 3) we can point out, in a preliminary way, that the distribution of cones at the central fovea is locally a regular triangular array. This is good agreement with previous detailed studies of the primate cone mosaic.[17] The outer ring that appears in Fig. 4 is due to the average of individual power spectra with approximately regular hexagonal structures but in different orientations. The imaged area of the fovea was slightly different for each instantaneous foveal image, and the relative orientation of the mosaic at different areas is also probably different.

In conclusion, we have presented an optical–digital method that is based on stellar speckle interferometry to obtain diffraction-limited information on the foveal cone mosaic *in vivo* for individual human eyes. The intercenter cone distance has been determined for the first time, to our knowledge, in a completely objective way. These data are useful for evaluating the physical limits of spatial resolution and aliasing artifacts in the sampling of retinal images. Further research to improve this methodology could help to achieve a better understanding of the actual spatial photoreceptor organization.

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