Photoreceptor inner and outer segments have a higher refractive index than their surrounding tissue. Sandwiched together between the external limiting membrane and the pigment epithelium, they act as dielectric light guides. Because their diameters are of the order of the wavelength of light, light intensity is not distributed homogeneously over their cross section but is guided by so-called “modes.” In this case, light guides are called “waveguides.”

During the second half of the last century, waveguide properties of photoreceptors were identified in the area called “photoreceptor optics.” The main results were summarized in the monography “Photoreceptor Optics.”

Answers could be given to questions such as the following: What kinds of modes are possible in vertebrate inner/outer segments? What explanations do we have for the two Stiles-Crawford effects? What is the smallest possible diameter of an outer segment before optical cross-talk between neighboring photoreceptors increases to such an extent that resolution is impaired?

During the past decade, it was suggested that, in addition to the photoreceptor inner/outer segment waveguides, a second type of retinal cell in the mammal retina, the Müller cell, can act as an optical fiber. Because some of the conclusions drawn in these papers are at variance with the results of photoreceptor optics, I have compared the methods and results of the two approaches.

In their seminal article, Franze and coworkers report that Müller cells extend from the inner to the outer limiting membrane, thereby spanning the entire retinal thickness. Because they can be seen to have higher refractive indices than the surrounding tissue, they can guide light (Fig. 1A). Because they are directed along the direction propagating light, these cells are believed to provide a low scattering passage of light from the retinal surface (inner limiting membrane) to the photoreceptor cells (external limiting membrane). According to this view, Müller cells form what is known as a fiberoptic plate-like structure in front of the photoreceptor layer.

Franze and coworkers conclude that the “fiber optic plate-like structure is especially characteristic for the retina of all mammals with the exception of the fovea centralis of humans and higher primates...: here the photoreceptor cells are not obscured by any inner retinal layers at all.” The question is whether Müller cells also form a fiberoptic plate-like structure outside the fovea. The results of several different approaches do not support this view.

Do Whole Müller Cells Act As Optical Fibers?

Histology. To be able to work as fiberoptic plates, Müller cells need to be straight (Fig. 1A); they cannot be curved or arranged in a zig-zag fashion, as light would then escape the guide due to the bending. Around the primate fovea, Müller cells are not straight but “Z-shaped.” To ascertain the course taken by the Müller cells, we only need to trace the course of the photoreceptor axons, that is, the Henle fibers as well as the bipolar cells that follow. This suffices because Müller cells are intertwined with the axons of the photoreceptors. Drasdo and coworkers calculated the length of the Henle fibers by comparing the lateral displacement of ganglion cells and photoreceptors. They observed a displacement close to the fovea of some 100 μm, which increased up to 500 to 600 μm at ±1 mm in the horizontal meridian, decaying to 100 μm at a distance of ±3 mm. A displacement of 100 μm means that, at this location, Müller cells are still Z-shaped. On the retina, 3 mm correspond to approximately 10 degrees. And therefore, due to their Z-shape, Müller cells seem to be unable to form a fiberoptic plate-like structure in front of the photoreceptor layer in the most important field of our view of a diameter of 20 degrees.

In fact, the structure of the retina provides proof, at least in the foveal region, that Müller cells do not guide light: Foveal cones are connected to Z-shaped Müller cells. If they were to guide light to the photoreceptors, this would, for obvious reasons, be detrimental for foveal resolution. And so we are left with the question, if we proceed from the fovea toward the periphery of the retina: at which point could Müller cells begin to guide light? A theoretical analysis cannot solve the problem because we know neither the refractive indices of the relevant...
Müller cells even further: If a subject wears a contact lens, Müllner cells, and not photoreceptors, it would no be necessary of light rays coming from the pupil. If light was accepted by increasingly acute angles with pigment epithelium and sclera. The consequence is that receptors near the posterior pole lie perpendicular to the sclera, whereas those located more and more anteriorly (i.e., closer to the ora serrata), form increasingly acute angles with pigment epithelium and sclera. This arrangement is interpreted as optimizing the acceptance of light rays coming from the pupil. If light was accepted by Müller cells, and not photoreceptors, it would not be necessary to adjust the photoreceptors in the way described. Instead, such an arrangement would be expected for Müller cells, albeit it has not been observed to date.

The following finding excludes a light-guiding function of Müller cells even further: If a subject wears a contact lens containing an artificial displaced pupil, one can show that the peak of the Stiles-Crawford effect of the first kind (SC1),\textsuperscript{7} indicative of the orientation of the light-receiving elements, moves to the center of the displaced pupil within 5 days. After removing the artificial pupil, the SC1 peak reverts after approximately 5 days to its original location.\textsuperscript{8} This finding is interpreted as follows: An active mechanism arranges the orientation of photoreceptors such as to optimize light acceptance. Even if it is not yet clear as to how this mechanism is realized, the following is a necessary condition: the elements that receive light must be capable of detecting the efficiency of light acceptance. This information is available to photoreceptors, but not to Müller cells: when guiding light, it would make no difference to the Müller cells whether they guide strong or weak light, because there is no light-absorbing pigment.

Direct Observation of Photoreceptors in the Living Eye. Using scanning laser ophthalmoscopes combined with adaptive optics, it is possible to resolve individual rods and cones in the living eye.\textsuperscript{9} The results have been confirmed by comparing rod and cone spacing with equivalent measures from histology. Meanwhile, the cone and rod mosaic in the human eye has been observed over large retinal areas. In the article by Marcos and coworkers,\textsuperscript{10} for example, these areas span from nasal 30 degrees over the fovea to 30 degrees temporal. Such observations with resolution of individual cones and rods are not compatible with the idea that a fiberoptic plate-like structure, as formed by Müller cells, lies in front of the photoreceptor layer.

The fact that photoreceptors can be observed directly without a fiberoptic plate-like structure in-between comes as no surprise, given that the Henle fibers and Müller cells form a weakly reflecting, dark band in optical coherence tomography (OCT).\textsuperscript{11} This indicates that Müller cells do not backscatter or reflect the incident light significantly, meaning that these layers are optically transparent, at least at the wavelength of light used in OCT recording.

Entoptic Image of the Retina. By illuminating the eye side-on, it is possible to observe one’s own retina. In this case, light enters the eye behind the lens ("retrolental illumination") and the retinal vessels cast a shadow onto the photoreceptors so that the subject is granted a wonderful view of his/her own vessels, known as the entoptic image of the retina. This phenomenon was first described by Purkinje.\textsuperscript{12} It is elicited by focusing light from the sun or from a penlight onto the sclera. The phenomenon also can be easily generated by a light-emitting diode (LED), which is found in many laser pointers in addition to the laser output.\textsuperscript{13}

When RLI is used, the fovea is seen as a grainy spot in the area without vessels. These grains prompted v. Helmholtz\textsuperscript{14} to describe this area as having the appearance of “shagreen leather.” By estimating the grain size, Ehrich\textsuperscript{15} came to the conclusion that each grain could correspond to the activity of a single cone. If the LED-lamp is moved, the grainy area can be seen to move in relation to the vessels. This conspicuous phenomenon, which is a necessary consequence of the fact that vessels and receptors are not located on the same plane of the retina, had already been observed by v. Helmholtz.\textsuperscript{14} As illustrated in Figure 2B, when the direction of incidence of the light is altered, the image of the vessels is displaced in relation to that of the photoreceptors (Fig. 2B, double arrowheads). Given the anatomical dimensions of the retina, a displacement of the light incidence of ±10 degrees leads to a relative displacement between fovea and vessels of approximately a quarter of a degree, corresponding to the observation.\textsuperscript{13} This can occur only if the Müller cells do not act as a fiberoptic plate-like structure. In this case, no displacement would be expected (Fig. 2B, single arrowhead). We can therefore also conclude from this experiment that Müller cells cannot act as optical fibers in the periphery of the fovea.

Are Müller Cells Wavelength-dependent Wave Guides in the Human Retina?

Labin and coworkers\textsuperscript{16} proposed that Müller cells function not only as optical fibers in the retina, but also as wavelength-dependent light guides, concentrating the green-red part of the visible spectrum onto cones and allowing the blue-purple part to leak onto nearby rods. These conclusions were drawn from computational analyses that have been confirmed by experiments in the guinea pig retina. For their computation, they assumed that the Müller cells in the nerve fiber layer have a proximal cup-like funnel followed by a rod-like structure that extends to the outer limiting membrane. Such a structure may be adequate to describe the situation in the guinea pig, but it is not appropriate for the human retina. Here, as discussed above, Müller cells are Z-shaped. Therefore the conclusions drawn by Labin and coworkers\textsuperscript{16} may well be relevant in the...
They furthermore investigated wholemount preparations from human retinae. The condenser of the microscope was replaced by a light beam, the angle of incidence of which could be modified on the sample. Light entering the fovea center at an angle of 0 degrees caused a very bright spot observable by the microscope after passing through this area. However, when the angle of the light beam was changed to 10 degrees, less light was observed or measured after passing through the retina: the foveolar center became darker and a Stiles-Crawford effect-like phenomenon became directly visible. Tschulakow and coworkers\textsuperscript{17} ascribed this phenomenon to properties of Müller cells, because the effect persisted after they carefully brushed the outer segments away.

Several findings speak against this interpretation:

1. As can be observed in Figure 1B, the diameter of that part of the Müller cell believed to be an element of a fiberoptic plate-like structure in the human foveola is of the order of 10 \( \mu \text{m} \). The resolution in the human fovea corresponds approximately to 1 arcmin. This corresponds to a mosaic of scanning elements of the order of 3 \( \mu \text{m} \).\textsuperscript{18} This mosaic, in turn, corresponds to the distance of cones in the human fovea. An optic plate-like structure, formed from elements of a diameter of approximately 10 \( \mu \text{m} \) in front of the foveal cones, was not compatible with the measured human acuity and would be detrimental to acuity.

2. It is possible to observe cones and rods in healthy subjects. In the fovea, the cones have center-to-center distances of the order of 3 arcmin.\textsuperscript{15} Using specific bleaching procedures, the three cone types L, M, and S\textsuperscript{20} can be distinguished from each other. It turned out that the reflectance of individual cones changes over time, that these changes are independent from cone to cone, and that they are present in all cone classes. This change in reflectance is explained by the “sheding” of discs, but could not be explained by any property of Müller cells.

It also transpired that all three types of cones reflect more light to a point close to the center of the pupil than toward the pupil margin. Such behavior is closely related to the SC1 effect, that is, the SC1 effect can be explained by the collective directional properties of the cones themselves, and no Müller cells are required.

3. In their paper, “The Stiles-Crawford effect: a theoretical revisit,” McIntyre and Pask\textsuperscript{21} introduced some refinements into the original theory, in an aim to explain the SC1 effect with the optical waveguide theory\textsuperscript{22} and considered new experimental results. Theory and experimental results were in such good agreement that the authors concluded that, with some minor adjustments, the waveguide theory constitutes the theoretical basis for the comprehension of the SC1 effect.

In fact, it was recently proposed that waveguiding may not be as fundamental for vision as commonly assumed, because a number of observations do not seem to be compatible with this concept.\textsuperscript{23} A “Volumetric integration model of the Stiles-Crawford effect of the first kind and its experimental verification” was therefore developed.\textsuperscript{24} However, in this model too, the outer segments, and not the Müller cells, are responsible for the generation of the SC1 effect.

**DISCUSSION**

The evidence for the conclusion that Müller cells form living optical fibers emanates from theoretical considerations and...
experiments alike. It is well documented that Müller cells have higher refractive indices than the surrounding tissue. Furthermore, by means of the so-called waveguide parameter \( V \), it is possible for a cylindrical waveguide to calculate whether the waveguide parameter is high enough for the structure to be able to guide light in such a way that the main part of the energy is maintained within this structure.\(^3\)

In Figure 1A, \( V \) values for light of 500 and 700 nm (upper and lower number, respectively) are indicated at different sections of a Müller cell from a guinea pig. Because these numbers are larger than 2, light-guiding capability is provided. What remains unclear is whether or not a notable loss in the guided light could be due to the uneven surface of the Müller cells: in the theoretical derivation of the waveguide parameter \( V \), the boundary conditions were such that the border between the core of a circular fiber and the cladding surround was even.\(^3\)

Experiments have shown that Müller cells can guide light. Both Franze et al.\(^2\) and Labin and coworkers\(^16\) used retinas of guinea pigs, but not of primates. Their experiments are therefore not relevant for primate retinae. Tschulakow and coworkers\(^3\) also used the retinae of five human eyes. Why an SCI-like effect could be observed in their wholemount preparations therefore remains unclear. However, the evidence presented above (i.e., that Müller cells in the human retina cannot act as light guides), together with the finding that an effect like the SCI effect can be observed in single photoreceptors\(^20\) in the living human retina, justifies the conclusion that the SCI effect is due to the collective directional properties of individual cones.

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**References**