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There is more to accommodation of the eye than simply minimizing retinal blur

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Abstract: Eyes of children and young adults change their optical power to focus nearby objects at the retina. But does accommodation function by trial and error to minimize blur and maximize contrast as is generally accepted? Three experiments in monocular and monochromatic vision were performed under two conditions while aberrations were being corrected. In the first condition, feedback was available to the eye from both optical vergence and optical blur. In the second, feedback was only available from target blur. Accommodation was less precise for the second condition, suggesting that it is more than a trial-and-error function. Optical vergence itself seems to be an important cue for accommodation.

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References and links


1. Introduction

The optical system of human eyes projects 2-dimensional images of the 3-dimensional world onto the light-sensitive retina at the back of the eye. Yet, dependent on the optical power of the cornea and crystalline lens, only objects at a certain distance, the retinal conjugate, can be imaged sharply. Objects closer or further away from the retinal conjugate are imaged out of focus. Luckily, the optical system of healthy children and young adults can adjust its power to form clear images of objects over a wide range of distances. This relatively fast and precise adaptive autofocus system called accommodation [1–5] was first described in 1619 [1].

Although binocular distance cues improve accommodative accuracy [6–8], monocular depth cues such as apparent distance, changing size, and interposition of objects are also used to control accommodation [9–11]. But these are not the only cues that the visual system uses. Normal eyes have irregularly shaped pupils [12,13] and chromatic and monochromatic aberrations that lead to different retinal images of the same object depending on whether they are formed in a plane behind or in front of the retina [13–19]. Therefore, irregular pupils [12,13] and chromatic [8,14–17,19] and monochromatic [13,18,19] aberrations introduce information that can be used by the eye to recover the sign of defocus and not only its magnitude. In other words, the optical imperfections of the eye provide signed cues for accommodation, as opposed to unsigned cues in which only magnitude but not sign of defocus is available. Signed cues from chromatic aberration are used by the eye to accommodate [8,14–17,19]. Yet, even if the neural system is adapted to the eye’s own natural aberrations [20], signed cues from monochromatic aberrations are not used by most subjects. Except in one case [21], all eyes tested have responded equally well to step stimuli [21–23] and sinusoidally moving stimuli [24–26] when the monochromatic aberrations are completely removed.

If all these cues are removed, then there is only one physical property of the light reaching the retina from which the eye can extract cues for accommodation: optical defocus. One way the visual system can exploit optical defocus to accommodate is to minimize retinal image blur that defocus generates, by trial and error. Microfluctuations in accommodation [27,28] are thought to be the physiological trial-and-error mechanism that drives accommodation [29–36]. Yet, as pointed out by Charman and Heron [28], the accommodation response seems too fast compared to the “relatively sluggish frequency characteristics of microfluctuations”.

Fincham [8,16] argued that there must be a faster, more direct way to determine the sign of defocus. He speculated that the visual system could somehow determine whether light rays reaching the retina are convergent or divergent and obtain the sign and magnitude of defocus from this direct observation. In an under-accommodated eye light rays converge as they arrive at the retina, whereas in an over-accommodated eye they diverge. He envisioned that optical vergence itself is a signed cue that the eye uses for accommodation. Despite being only theoretical models, Vohnsen [37] and López-Gil et al [38] proposed ways in which a single cone photoreceptor or patches of photoreceptors may be able to exploit the signed cues provided by optical vergence.

The aim of this work was to test whether accommodation under monocular and monochromatic conditions is driven only by a trial-and-error mechanism to minimize blur [29–36]. The trial-and-error mechanism was put to the test in three different experiments and two conditions. In both conditions, adaptive optics (AO) was used to correct astigmatism and higher-order aberrations and an image of the object was blurred if the accommodative response of the eye did not correspond to the distance at which the stimulus was placed. In the first, more natural viewing condition, the retinal image was blurred because the rays from the target did not converge onto the retina but rather behind or in front of it (optical blur). In the second, less natural viewing condition, the target itself was blurred and the rays from the target were made to converge onto the retina (target blur). In the optical-blur condition, the eye potentially had access to signed cues from optical vergence [37,38] as well as the unsigned cue blur. In the target-blur condition, the eye only had access to the unsigned cue.
blur, as optical vergence was constant regardless of how the eye changed its optical power. In the first of the three experiments, the accommodative stimulus was a stationary target. In the second experiment, the target moved abruptly in steps. In the third experiment, the target moved sinusoidally. If accommodation is achieved by trial and error to minimize blur, then the response for all three experiments ought to be the same for both experimental conditions.

In a previous work [39], the authors ran a similar experiment but without feedback from accommodation. In that experiment, the accommodative response of the eye was always corrected with an AO system so that neither optical blur nor target blur were generated at the retina, regardless of the response of the eye. Their results suggest that the eye is able to extract the sign of defocus from optical vergence as predicted by Fincham [8]. This work extends that presented in [39] to a setup where the eye is rewarded appropriately with a clearer image if it accommodates in the correct direction and punished with a more blurred image if it accommodates in the wrong direction. The feedback conditions of these three experiments are more closely related to the normal feedback control of accommodation under natural conditions.

2. Methods

2.1 Apparatus

Binocular and monocular cues, cues from imperfect pupils, and cues from chromatic and monochromatic aberrations were removed with the help of a custom-made AO system, which has been described elsewhere [39]. The AO system consists of an infrared-sensitive Shack-Hartmann wavefront sensor with 40 × 32 micro-lenses (HASO4 First, Imagine Eyes, France), a deformable mirror with 52 actuators (Mirao 52e, Imagine Eyes, France), a motorized user-controlled Badal system, and a monochromatic green microdisplay of 800 × 600 pixels and 15-micron pixel pitch (SVGA + OLED Micro-display, eMagin, NY, USA). The subjects viewed the microdisplay through a narrowband (± 5 nm) green interference filter with peak transmission at 550 nm. The Badal system allows the operator and subjects to change the target stimulus distance (optical vergence) without changing its apparent size. Customized dental molds (bite-plates) for each subject mounted on a 3-dimensional linear stage were used to align the eye and the AO system and to reduce head movements. The alignment of the eye with the AO system eye was monitored in real time during each experimental trial with an infrared camera. Measurements were taken with a low-intensity (102.5 μW) beam of near-infrared light (830 nm).

With this setup, the accommodative response of the eye can be calculated from aberrometry measurements recorded with the Shack-Hartmann wavefront sensor [21,39] together with the positions of the Badal system and the deformable mirror [40]. Custom-made software implemented with the analysis and simulation software library and software development kits provided by the manufacturer (Imagine Eyes, France) for MatLab (Mathworks, Inc., Natic, MA, USA) were used to control the system in all experiments.

2.2 Subjects

Preliminary trials were run to recruit participants who could accommodate effectively to the monocular, monochromatic target without correcting their natural aberrations [39]. Nine subjects, from 21 to 40 years of age were enrolled to participate in this study [39]. The refractive error of participants varied from 5 diopters (D) of myopia to 0.5 D of hyperopia, their astigmatisms were smaller than 1 D, and presented no ocular or accommodative anomalies. Informed consent was obtained from all subjects. The study adhered to the tenets of the declaration of Helsinki.
2.3 Experimental conditions
The key difference between the optical-blur condition and the target-blur condition relied on how retinal image blur was generated. For an emmetropic eye, or a corrected ametropic eye, the goal was to present a stimulus at a certain distance from the eye, say, at half a meter or equivalently at 2 diopters (D), demanding the eye to accommodate in order to see the target clear. In both conditions, a clear image of the target was formed at the retina only if the accommodation response of the eye was equal to the accommodation demand, 2 D. In both conditions, the amount of blur depended exclusively on the accommodative error of the eye, that is, the difference between accommodation demand and accommodation response. Thus, if the accommodation response of the eye is 1.5 D, then the retinal image would have blur corresponding to an accommodative error of −0.5 D. The nature of the blur, however, is different in the two conditions. Figure 1 illustrates both conditions schematically. For the optical-blur condition, the eye had feedback from both retinal image blur and optical vergence. In the target-blur condition, the eye only had feedback from retinal blur, but not from optical vergence, so that the only way for the eye to accommodate correctly was by trial and error.

Fig. 1. Schematic illustration of the two experimental conditions for the three experiments: optical-blur condition (light blue box) and target-blur condition (light green box). In both conditions, the accommodative error is the same and the monochromatic Maltese crosses imaged on the retina have same amount of blur. The nature of the blur, however, is different. In the optical-blur condition, blur is produced by natural optical defocus. In the target-blur condition, the blur is produced by artificially blurring the Maltese cross itself while the AO system images the target on the retina.

2.4 Experimental procedure
In all experiments and conditions, the target was a monochromatic green Maltese cross (550 ± 5 nm) with a luminance of about 20 cd m⁻² spanning 1.95 degrees of visual angle. The target was monocularly seen through a fixed circular artificial pupil of 4 mm in diameter that was imaged at the entrance pupil plane of the eye. Before starting each experiment, ametropic subjects were corrected with the Badal system. They were asked to find their far point 3 times
with the help of the Badal system using a fogging methodology. More precisely, participants were instructed to move an ETDRS chart presented on the microdisplay away from their eye until they could not see the letters clearly, using a computer mouse that controlled the Badal system. Then, they were asked to move the target slowly towards the eye until it first became clear, thus avoiding unintentional use of their accommodation. For each subject, the accommodative demands in all experiments were defined with reference to the average of the three far point measurements. In all experimental trials, astigmatism and higher-order aberrations of the eye were corrected in real time at 20 Hz with the AO system. In the target-blur condition, the accommodative response of the eye was also compensated in real time at 20 Hz, while target blur was generated with the Fourier optics calculator [41], with the amount of blur determined by the accommodative error. Each of the 9 subjects preselected in the preliminary trials underwent three experiments, which were run 6 times under each of the two conditions.

In the first experiment, a stationary target was presented at an accommodative demand of 2 D during trials lasting 50 seconds (s). The accommodative response was recorded throughout the period of the trial.

In the second experiment, the target always started the trial with an accommodative demand of 2 D and then stepped randomly ± 1 D to an accommodative demand of 1 D or 3 D. The times at which the target stepped were random with a mean Gaussian distribution of 10 s and standard deviation of 1.25 s. Thus, if the target was at 2 D, then it moved 1 D either towards or away from the eye. If the target demand was 1 D or 3 D, then it returned back to 2 D before stepping again. For each of the 6 trials, a different step profile of accommodative demands over time was generated. The same profile of steps was used in both conditions, so each subject was tested using 6 different step patterns in each condition. Trials with different step profiles and conditions were presented in randomized order. The accommodative response was recorded for 50 s during each trial.

In the third experiment, the target started each trial at an accommodative demand of 2 D and moved sinusoidally towards and away from the eye between 1 D and 3 D at temporal frequencies of 0.05 Hz, 0.1 Hz, 0.2 Hz or 0.4 Hz. The initial direction of the target movement was random. The accommodative response was recorded for the period of the trial, which was different for different temporal frequencies (25 s for 0.2 Hz and 0.4 Hz, 30 s for 0.1 Hz, and 40 s for 0.05 Hz).

2.5 Experimental limitations

In practice, the AO system provided a good, albeit not perfect, correction of aberrations and defocus as required. The correction of astigmatism and higher-order aberrations in both conditions was quite precise. For the stationary stimulus and the step stimulus, the median root mean square (RMS) errors computed for a 4-mm pupil over the period of the trial were always smaller than 0.07 microns. For the sinusoidal stimulus, the median RMS errors were smaller than 0.07 microns in all but 14 out of 432 trials. Median RMS errors were greater than 0.1 microns in only 2 trials.

For the optical-blur condition, the deformable mirror changed the optical vergence of the target very accurately for the step stimulus and the sinusoidal stimulus once drifts associated with partial wavefront correction were corrected [40]. The median defocus errors over the periods of the trial were smaller than 1.1 × 10⁻³ D for all trials and all experiments. The median absolute defocus errors were always smaller than 0.01 D. For the target-blur condition, the median defocus errors were all smaller than 0.01 D. The median absolute errors were all smaller than 0.05 D. Since for pulses of duration of less than 100 ms, accommodation response to changes in demand of more than 1 D are absent or lower than 0.2 D [42], and since the correction rate was 20 Hz, so that correction lag was 50 ms, it seems unlikely that the defocus errors committed could elicit significant responses. A correction
speed of 20 Hz is also fast enough to eliminate any feedback from microfluctuations in accommodation, since the amplitude for frequencies beyond 20 Hz are miniscule [27,28,43].

Although a 4-mm artificial pupil was used to control that the size was about the same for all subjects, conditions, and trials, it was not possible to ensure that the real pupil was not smaller than the artificial one. Nevertheless, the young age of the subjects, the low values of accommodative demand, and the luminance and low field angle of the stimulus [44], allowed to have a pupil size greater or equal to 4 mm most of the time (89.6% of the time), dropping in diameter below 3.7 mm only occasionally.

2.6 Data analysis

Figure 2 shows individual results for a trial under the optical-blur condition and the stationary stimulus (top panel), the step stimulus (middle panel), and the sinusoidally moving stimulus at a temporal frequency of 0.2 Hz (bottom panel).

![Graphs showing data analysis](image)

**Fig. 2.** Data analysis for each of the three experiments. The top panel shows a stationary-stimulus trial, the middle panel shows a step-stimulus trial, and the bottom panel shows a sinusoidally moving stimulus trial at 0.2 Hz. The accommodative demand is represented as black lines and curves. The accommodative response is represented as light gray circles. In the first stationary stimulus in upper panel the average response is shown as a solid red line. The standard deviation (std) of the response for the stationary stimulus is shadowed in light red in the upper panel. For the step stimulus and the sinusoidally moving stimulus, the mid demand is shown as a black dotted line, whereas the mid response is shown as a red dotted line. The step and sinusoidal functions fitted to the accommodative responses for both moving stimuli are shown in red. See the text for details.
For the stationary stimulus, the average error and the standard deviation (std) of the accommodative response were calculated for each trial. An accommodative error of zero means that the subject’s response equals the stimulus demand, a positive error represents an accommodative lag, and a negative error a lead. Greater std in the accommodative response means that there was greater activity (energy) in the response signals, which can be understood as greater uncertainty in accommodative response.

For the step stimulus, a step function with the same pattern of jumps as the demand (in black in middle panel of Fig. 2) and three parameters; namely, mid response, amplitude, and latency, were fitted to the data using least squares with the robust bisquare weights method. The fitted step function is shown in solid red in Fig. 2. The mid response is shown as a red dotted line, whereas latency and amplitude are denoted by the blue arrows. Subject’s response would be perfect if it had a mid response of 2 D, an amplitude of 1 D, and a latency of 0 s, thus matching exactly the demand step function, i.e. red and black step functions would be equal. Negative amplitude would mean that the steps of the fitted function are reversed, or in other words, that the response is in counter-phase with the demand. Since the amplitude of the response ought to be smaller than the amplitude of the demand, the gain, i.e., response amplitude over the demand amplitude, is reported.

For the sinusoidally moving stimulus, a similar analysis to that of the step stimulus was conducted, but with a sinusoidal function with the same frequency as the demand. For sinusoidal signals, the third parameter is typically called (temporal) phase lag, but the interpretation is analogous to that of latency for step functions. Note that here, ordinary least squares fitting of a sinusoidal function yields the same result as performing a Fourier transform and collecting amplitude and phase at the frequency of interest. Fitting the sinusoidal function directly allows the use of robust methods that mitigate the effects of outliers without smoothing the data. The same robust bisquare least squares methods was used to fit all the sinusoidal functions.

Since the data in the different experiments, conditions, and trials were typically not well described by Gaussian distributions (as tested by the Shapiro-Wilk test), the non-parametric version of the paired t-test, the Wilcoxon signed-rank significance test, was performed systematically to compare the optical-blur condition against the target-blur condition. Significance was set as 0.05 as usual.

3. Results and comment

The left panel of Fig. 3 shows the average accommodative error over 6 experimental trials for 9 subjects and both conditions. The right panel shows the average over the 6 trials of the standard deviations of the accommodative responses over the 50 s of each trial. The video in Visualization 1 shows the data recorded for a single trial of the experiment with a stationary stimulus and both conditions for subject s03. Reconstructions of the Maltese cross with defocus blur (optical-blur condition) and target blur (target-blur condition) are also shown.
Fig. 3. Response to the stationary stimulus. The left panel shows the mean accommodative error over 6 trials for 9 subjects labeled from s01 to s09. Solid circles show averages for the optical-blur condition (upper panel in Fig. 1) and open leftward triangles show averages for the target-blur condition (lower panel in Fig. 1). Data were sorted from least to most accommodative error for the optical-blur condition. The right panel shows the mean std of the accommodative response over the 6 trials per subject. Horizontal bars are ± 2 standard errors of the mean.

Except for one subject (labeled s03 in the graph), the accommodative error was not too different between both conditions. Yet, the standard deviations were almost always greater for the target-blur condition than for the optical-blur condition, suggesting a greater uncertainty in accommodation when blur but not optical vergence was available to the eye. These results for stationary targets are not conclusive, however. See, for instance, subjects labeled s06 and s07 for which there was no clear difference in response between both conditions. The mean difference in accommodative error between conditions, ± 2 standard errors of the mean, was −0.09 ± 0.19 D with a p-value for the Wilcoxon signed-rank significance test of 0.496. The mean difference in the standard deviation of response was −0.21 ± 0.15 D with a p-value of 0.004.

Fig. 4. Response to the step stimulus. The left panel shows the mean gain for a stimulus changing vergence in steps of 1 D over 6 trials for 9 subjects sorted from greatest to smallest gain for the optical-blur condition. The right panel shows the mean latency over the 6 trials per subject. Other details as for Fig. 3.

The left panel of Fig. 4 shows the average gain over 6 experimental trials for 9 subjects and both conditions. The right panel shows the average latency. The video in Visualization 2.
shows the data recorded for a single trial of the experiment with a step stimulus and both conditions for subject s04.

Except for subject labeled s06, the gain was clearly greater and the latency smaller for the optical-blur condition than for target-blur condition. Unlike the rest, subject s06 did not seem to take advantage of optical vergence for the stationary stimulus (Fig. 3) or the step stimulus (Fig. 4). The mean difference in gain was 0.40 ± 0.20 D with a $p$-value of 0.004. The mean difference in latency was $-1.11 \pm 0.69$ s with a $p$-value of 0.004.

From left to right, Fig. 5 shows the average gain for each subject to sinusoidal changes in stimulus at temporal frequencies of 0.05 Hz, 0.1 Hz, 0.2 Hz, and 0.4 Hz. The video in Visualization 3 shows the data recorded for a single trial for both conditions of the experiment with a sinusoidally moving stimulus at 0.2 Hz for subject s07.

For subjects labeled s04 and s05, average gains were similar for both conditions for a sinusoidally moving stimulus at 0.05 Hz. These two subjects accommodated just as effectively when there was no optical vergence and they had to use trial and error to accommodate. Yet, as the temporal frequency increased, the gain for the target-blur condition decreased much more (from 0.7 to 0.1 for s04 and from 0.7 to 0.2 for s05) than the gain for the optical-blur condition (from 0.8 to 0.6 for s04 and from 0.8 to 0.7 for s05). The mean differences in gain for 0.05 Hz, 0.1 Hz, 0.2 Hz, and 0.4 Hz were, respectively, 0.36 ± 0.17 D, 0.43 ± 0.15 D, 0.44 ± 0.13 D, and 0.19 ± 0.23 D with $p$-values smaller than 0.04. Phase data are not presented because the differences in gain between conditions are already very clear and because phase for those trials with zero gain can artifically take any value between 0 and 1 / temporal frequency and are therefore physically meaningless.

4. Discussion

The experimental results presented here show that there is more to accommodation of the eye than simply minimizing defocus blur by trial and error. Accommodation response was considerably slower and less reliable overall and for each particular individual when optical vergence was removed. Remarkably, if feedback from accommodation is also removed, so that the closed-loop negative feedback system is negated, the eye is still able to accommodate correctly as long as optical vergence is present [39].

Fincham’s conjecture that the eye detects optical vergence and obtains the sign and magnitude of defocus [8] was based on subjective observations from several experiments. But
at the time, the experimental conditions could not be controlled with sufficient precision. In particular, astigmatism and higher-order aberrations could not be removed. At the time, it was also not possible to measure the accommodation response to moving stimuli fast enough. These two important limitations were overcome here with the use of high-speed wavefront aberrometry and AO that corrected astigmatism and higher-order aberrations continuously. Still, although the correction of the AO system is very good (see Section 2.5), it is not perfect. In addition, blur generated in the target-blur condition is based on Fourier optics and a reduced eye model [41] (see Section 2.4), which may not represent exactly any of the 9 eyes tested. Therefore, slight differences in the blurred Maltese cross presented in each condition are to be expected. Nevertheless, if feedback was the sole driver of accommodation, these small differences should have little to no effect on the different responses to the two conditions.

Since, as mentioned in the introduction, the neural system is adapted to the eye’s own natural aberrations, it is reasonable to think that the response to the target-blur condition would be improved if the natural aberrations of the eye were included. Nevertheless, the effect of monochromatic aberrations have been shown to have little or no effect on the accommodation to step stimuli [21–23] and sinusoidally moving stimuli [24–26]. A previous experiment by the authors, in which the natural aberrations of the eye were simulated in the target-blur condition but without feedback [25], showed that the eye does not accommodate correctly to blur due to astigmatism and higher-order aberrations.

The results of the target-blur condition of the experiments presented here are in agreement with a trial-and-error mechanism that maximizes retinal contrast. In particular, the results here are consistent with the examples shown by Phillips and Stark [34] that show that eyes are able to accommodate to step changes, but with more difficulty and uncertainty when only target blur is present than when optical vergence is also present —compare Fig. 2 in Ref [34], for optical vergence and defocus blur (optical-blur condition) with Figs. 7 and 9 in Ref [34], for target blur without optical vergence (target-blur condition).

Phillips and Stark concluded that the accommodation control system can be stimulated by blur and that no additional sensory information is required. The results presented here show that, even though their hypothesis seems correct, especially for stationary stimuli, all eyes invariably performed better when optical vergence was available. Furthermore, the speed at which the accommodative mechanism breaks down is greater when optical vergence is available to the eye than when it is not. In Fig. 5, for the temporal frequencies 0.1 Hz and 0.2 Hz, at least 4 subjects could accommodate in the optical-blur condition but not in the target-blur condition. Optical vergence itself is thus an important cue used by the eye, presumably in concert with all other binocular and monocular cues and mechanisms, including trial and error to reduce blur and maximize contrast.

Not all cues and mechanisms are used by all subjects. Indeed, different subjects use different strategies to achieve accommodation and some are unable to accommodate when chromatic information is removed [14,45], at least until trained. Only subjects that could accommodate effectively to the monocular, monochromatic target moving sinusoidally at 0.2 Hz without correcting their natural aberrations [39] were selected for this study. Of all the subjects included in this study, all could accommodate when astigmatism and higher-order aberrations were removed (optical-blur condition), and all but one (subject s07) when optical vergence was removed (target-blur condition).

Despite the evidence that the visual system uses optical vergence to obtain the sign of defocus, the experiments presented here and in Ref [39] do not provide an explanation of how the sign of defocus can be extracted from optical vergence. A physiologically plausible theoretical model based on the antenna-like properties of cone photoreceptors [46] theorizes about how optical convergence or divergence of rays reaching the retina could be detected by single cone photoreceptors and by groups of cones [37]. Alternatively, or complementarily, the sign and magnitude of defocus can be extracted from the interaction of light with retinal
blood vessels in the macula [38]. Blood vessels outside the avascular zone are in front of the photoreceptor layer and generate different patterns of shadows depending on the sign of optical vergence. More precisely, there is an increase in higher spatial frequency content if light converges behind the retina than if it converges in front of the retina. From these observations, it is speculated that the visual system detects these changes even though they are not perceivable. Eye movements may also provide information about the sign of defocus from vignetting generated by blood vessels, which can create a local monocular motion parallax cue [47].

Beyond these theoretical models and the unambiguous psychophysical evidence presented here that accommodation is less accurate with blur but without optical vergence (target-blur condition), the neurophysiology and the visual pathways involved for detection and processing of optical vergence are still unknown.

It is possible that the same neurophysiological mechanisms that the visual system of humans and many vertebrates use for ocular accommodation are also used for the long-term focusing process called emmetropization [48]: the coordinated development of the optical components and growth of axial length of the eye. Indeed, although on different time-scales, both accommodation and emmetropization may share a similar feedback loop in which ocular adjustments are made to place the optical image in the eye coincident with the retina. Of course, during accommodation, these adjustments are optical in nature and the image is moved toward the retina [8], whereas in emmetropization, the retina is moved towards the image plane [49]. Both control systems must detect differences between the retinal and image planes. Lessons learned from studying the defocus signal in accommodation may provide important insights into the signal detection component of emmetropization. This, in turn, may help define new clinical treatments for the control of myopia, many of which are specifically designed to alter the defocus signal in the eyes of developing myopes [49].

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