Accommodative lag and fluctuations when optical aberrations are manipulated

Enrique Gambra
Instituto de Optica, Consejo Superior de Investigaciones Científicas (CSIC), Madrid, Spain

Lucie Sawides
Instituto de Optica, Consejo Superior de Investigaciones Científicas (CSIC), Madrid, Spain

Carlos Dorronsoro
Instituto de Optica, Consejo Superior de Investigaciones Científicas (CSIC), Madrid, Spain

Susana Marcos
Instituto de Optica, Consejo Superior de Investigaciones Científicas (CSIC), Madrid, Spain

We evaluated the accommodative response to a stimulus moving from 0 to 6 D following a staircase function under natural, corrected, and induced optical aberrations, using an adaptive-optics (AO) electromagnetic deformable mirror. The accommodative response of the eye (through the mirror) and the change of aberrations were measured on 5 subjects using a Hartmann–Shack wavefront sensor operating at 12.8 Hz. Five conditions were tested: (1) natural aberrations, (2) AO correction of the unaccommodated state and induction (over 6-mm pupils) of (3) +1 μm and (4) −1 μm of spherical aberration and (5) −2 μm of vertical coma. Four subjects showed a better accommodative response with AO correction than with their natural aberrations. The induction of negative spherical aberration also produced a better accommodative response in the same subjects. Accommodative lag increased in all subjects when positive spherical aberration and coma were induced. Fluctuations of the accommodative response (computed during each 1-D period of steady accommodation) increased with accommodative response when high-order aberrations were induced. The largest fluctuations occurred for induced negative spherical aberration and the smallest for natural and corrected aberrations. The study demonstrates that aberrations influence accommodative lag and fluctuations of accommodation and that correcting aberrations improves rather than compromises the accommodative response.

Keywords: accommodation, lag, fluctuations, high-order aberrations, adaptive optics


Introduction

The young human eye has the ability to accommodate to near and far targets. However, the mechanism that drives accommodation and the factors that determine the accommodative response are not well understood. Diverse optical signals (cues) that may specify the sign of defocus and its direction have been suggested. These cues include chromatic aberration (Fincham, 1951), Stiles–Crawford effect (Fincham, 1951), and blur (Campbell & Westheimer, 1959).

Several studies have shown that the longitudinal chromatic aberration plays a role in reflex accommodation (Aggarwala, Kruger, Mathews, & Kruger, 1995; Aggarwala, Nowbotsing, & Kruger, 1995; Kotulak, Morse, & Billock, 1995; Kruger, Aggarwala, Bean, & Mathews, 1997; Kruger, Mathews, Aggarwala, & Sanchez, 1993; Kruger, Nowbotsing, Aggarwala, & Mathews, 1995; Kruger & Pola, 1986; Lee, Stark, Cohen, & Kruger, 1999; Stark, Lee, Kruger, Rucker, & Fan, 2002) although other studies have provided evidences of the contrary (Charman & Tucker, 1978; Kotulak et al., 1995). See Lee et al. for a further discussion on this topic. Lee et al. showed that chromatic aberration drives accommodation to both moving and stationary objects, viewed through a 0.75-mm pinhole and simulated defocus of +1 D or −1 D. Kruger et al. (1997) showed that some individuals are able to accommodate in the absence of chromatic aberration, which suggested the existence of other achromatic cues driving reflex accommodation. Few studies have studied the role of cone receptor directionality on accommodation. Kruger, López-Gil, and Stark (2001) showed that the Stiles–Crawford effect did not mediate the accommodative response to defocus in the only subject of their study. Finally, blur of the retinal image has been generally considered the primary even-error stimulus for accommodation (Kruger & Pola, 1986; Phillips & Stark, 1977; Tucker & Charman, 1979).

Monochromatic high-order aberrations have also been identified as possible odd-error cues for accommodation...
(Charman & Tucker, 1977; Walsh & Charman, 1989). Wilson, Decker, and Rooorda (2002) showed with natural pupils that the presence of high-order aberrations will result in different point spread functions in combination with either hyperopic or negative defocus. They suggested that these differences might be used by the visual system to identify the correct direction of focus shift. Several studies have further explored the possible impact of aberrations on determining the direction of accommodation, altering the aberration pattern either using adaptive optics—a deformable mirror to correct totally or partially the subject’s aberrations—or lenses. Chen, Kruger, Hofer, Singer, and Williams (2006) measured the accommodative response to a 0.5-D step change in vergence on six subjects. One subject clearly required higher order aberrations to accommodate, while four did not. None of the subjects improved their accommodation to a small change of focus when high-order aberrations were removed. Fernández and Artal (2005) measured the accommodative response to a change of 1.5 D or 2 D in two subjects with their normal aberrations and with the asymmetric Zernike terms corrected. They found a significant and systematic increase in the accommodation response time and a reduction in the peak velocity in both subjects when the aberrations were corrected in real time. However, neither the latency time nor the precision of the accommodation was affected. To our knowledge, only one study (Collins, Goode, & Atchison, 1997) attempted to evaluate the influence of induced spherical aberration on accommodation, by adding $-3$ D to $+3$ D of spherical aberration through the use of aspheric surface rigid contact lenses. They found that negative spherical aberration caused an increase of the accommodative response and positive spherical aberration caused a decrease of it. Another study looked at the influence of coma and trefoil, induced by contact lenses on the accommodative gain (López-Gil et al., 2007). Several studies have also studied the dynamic accommodative response in the presence of astigmatism (Stark, Strang, & Atchison, 2003), although the conclusions differ across studies.

Alternatively, the presence of high-order aberrations may result in a reduction of the accuracy of accommodation (i.e., larger accommodative lag), as aberrations increase the depth of focus (Marcos, Moreno, & Navarro, 1999) and changing focus beyond a certain amount will not significantly increase image sharpness. Furthermore, accommodative lag has been related to myopia development. Some studies have suggested that the increased accommodative lag during near tasks in certain subjects can be a potential trigger for myopia development (Gwiazda, Thorn, Bauer, & Held, 1993). On the other hand, other studies have suggested that increased hyperopic defocus from accommodative lag may be a consequence rather than a cause of myopia (Mutti et al., 2006). As several studies have shown that myopic eyes may show larger amounts of high-order aberrations than emmetropes (Collins, Wildsoet, & Atchison, 1995; He et al., 2002; Marcos, Moreno-Barriuso, Llorente, Navarro, & Barbero, 2000; Paquin, Haman, & Simonet, 2002), the increase in accommodative lag found in myopes could be just the result of increased aberrations in these eyes. He, Gwiazda, Thorn, Held, and Vera-Diaz (2005) found that accommodative lags and Strehl ratio (derived from the wave aberrations) were significantly correlated in myopes.

Aberrometers are extensively used to measure the wave aberration of the eye, and in recent years they have been used to assess the optical quality of the eye as a function of accommodation either statically (He, Burns, & Marcos, 2000; Wilson et al., 2002) or dynamically (Hampson, Paterson, Dainty, & Mallen, 2006; Hofer, Artal, Singer, Aragón, & Williams, 2001; Plainis, Ginis, & Pallikaris, 2005). Several authors have measured the change of low- and high-order aberrations of the accommodated eye (Atchison, Collins, Wildsoet, Christensen, & Waterworth, 1995; Cheng et al., 2004; He et al., 2000; Lu, Munger, & Campbell, 1993). It is widely accepted that the only systematic change across subjects occurs for spherical aberration, which shifts toward more negative values with accommodation, and that these changes must be primarily related to changes in shape and structure of the crystalline lens as the eye accommodates (Kotulak & Schor, 1986b; Miege & Denieul, 1988; Rosales, Wendt, Marcos, & Glasser, 2008). While photodynamic retinoscopy or dynamic autorefractometry are typically used to measure the accommodative response, aberrometers have been shown to provide accurate estimates of refractive error, based on the wave aberration or on retinal image quality metrics (Guirao & Williams, 2003; Thibos, Hong, Bradley, & Applegate, 2004). Plainis et al. (2005) used an aberrometer to monitor dynamically the accommodative response (from wave-aberration estimates of the residual refractive error) for accommodative stimuli up to 8 D.

The accommodative response when focusing on a stationary target is not constant throughout time, but it fluctuates (see Charman & Heron, 1988, for a review on fluctuations of accommodation). Fluctuations of accommodation have been suggested to be an active method to maintain accommodation response and to play a role in obtaining directional cues for the dynamic accommodative response (Gray, Winn, & Gilmartin, 1993a; Kotulak & Schor, 1986a). However, other authors have suggested that fluctuations of accommodation could be a passive consequence of the reduction in zonular tension with increasing accommodative response, which would allow increased freedom of movement of the crystalline lens (Miege & Denieul, 1988). The magnitude of the fluctuations of accommodation has been shown to depend also on different factors affecting the depth of focus, such as pupil size (Stark & Atchison, 1997) or luminance (Gray, Winn, & Gilmartin, 1993b). The fluctuations of accommodation to steady target have been reported to be higher in myopes than emmetropes (Harb, Thorn, & Troilo, 2006). They have also been reported to increase with accommodative response (Kotulak & Schor, 1986b), although some studies have found a maximum for intermediate values.
of accommodation response (Miege & Denieul, 1988; Plainis et al., 2005). As aberrations affect depth of focus, it is likely that they also play a role in the fluctuations of accommodation.

In this study, we address the influence of ocular aberrations in the accommodative response, in particular the accommodative lag and fluctuations of accommodation, to accommodative demands ranging from 0 to 6 D. We have developed a custom Hartmann–Shack/Adaptive-Optics setup to measure dynamically wave aberrations (from which the accommodative response is estimated) under different states of correction/induction of aberrations using an electromagnetic adaptive-optics deformable mirror. Conditions include the correction of ocular aberrations of the unaccommodated state and induction of positive and negative spherical aberration or coma (in amounts consistent to those found in post-refractive surgery or keratoconus patients). Dynamic changes of ocular aberrations and pupil size in the different conditions will be also assessed.

Adaptive optics is an ideal tool to simulate the effect of a potential customized correction and clinical conditions or procedures that induce aberrations on the accommodative response. The results obtained from these simulations may have implications in the understanding of the role of ocular aberrations in the accommodative lag, allowing to test the hypothesis that the presence of aberrations may reduce the accuracy of the accommodative response, particularly at high accommodative demands. The results will also provide further insights into the nature of the fluctuations of accommodation.

**Methods**

**AO setup**

*Figure 1* shows a view of the adaptive-optics setup used in the accommodation experiments. A detailed description of the system has been presented in a recent study (Marcos, Sawides, Gambra, & Dorronsoro, 2008), where it was used to assess the improvement of visual acuity (at different luminance and contrast polarities) upon correction of ocular aberrations. The primary components of the system are a Hartmann–Shack wavefront sensor (HASO 32 OEM, Imagine Eyes) composed by a matrix of 32 × 32 microlenses with 3.6-mm effective diameter and a CCD camera and an electromagnetic deformable mirror (MIRAO, Imagine Eyes) with 52 actuators, a 15-mm effective diameter, and 50-μm stroke. Illumination arises from a SuperLuminescent Diode emitting at 827 nm. The beam is collimated and enters the eye slightly (1 mm) off-centered, with a diameter of 1 mm and with an irradiance of 6.95 μW on the cornea. Light reflected off the retina passes through a Badal system, the deformable mirror, and is focused on the CCD camera by the microlens array. The Badal system is mounted on a motorized stage (VXM-1, Velmex) and is used both for compensating for spherical refractive error and for inducing accommodative demands. Deformable mirror and microlens array are conjugated to the pupil with a 2 and 0.5 magnification, respectively. A cold mirror behind the wavefront sensor allows inserting the accommodation stimulus, a black and white Maltese cross with eight arms (see *Figure 1*) in the deformable mirror path. Maltese cross has been extensively used in accommodation experiments and its appropriateness has been reported (Mathews & Kruger, 1994). The stimulus is presented on a 12 mm × 9 mm SVGA OLED minidisplay (LE400, LiteEye Systems) at optical infinity to the observer and subtended 2.58 deg on the retina. The effective luminance of the white lines of the stimulus (after light losses in the system) is 50 cd/m². A pupil monitoring channel, consisting of a CCD camera (TELI, Toshiba), is inserted in the system by means of a plate beam splitter. Subjects are stabilized by means of a bite bar and aligned to the system (using an x–y–z stage) using the line of sight as a reference.

Residual aberrations of the system were calculated by using an artificial eye composed of an achromatic lens and a diffuser acting as a retina. A closed-loop correction was performed to assess the mirror state that compensated for these residual aberrations and used to correct the aberrations of the optical system.

A custom-built software programmed in VC++.Net 2005 (Microsoft) was specifically developed to control the Hartmann–Shack, the deformable mirror (by means of a Software Development Kit from Imagine Eyes), and the motorized Badal system. This software allowed us to move the motor both manually and automatically, capture Hartmann–Shack images, and drive the deformable
mirror, correcting or inducing different pattern of aberrations. Besides, software programmed in VB.Net 2005 (Microsoft) was used to continuously monitor the pupil.

**Experimental protocol**

Ocular aberrations were measured dynamically at a rate of 12.8 Hz for different accommodative stimuli, ranging from 0 to 6 D. The stimulus followed a staircase function (Figure 2) in 1-D steps and was produced by means of the motorized Badal optometer. Each step lasted 5 s. Around 65 Hartmann–Shack images were captured in each step. Between steps, the Badal optometer moved during 0.78 s with a speed of 10 mm/s (1.28 D/s). The entire sequence lasted 40 s and was typically repeated 5 times for statistical purposes.

The experiment was performed under different states of the deformable mirror. Five different conditions were studied:

1. the subject viewed the targets under his/her natural aberrations (*Nat*). In this case, the mirror only compensated for the residual aberrations of the system;
2. the subject viewed the targets under corrected aberrations (*Corr*). In this case, the mirror state compensated for the subject’s aberrations in the unaccommodated state. Best AO correction was found in a closed-loop mode immediately before the measurement;
3. the subject viewed the target with 1 μm of positive spherical aberration induced by the mirror (for 6-mm pupil) and added to his/her natural aberrations (*PSph*);
4. the subject viewed the target with 1 μm of negative spherical aberration induced by the mirror (for 6-mm pupil) and added to his/her natural aberrations (*NSph*);
5. the subject viewed the target with −2 μm of vertical coma (for 6-mm pupil) and added to his/her natural aberrations (*Coma*).

The residual aberrations of the system were corrected in all cases. The induced aberrations and their amounts were not arbitrary chosen: spherical aberration is a symmetric aberration that changes systematically during accommodation, and previous studies have reported induction of similar amounts of aberration after myopic (Marcos, Barbero, Llorente, & Merayo-Lloves, 2001) or hyperopic (Llorente, Barbero, Merayo-Lloves, & Marcos, 2004) LASIK. On the other hand, similar amounts of coma have been reported in keratoconic eyes (Barbero, Marcos, Merayo-Lloves, & Moreno-Barriuso, 2002). Mirror states inducing aberrations were actually achieved for a 7-mm pupil but aiming at the desired amount of aberrations for a 6-mm pupil. The absolute values of induced aberrations change across experiment due to pupillary miosis. The aberrations imposed on the mirror affected the quality of the image of the accommodative stimulus and the aberrations measured by the Hartmann–Shack system, allowing possible interactions between defocus and high-order aberrations.

Subjects were aligned to the system by centering the pupil to the optical axis of the system (using the pupil’s camera) while fixating at the Maltese cross. Best refractive correction was subjectively achieved by each subject by moving the Badal optometer in 0.125-D steps, and it was independently obtained for each of the five experimental conditions. Objective refraction was measured immediately before the experiment using a commercial autorefractometer (Zeiss/Humphrey), and the correction was initially set more hyperopic in the Badal system to avoid the subject accommodating while searching the best focus. Subjects were familiarized with the setup and procedure by performing some preliminary experimental sequences. All the conditions were measured consecutively in the same session. Each condition was repeated five consecutive times.

AO closed-loop correction was performed using our custom-developed software. Final and initial RMS wavefront error values were compared and a correction of at least 80% (astigmatism plus high-order aberrations) was required to deem the mirror state appropriate for measurements.

As pupil size decreased with accommodation, we made sure that AO correction/induction of aberrations was achieved for the largest pupil size (unaccommodated state). Therefore, correction/induction should not be affected by pupil change (if constriction happens concentrically). The Hartmann–Shack images were used to calculate the pupil size during the experiment, with a precision of 0.11 mm.

**Subjects**

Five young subjects (age: 25.3 ± 2.4) with low amounts of spherical error (0.35 ± 0.72 D) and astigmatism (<0.5 D) participated in this study. Two of them were trained subjects and the other three were naive. All of them were

![Figure 2. Staircase function followed by the accommodation test.](image-url)
capable of accommodating 6 D, as assessed with IR dynamic retinoscopy (PowerRef II, Plusoptix) prior to the experiment. LR was unable to perform the experiment under coma condition. Subjects signed a consent form approved by the Institutional Review Boards after they had been informed on the nature of the study and possible consequences. All protocols met the tenets of the Declaration of Helsinki.

Data analysis

Aberrations

Wave aberrations were fitted to seventh-order polynomials (with criteria following the OSA standards) using a least-mean square procedure. Sequences of Zernike polynomials along with the corresponding pupil diameter and the pupil center coordinates were analyzed. Typical 40-s sequences of data contained 482 wave aberration measurements and were processed using routines written in Matlab (version 7.3; The Mathworks). Measurements affected by blinks were automatically removed by the software (as no signal was detected in the Hartmann–Shack), while data captured immediately before and after were supervised and excluded if necessary. We used as a criterion that pupil size and centration should not change significantly from the data previous to the blink. Each accommodative step contained on average 51 ± 12 (between 18 and 65) useful measurements. Zernike coefficients were fitted to individual measurements (to assess dynamic changes in aberrations and accommodative response). Accommodative response was calculated for each measurement and then averaged to estimate its mean value at each accommodative demand. Similarly, pupil diameter at each accommodative demand was obtained as average of individual measurements. The results of five repeated sequences were eventually averaged to achieve the final data for each condition and accommodative demand.

Unless otherwise noted, results are presented for the natural pupil (which varied dynamically). In some cases, Zernike coefficients were resized to the same pupil size (generally a 4-mm pupil). In some cases, the spherical aberration coefficient is reported in terms of diopters by considering its contribution to the accommodative response:

\[
SE(D) = \frac{12\sqrt{5} \cdot C_4^0}{R^2}.
\]

(1)

Accommodative response

We estimated the accommodative response from wave aberrations, using a definition for spherical equivalent error, based on the paraxial curvature matching of the wavefront aberration map (Thibos et al., 2004). Therefore, the residual refractive error \((M)\) for each accommodative demand was

\[
M = -\frac{4\sqrt{3} \cdot C_2^0 + 12\sqrt{5} \cdot C_4^0 - 24\sqrt{7} \cdot C_6^0}{R^2}.
\]

(2)

For comparative purposes, we also used as a definition of spherical error the defocus that optimizes the volume under the MTF. This definition (or an alternative that uses Strehl ratio) has been shown to provide the best prediction of subjective refractive error in previous works (Guirao & Williams, 2003; Marcos et al., 2008), and takes into account interactive effects between different Zernike terms as well as diffraction. We used the average volume under the MTF, rather than normalized (Strehl ratio) to allow comparisons across accommodation states (with different pupil sizes). The volume under the MTF was truncated at 100 c/deg, as higher frequencies are not relevant to the visual system (Marcos, Burns, Moreno-Barriuso, & Navarro, 1999).

The accommodative response was estimated as the corresponding accommodative demand minus the residual refractive error. Residual refractive error was assumed to be zero at 1.5 D of accommodative demand (He et al., 2000; Plainis et al., 2005), which has been found to be the average accommodative resting state (Leibowitz & Owens, 1975, 1978; Maddock, Millodot, Leat, & Johnson, 1981; Smith, 1983; Wolfe & O’Connell, 1987). Therefore, the estimated accommodative responses are shifted so that the average response at 1.5 D of accommodative demand is 1.5 D. The refractive correction for the unaccommodated state agreed well with previously measured refraction (autorefractometer) and the residual defocus computed from the Zernike term was consistent with the longitudinal chromatic aberration between the visible wavelength of the target and IR light of the test source (Llorente, Diaz-Santana, Lara-Saucedo, & Marcos, 2003). For each accommodative demand, the average accommodative response was calculated by averaging the estimated individual response during each period of 5 s. The average accommodative response for each trial was then averaged across the five trials. The accommodative lag is defined as the difference between accommodative demand and accommodative response. Thus, lag is directly the residual refractive error.

Fluctuations of accommodation

The fluctuations of the accommodative response were estimated as the standard deviation of the latter during sustained accommodation. These were computed for each accommodative demand (5-s periods) and AO aberration correction/induction conditions.

Alternatively, we obtained the frequency spectra for each of the 5-s sequences (for the different accommodative
demands and AO correction condition), using Fourier
analysis. The area under the frequency spectra was
numerically calculated for low (0–0.6 Hz) and high (0.9–
2.5 Hz) frequency regions and compared across conditions.

Control experiments
In a previous study (Gambra, Sawides, Dorronsoro,
Llorente, & Marcos, 2007), we had presented calibrations
of the system, including accuracy of wave aberration
measurements on artificial eyes with known high-order
aberrations—as calibrated from the manufacturer and also
measured by a Laser Ray Tracing system in our laboratory
(Llorente, Barbero, Cano, Dorronsoro, & Marcos, 2004;
Llorente et al., 2003)—and capabilities of the AO system.
Discrepancies in the measured aberrations were typically
less than 5% with respect to nominal values. We found that
the RMS (excluding tilt and defocus) of the artificial eye
decreased from 0.960 μm to 0.033 μm after 8 iterations
(0.6 s) in a closed-loop compensation. For this study, we
also performed a series of control experiments aimed at
testing deformable mirror stability throughout a session,
accuracy of induced aberrations (particularly, as we are
inducing large amounts of spherical aberration and coma),
and potential changes of system’s aberration for the
different positions of the Badal system.

The mirror stability was checked by measuring wave
aberrations of an artificial eye every 30 min during 3 h,
i.e., more than the total duration of the experimental
session in a single subject. Changes in the RMS (excluding
tilt and focus) were less than 0.003 μm standard deviation
(0.3%) and showed no particular trend with time. We also
simulated an accommodation experiment on an artificial
eye by changing the Badal system (in similar steps as for
the experiments in real eye) and compensating the induced
defocus with trial lenses. The experiment was conducted
for different states of the deformable mirror (inducing
spherical aberration, etc.). Pupil size measured with the
Hartmann–Shack was independent of the condition. Most
Zernike coefficients varied less than 0.02 μm (for 4-mm
pupils) with simulated accommodation, although some
specific terms $C_{3}^{+1}$, $C_{2}^{−2}$, and $C_{4}^{0}$ changed systematically.
These calibrations were considered to discount the effects
of the instrument on the eye’s measurements.

Results

Aberration correction and induction

Figure 3 shows examples of wave aberration maps in
the unaccommodated state for the five experimental
conditions (natural, corrected, induced positive and nega-
tive spherical aberration, and induced coma) for all
subjects. Each map has been plotted for the corresponding
natural pupil diameter (between 4.7 and 6.8 mm). Figure 4
shows the amount of spherical aberration, third-order
RMS, and total higher order RMS in each of the wave
aberration maps in Figure 3, for the natural pupil. Table 1
shows the average amount of high-order RMS in the
natural and AO-corrected condition (across all measure-
ments of the unaccommodated state) and a 4-mm pupil.

Changes in pupil with accommodation and
aberration condition

Changes in pupil diameter with accommodation play a
role in the relative change of aberrations with accommo-
dation and the accommodative response. Figure 5A shows
the pupil diameter change with accommodative response
for the different experimental conditions (averaged across
subjects). There is a systematic decrease of pupil diameter
with accommodation, as expected (Kasthurirangan &
The rate of change in pupil diameter differs across
subjects. In addition, several subjects showed different
pupil diameter change rates across conditions. Figures 5B
and 5C show examples for two subjects. LS showed
differences in pupil diameter across conditions, while for
LR the pupil diameter was nearly independent of the
aberration condition.
Linear regressions to the data of Figure 5A show a highly linear pupil diameter change with accommodation. The average slope of the change ranged from $-0.23$ mm/D (for induced negative spherical aberration) to $-0.6$ mm/D (for induced positive spherical aberration). On average, the pupil diameter was significantly smaller than in the rest of the conditions when the aberrations were corrected, and (for the highest accommodative demands) also when positive spherical aberration was induced (ANOVA, Bonferroni T2, with SPSS 15.0 for Windows).

![Figure 4](https://jov.arvojournals.org/pdfaccess.ashx?url=/data/journals/jov/933553/)

**Figure 4.** Contribution of different Zernike terms to the wave aberration maps in Figure 3: spherical aberration $C_4^0$ (red), third-order RMS (green), and total high-order RMS (blue). Pupil diameters are indicated under each condition: natural (Nat), AO-corrected (Corr), induced positive spherical aberration (PSph), negative spherical aberration (NSph), and coma (Coma).

Table 1. Natural and AO-corrected RMS wavefront errors (for high-order aberrations). Pupil diameter = 4 mm.

<table>
<thead>
<tr>
<th>Subject</th>
<th>Natural</th>
<th>AO-corrected</th>
</tr>
</thead>
<tbody>
<tr>
<td>LS</td>
<td>0.138</td>
<td>0.075</td>
</tr>
<tr>
<td>LR</td>
<td>0.107</td>
<td>0.050</td>
</tr>
<tr>
<td>IG</td>
<td>0.202</td>
<td>0.097</td>
</tr>
<tr>
<td>PK</td>
<td>0.169</td>
<td>0.151</td>
</tr>
<tr>
<td>JP</td>
<td>0.120</td>
<td>0.058</td>
</tr>
<tr>
<td><strong>Average</strong></td>
<td><strong>0.147</strong></td>
<td><strong>0.086</strong></td>
</tr>
</tbody>
</table>

**Change of aberrations with accommodation**

Movie 1 shows the change of the wave aberration (second- and higher order terms) with the accommodative demand (left) and the corresponding simulated PSF (right), for natural pupil sizes. The example is for a particular sequence, for subject LS and AO-corrected condition. Data were acquired at a 12.8-Hz rate and the variations in pupil size are truly represented.

**Table 2** shows the slopes from regression lines to data from all subjects. As expected, the term that varied the most was the spherical aberration, which shifts toward more negative values with accommodation. Interestingly, the condition under test influenced significantly the rate of variation of spherical aberration with accommodation. In all subjects, the measured spherical aberration (corresponding to the eye plus the mirror) changed more rapidly toward negative values when positive spherical aberration was induced by the deformable mirror, whereas the slope of this change was greatly reduced when negative spherical aberration was induced. The tendency was the same (not...
shown) when spherical aberration was plotted against the accommodative demand (which was independent of the actual change in spherical aberration). It is expected that for the same accommodative response the accommodation-related physical changes of the crystalline lens and therefore the relative change of the ocular spherical aberration are similar, regardless of the experimental condition (or overall degradation) of the target.

We explored the causes for the relative differences in the rate of change of spherical aberration across conditions shown in Figure 6. Figure 7 shows the isolated ocular contribution to the measured change of spherical aberration with ocular accommodative effort for natural and positive and negative spherical aberration induced conditions. The ocular contribution to the accommodative response (ocular effort) has been calculated by resizing all wavefronts to a 4-mm pupil, which eliminates the influence of pupil constriction on spherical aberration change. Besides, Zernike coefficients of the resized pupils have been used to assess ocular accommodative effort, using Equation 2. Figure 7 shows average data across four subjects (PK was not included as his pupil was smaller than 4 mm for the highest accommodative demands).

The rate of change for the three conditions (natural and induced positive/negative spherical aberration) is much more similar (Figure 7), as expected, and primarily driven by the structure-related changes in spherical aberration of the crystalline lens with accommodation.

Table 2. Slope of the regressions of $C_{2-2}$, $C_{4-0}$, and $C_{3-1}$ (in microns) vs. accommodative response for each subject and condition.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Subject</th>
<th>$C_{2-2}$</th>
<th>$C_{3-1}$</th>
<th>$C_{4-0}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nat</td>
<td>LS</td>
<td>-0.027*</td>
<td>-0.011</td>
<td>0.023</td>
</tr>
<tr>
<td></td>
<td>LR</td>
<td>-0.013*</td>
<td>-0.002</td>
<td>-0.034*</td>
</tr>
<tr>
<td></td>
<td>IG</td>
<td>0.012*</td>
<td>-0.007*</td>
<td>-0.012</td>
</tr>
<tr>
<td></td>
<td>PK</td>
<td>-0.063*</td>
<td>0.018*</td>
<td>-0.028*</td>
</tr>
<tr>
<td></td>
<td>JP</td>
<td>0.008</td>
<td>-0.056*</td>
<td>-0.013*</td>
</tr>
<tr>
<td></td>
<td>Avg</td>
<td>-0.017</td>
<td>-0.012</td>
<td>-0.013*</td>
</tr>
<tr>
<td>Corr</td>
<td>LS</td>
<td>$4 \times 10^{-5}$</td>
<td>$6 \times 10^{-5}$</td>
<td>-0.021</td>
</tr>
<tr>
<td></td>
<td>LR</td>
<td>-0.058*</td>
<td>-0.003</td>
<td>-0.028*</td>
</tr>
<tr>
<td></td>
<td>IG</td>
<td>-0.012*</td>
<td>0.002</td>
<td>-0.030*</td>
</tr>
<tr>
<td></td>
<td>PK</td>
<td>0.012*</td>
<td>0.003</td>
<td>-0.016*</td>
</tr>
<tr>
<td></td>
<td>JP</td>
<td>0.004</td>
<td>-0.002</td>
<td>-0.014*</td>
</tr>
<tr>
<td></td>
<td>Avg</td>
<td>-0.011</td>
<td>$1 \times 10^{-5}$</td>
<td>-0.022*</td>
</tr>
<tr>
<td>PSph</td>
<td>LS</td>
<td>0.009</td>
<td>0.052*</td>
<td>-0.157*</td>
</tr>
<tr>
<td></td>
<td>LR</td>
<td>-0.013</td>
<td>0.081*</td>
<td>-0.190*</td>
</tr>
<tr>
<td></td>
<td>IG</td>
<td>0.014*</td>
<td>0.044*</td>
<td>-0.065*</td>
</tr>
<tr>
<td></td>
<td>PK</td>
<td>-0.051</td>
<td>0.044</td>
<td>-0.117*</td>
</tr>
<tr>
<td></td>
<td>JP</td>
<td>0.029*</td>
<td>-0.009</td>
<td>-0.505*</td>
</tr>
<tr>
<td></td>
<td>Avg</td>
<td>-0.002</td>
<td>0.042*</td>
<td>-0.207*</td>
</tr>
<tr>
<td>NSph</td>
<td>LS</td>
<td>0.006</td>
<td>-0.044*</td>
<td>0.078*</td>
</tr>
<tr>
<td></td>
<td>LR</td>
<td>-0.005</td>
<td>-0.010</td>
<td>0.045*</td>
</tr>
<tr>
<td></td>
<td>IG</td>
<td>-0.001</td>
<td>-0.049*</td>
<td>0.039*</td>
</tr>
<tr>
<td></td>
<td>PK</td>
<td>-0.041*</td>
<td>0.033</td>
<td>0.084*</td>
</tr>
<tr>
<td></td>
<td>JP</td>
<td>0.005</td>
<td>-0.093*</td>
<td>0.042*</td>
</tr>
<tr>
<td></td>
<td>Avg</td>
<td>-0.007*</td>
<td>-0.033*</td>
<td>0.058*</td>
</tr>
<tr>
<td>Coma</td>
<td>LS</td>
<td>-0.082*</td>
<td>-0.026*</td>
<td>-0.044*</td>
</tr>
<tr>
<td></td>
<td>IG</td>
<td>-0.010</td>
<td>-0.002</td>
<td>-0.005</td>
</tr>
<tr>
<td></td>
<td>PK</td>
<td>-0.079*</td>
<td>0.006</td>
<td>-0.033*</td>
</tr>
<tr>
<td></td>
<td>JP</td>
<td>-0.205</td>
<td>0.205*</td>
<td>-0.127*</td>
</tr>
<tr>
<td></td>
<td>Avg</td>
<td>-0.094*</td>
<td>0.046</td>
<td>-0.052*</td>
</tr>
</tbody>
</table>

Figure 6. Change of different individual Zernike terms ($C_{2-2}$, $C_{2+2}$, $C_{3-1}$, $C_{3+1}$, and $C_{4-0}$) with accommodative response for different conditions [(A) natural, (B) AO-corrected, (C) induced positive spherical aberration, and (D) induced negative spherical aberration]. Data are for subject LR with natural pupil.

Table 2. Slope of the regressions of $C_{2-2}$, $C_{4-0}$, and $C_{3-1}$ (in microns) vs. accommodative response for each subject and condition. Note: *There is a significant dependence with accommodative response (Z-test).
pupil-dependent contribution of the induced/corrected spherical aberration, which varies across accommodative responses and conditions. When positive spherical aberration is induced, its effective positive contribution relatively decreases as the pupil decreases with accommodation. The result is a change of measured spherical aberration shifted to more negative values, i.e., the effect is added to the effect of the crystalline lens. On the other hand, if negative spherical aberration is induced, its effective negative contribution relatively decreases as the pupil decreases with accommodation counteracting the change in spherical aberration of the crystalline lens and the slope becoming closer to zero.

We also evaluated the dynamic change of other aberrations (astigmatism and third-order Zernike terms) as a function of the accommodative response for the conditions under test (see Figure 6 for graphical example on subject LR, and Table 2 for regression line fits to data from all subjects). We did not find a general tendency across subjects, neither in the natural or aberration corrected/induced conditions. Although the change in certain Zernike terms with accommodation is significant in some individual subjects, it usually does not occur in all measured conditions (less frequently in the natural conditions), and slope for the change is very small.

**Influence of aberrations on the accommodative response**

Figure 8 shows examples of the accommodative response for subject LS under the five conditions under test (natural aberrations, corrected aberrations, induced positive spherical aberration, induced negative spherical aberration, and induced coma). The data are for a single measurement and are representative of typical responses in this group of subjects. One of the subjects (LR) was unable to perform the task under induced coma. The accommodative response (and from it, the accommodative lag) was estimated from the residual spherical error (Equation 2).

Figures 9A–9E show the accommodative lag, averaged across measurements (5 runs) and 5-s steps as a function of the accommodative demand. Data are for all five subjects and conditions. Most subjects showed a better accommodative response (lower lag) with corrected than with their natural conditions (4 out of 5 subjects). The induction of negative spherical aberration resulted also in a better accommodative response for the same 4 subjects. On the other hand, the accommodative response is poorer in all the cases when positive spherical aberration and vertical coma were induced. Only one subject (IG) showed best accommodative response under natural aberrations.

Figure 9F shows the accommodative lag averaged across subjects. On average, lag with AO-corrected aberrations and with induced negative spherical aberration were significantly different from lag with coma ($p < 0.05$) for high accommodative demands. Differences between lag for induced positive spherical aberration and all other conditions (except coma) were statistically significant (ANOVA, Bonferroni T2, with SPSS 15.0 for Windows).
These general tendencies were followed by three of the individual subjects (LS, LR, and JP). The other two showed significant differences for a few accommodative demands and conditions.

Alternatively, residual error (and accommodative lag) was computed from the defocus that optimized the volume under the MTF. Figure 10 shows through-focus optical quality (in terms of volume under the MTF) for the different accommodative demands and four conditions [natural (Figure 10A); AO-corrected (Figure 10B); induced positive spherical aberration (Figure 10C); induced negative spherical aberration (Figure 10D)], for subject LR. The defocus shift that produces a maximum in the through-focus function represents the accommodative lead (for the lower accommodative demands) and the accommodative lag (for the higher accommodative demands). The arrow represents the accommodative lag for a 6-D stimulus. The amplitude and width of the through-focus functions, as well as the accommodative lag, change across conditions.

Correcting the aberrations of the unaccommodated state produces an increase in the peak values and a narrowing of the through-focus functions. Inducing positive spherical aberration produces an enhancement of the through-focus functions for the highest accommodative demands as well as an increase in the accommodative lag. Inducing negative spherical aberration broadens the curves for all accommodative demands and reduces the accommodative lag (which, for this particular subject and condition, results in a negative value). We have compared the accommodative response and accommodative lag obtained from the volume under the MTF through-focus function and from other spherical error definitions. We found a better agreement between the volume under the MTF and the paraxial curvature metric, considering up to sixth-order spherical aberration in the equation (standard deviation of the difference in accommodative lag across metrics: $SD = 0.27$ D). However, when the spherical error was estimated considering the Zernike defocus term only, the accommodative response was properly described for natural and AO-corrected conditions but failed for the conditions in which spherical aberration was induced ($SD = 0.50$ D).

Figure 9. Accommodative lag for all subjects (A–E) and averaged across subjects (F) for all conditions. Positive lag means underaccommodation (lag) while negative lag means overaccommodation (lead). Each point has been calculated by averaging responses in each accommodative demand and from five repeated measurements.

Figure 10. Through-focus volume under the MTF (as an optical quality metric), for the different accommodative demands and different conditions [(A) natural aberrations, (B) AO-corrected aberrations of the unaccommodated state, (C) induced positive spherical aberration, (D) induced negative spherical aberration], for subject LR. The defocus shift that produces a maximum in the through-focus function represents the accommodative lead (for the lower accommodative demands) and the accommodative lag (for the higher accommodative demands). The arrow represents the accommodative lag for a 6-D stimulus. The amplitude and width of the through-focus functions, as well as the accommodative lag, change across conditions.
Considering only defocus and 4th spherical aberration in the definition of residual spherical error tended to overestimate the accommodative response (SD = 0.86 D) with respect to the paraxial definition that includes terms up to the sixth order.

**Influence of demand and aberrations on the fluctuations of accommodation**

Figure 11 shows the fluctuations of accommodation (standard deviation of the accommodative response) as a function of accommodative demand, for all conditions tested, and averaged across subjects. We found that fluctuations increased systematically with accommodation in all conditions (with slopes ranging from 0.033 when positive spherical aberration was induced to 0.077 when coma was induced). For a given accommodative demand, fluctuations tend to be lowest under natural and corrected aberrations, and highest under induced spherical aberration (particularly negative) and induced coma. Fluctuations were significantly higher (p < 0.05) than for natural aberrations when negative spherical aberration was induced (ANOVA, Bonferroni T2, with SPSS 15.0 for Windows). The induced positive spherical aberration condition also produced significantly higher fluctuations for the lowest accommodative demands.

Alternatively, the area under frequency spectra (up to a frequency of 2.5 Hz) was also used to define the fluctuations of accommodation. We found a good correlation (slope = 0.78 ± 0.03, R = 0.94, p < 0.0001) between the fluctuations estimated from the frequency spectra and the standard deviation of the accommodative response. Restricting the area to low frequency range (0–0.6 Hz), primarily associated to the fluctuations of the accommodation plant, does not increase the correlation between definitions, while restricting the area to a higher frequency range (0.9–2.5 Hz), typically related to cardiac pulse slightly worsened the correlation (slope = 0.34 ± 0.02, R = 0.88, p < 0.0001).

**Discussion**

Our results show that the presence or absence of high-order aberrations (controlled with adaptive optics) alters the accommodative response and the fluctuations of accommodation. We did not find that correcting high-order aberrations had a negative impact on the accommodative response. Moreover, the precision of the accommodation response increases if aberrations are corrected and worsens if some aberrations such as coma (which broadens the depth of focus) are induced. We can conclude from this study that the presence of larger amounts of high-order aberrations produces an increase in accommodative lag. This result is interesting in the understanding of the causes for the accommodative lag in young subjects. It also suggests that the increased accommodative lag found in myopes (Mutti et al., 2006) may be linked to larger amounts of high-order aberrations in myopes (He et al., 2002; Marcos et al., 2000; Paquin et al., 2002), and therefore be a consequence rather than a preceding factor in myopia development (Mutti et al., 2006). Although not all studies have found higher amounts of aberrations in myopes compared to emmetropes or hyperopes (Carkeet, Luo, Tong, Saw, & Tan, 2002; Cheng, Bradley, Hong, & Thibos, 2003), there is evidence that this is the case for high myopes. Whether increased amounts of aberrations may trigger myopia development has also been a matter of debate (Collins et al., 1995; Thorn, Held, Gwiazda, & He, 2008). Recent studies on animal models (Garcia de la Cera, Rodriguez, De Castro, Merayo, & Marcos, 2007) suggest that increased aberrations may be rather a result of the structural properties of myopic eyes, rather than a cause of myopia.

The presence of spherical aberration also influences the accuracy of the accommodative response, with the effect being highly dependent on the sign of the induced spherical aberration. In agreement with a previous observation by Collins et al. (1997), we found that adding negative spherical aberration produced a decrease in the accommodative lag, despite the increase of high-order aberrations (and decrease of optical image quality of the unaccommodated state). On the other hand, adding positive spherical aberration produced an increase in the accommodative lag (less accurate accommodative response). These results indicate that the accommodative response may be affected in patients that had undergone corneal refractive procedures that increase high-order aberrations, as standard myopic LASIK induces significant amounts of positive spherical aberration (Marcos et al., 2001), and hyperopic LASIK of negative spherical
aberration (Llorente, Barbero, Merayo-Lloves et al., 2004). The influence of spherical aberration on the accommodative response also reinforces the importance of considering not only defocus but higher order aberrations for the estimation of the accommodative response, as had been emphasized by Plainis et al. (2005), similarly as in the calculation of refractive errors (Guirao & Williams, 2003; Thibos et al., 2004). To our knowledge, few studies have explored the influence of other high-order aberrations on accommodation. López-Gil et al. (2007) found a decrease of dynamic accommodation gain in subjects wearing contact lenses that induced coma and trefoil, which is consistent with the reduced accommodative response that was found in the presence of coma.

The change of pupil size diameter with accommodation is also important to account for the relative contribution of the induced/corrected aberrations and the relative change of high-order aberrations with accommodation to the accommodative response. We found that in our subjects, pupil size decreased with accommodative response at a rate of $-0.35$ mm/D (natural condition), within the range of previous studies, i.e., Plainis et al. ($-0.18$ mm/D) and Alpern, Mason, and Jardinico (1961) ($-0.45$ mm/D). Surprisingly, the pupil diameter varied significantly across conditions in several subjects, and the differences were observed at all accommodative demands. On average across subjects, the pupil was significantly smaller when aberrations were AO-corrected, and largest in the natural condition. Certain subjects (i.e., LS) differed as much as 1.66 mm between conditions, for the same accommodative demand, although for other subjects (i.e., LR) the differences across conditions were not significantly different. The rate of variation in pupil diameter with accommodation also varied across conditions. Pupil size did not vary with the condition tested when artificial eyes were used. We are uncertain on the reasons for this difference, which is very significant in some subjects, as the changes in retinal illuminance between the corrected/uncorrected aberration conditions are expected to be small. An alternative hypothesis is that the presence of unfamiliar distortion (or correction) in the image has an impact on pupil size. In any case, these differences contribute to the improved accommodative lag under corrected aberrations.

The accommodation-related changes of aberrations with accommodative demand that we found are in good agreement with previous studies. We did not find that correcting/inducing aberrations altered the relative change of aberrations (except for spherical aberration) with accommodation. The reported differences in the change of spherical aberration when the amount of spherical aberration of the unaccommodated state is altered are mainly a consequence of the relative contribution of the aberration induced by the mirror as the pupil decreases with accommodative response. When the ocular (primarily crystalline lens) contribution to the change in spherical aberration is isolated, the change of spherical aberration with accommodation is much more similar across conditions (see Figure 7). It should be noted, however, that the actual changes reported in Figure 6 (showing drastic differences in the change of spherical aberration under positive or negative spherical aberration) should be truly representative of the accommodation-related changes of spherical aberration after standard LASIK, where significant amounts of aberration are induced on the cornea.

Under natural conditions, spherical aberration shifted to more negative values with accommodation response at a rate of $-0.013$ μm/D (averaged across subjects). This rate of change is lower than that reported in earlier studies using a fixed pupil diameter ($-0.043$ μm/D of Cheng et al., for an artificial pupil of 5 mm; around $-0.083$ μm/D of He et al. for an effective 6.5-mm pupil, and $-0.048$ μm/D of Plainis for natural pupils). The differences arise primarily from the change pupil diameter with accommodation in our experiments, which were performed under natural viewing conditions. A comparison of the change of spherical aberration expressed in diopters (Equation 1) to minimize the impact of the pupil diameter change gives similar rate of change ($-0.153$ D/D in the current study, $-0.184$ D/D in Cheng et al., around $-0.230$ D/D in He et al., and $-0.170$ D/D in Plainis et al.).

Other aberration terms (astigmatism; $C_3^2$, $C_2^2$) orcoma ($C_3^{-1}$ and $C_1^2$) did not change systematically with accommodation across subjects, and their averaged slopes were similar to those reported in previous studies (Cheng et al., 2004; He et al., 2000; Plainis et al., 2005).

Fluctuations of accommodation systematically increased with accommodative response. For natural condition, we have obtained that fluctuations varied from 0.09 D to 0.31 D—in the 0–6D stimulus range—with a slope of 0.049 D/D. This is consistent with previous studies: Plainis et al. (2005) found that fluctuations increased with accommodation from 0.07 D to 0.22 D for an accommodative demand of 8 D; and Kotulak and Schor (1986b) found a slope of 0.047 D/D (plotting fluctuations vs. mean response). However, we did not find a maximum for intermediate demands—as reported by Miege and Denieul (1988) and Plainis et al. (2005)—either for averaged or for individual data. Furthermore, although differences did not always reach statistical significance, in general, fluctuations were greater when spherical aberration and coma were induced and smaller for natural and AO-corrected aberrations. This finding indicates that retinal image quality plays an active role in the fluctuations of the accommodative response, likely due to the increased depth-of-focus when aberrations are increased (Cheng et al., 2003; Marcos, Moreno et al., 1999).

**Acknowledgments**

This work was supported by a CSIC I3P Predoctoral Fellowship to EG, MÉyC FPI Predoctoral Fellowship to...


Commercial relationships: none.

Corresponding author: Enrique Gambra.

Email: e.gambra@io.cfmac.csic.es.

Address: Instituto de Óptica, CSIC, Serrano 121, 28006, Madrid, Spain.

References


