The Pupil Can Control an Artificial Lens Intuitively

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Purpose. After cataract surgery, the ability to accommodate is lost. For this reason, a mechatronic IOL is being developed at the moment: The Artificial Accommodation System. This device requires an easily measureable indicator of the distance of the observed object to determine the demand of accommodation. As the pupil constricts with near vision, pupil size might be such an indicator. Our research focused on whether the pupil can control an artificial lens.

Methods. A study with 14 healthy subjects aged between 24 and 64 years was conducted. An artificial lens with variable refractive power was mounted in front of one eye. In this eye, natural accommodation was greatly reduced or absent due to presbyopia, pseudophakia, or iatrogenic cycloplegia. The lens’ refractive power was changed in a computer-controlled manner depending on changes in the pupil diameter of the second eye, which could not see the fixation stimulus. The subject’s task was to get a clear focused image of the target in different distances.

Results. The lens can be controlled by the pupil intuitively ($P < 1.8 \times 10^{-10}$). Without prior knowledge, 11/14 subjects passed the first trial, and 31/41 trials were successful. Only one subject was not able to control the lens at all. Most subjects comprehended instantly how to use the unfamiliar lens control to bring a target into focus.

Conclusions. This study emphasizes the plasticity of the visual control system. Positioning accuracy was acceptable, but the control must be optimized to facilitate maintaining a defined refractive power.

Keywords: pupil, neural control, IOL, accommodation
power of the lens was coupled to the pupil diameter. The task of the subject was to bring the target located at different distances into focus.

The axis of sight. Opaque curtains occluded the left eye. During the experiment, the pupil of this eye was measured by a video pupillometer. The accommodation was reduced greatly or absent due to presbyopia, pseudophakia, or iatrogenic cycloplegia. The target could be shifted parallel to the axis of sight. Opaque curtains occluded the left eye. During the experiment, the pupil of this eye was measured by a video pupillometer. The power of the lens was coupled to the pupil diameter. The task of the subject was to bring the target located at different distances into focus.

10 consecutive values. Curves were low-pass filtered by moving average considering reliable pupil diameter was transferred to the lens control to changes in refractive power. In case of blink detection, the last erroneous enlargement of the pupil range and false rapid before and five after each blink were rejected to avoid removed eye blink artifacts. In addition, two measured values curves were low-pass filtered by moving average considering reliable pupil diameter was transferred to the lens control to changes in refractive power. In case of blink detection, the last erroneous enlargement of the pupil range and false rapid before and five after each blink were rejected to avoid removed eye blink artifacts. In addition, two measured values.

FIGURE 1. Experimental setup. The subjects looked with the right eye through a lens of variable refractive power at a target. In this eye, natural accommodation was reduced greatly or absent due to presbyopia, pseudophakia, or iatrogenic cycloplegia. The target could be shifted parallel to the axis of sight. Opaque curtains occluded the left eye. During the experiment, the pupil of this eye was measured by a video pupillometer. The power of the lens was coupled to the pupil diameter. The task of the subject was to bring the target located at different distances into focus.

MATERIALS AND METHODS

This study was performed in accordance with the Declaration of Helsinki. All 16 participants signed an informed consent. The study was approved by the Tübingen Ethics Committee.

The experimental setup is shown in Figure 1. The subject’s head was immobilized with a forehead support and a chin rest. The subject looked with the right eye monocularly through an Alvarez-Humphrey lens. This lens is composed of two complex-shaped, aspheric, not rotationally symmetric components. The refractive power of the system was varied continuously and linearly by shifting these elements laterally in opposite directions. In the setup, one of the lens elements was fixed. A step motor controlled by a LabVIEW program was used to move the other component.

Through the lens, the subjects fixated the target. The position of the target could be shifted on a rail parallel to the axis of sight.

The target image shown in Figure 2 was chosen, as it was composed of irregular details at any scale. This means that the power spectrum of the image contains a gapless spectrum of spatial frequencies of the same scale of power. This guarantees that the subjects can perceive contrasting shapes and features in the image, even if defocus blur, refractive errors, the individual visual acuity, or the target distance reduce its resolution. All these influences act as optical low-pass filters, which cut off high spatial frequencies. The continuous spatial spectrum guarantees that perceivable frequencies always are left.

The subject’s left eye was occluded from outer stimuli by opaque curtains. A self-made infrared video pupillometer measured the pupil diameter of this eye at a frequency of 30 Hz. Preprocessing based on a C++ program detected and examiner marked these time gaps in the measured data with a step, excluding the time required to move the target. The variability of the lens was reduced to steps of 0.125 D. This facilitated keeping the lens in a defined refractive state. The lens had to be calibrated for each subject. By this means, the defocus could be determined accurately, which enabled monitoring of the focusing success.

In addition, the range of the pupil diameter had to be determined to guarantee that every subject could bring the target into focus at any given distance. The task of the lens control was to relate the actual pupil diameter to the demanded refractive power of the lens. The power of the lens was related linearly to the pupil diameter, such that the maximum pupil diameter occurred at minimum refractive power and vice versa (Fig. 3). The pupil range defined the sensitivity of the lens control. As this range could increase during the trials, the subjects had to adapt to changes in sensitivity of the control.

The experiment was done in a dim room with an ambient illumination of 22 to 35 lux. The target image was illuminated homogeneously from the back to guarantee an equal luminous emittance in each distance. In 30 cm, that is the closest target distance, the difference in luminous emittance was 0.7 lux, corresponding to 3.2% or less of ambient illumination. Due to the logarithmic sensitivity curve of the retinal photoreceptor cells, no measurable change in pupil diameter was expected, which proved to be true in tests with the first subjects.

The experimental procedure was as follows: In 15 steps, the target was shifted to predefined positions by the examiner. The task of the subject was to bring the target into focus. The subjects got between 3 and 82 seconds before the target was moved to the next position. The time span for focusing depended on the trial. In the first run, the examiner decided when to proceed, taking into account the performance of each subject. The purpose was to give the subjects the time to familiarize themselves with the control of the lens. In the following trials, the time span was limited to 10 seconds per step, excluding the time required to move the target. The examiner marked these time gaps in the measured data with a step.
FIGURE 2. Target image. The size of the target image was $8 \times 5.2$ cm. The image is composed of irregular details at any scale. This means that the power spectrum of the image contains a gapless spectrum of spatial frequencies of the same scale of power. The subjects can perceive contrasted shapes and features in the image in spite of defocus blur, refractive errors, a low visual acuity, or an increased target distance.

FIGURE 3. Control scheme. The control is based on a linear relation between pupil width and refractive power of the lens. The target range plus a buffer of 0.5 D on both sides defines the upper and lower power limits. The maximum and minimum pupil diameters follow from the measured data, and have to be updated continuously. The sensitivity of the control decreases with increasing range of the pupil diameter. The resolution is restricted to steps of 0.125 D to allow for small changes in pupil diameter without changing the refractive power.
manual trigger during the trial. Data measured during the interval when the target was moved were rejected, as the defocus could not be determined reliably.

The target positions were distributed in steps of equal refractive power of 0.5 D (Fig. 4A, black curve). The target initially was shifted in 0.5 D steps from the farthest position to the 3 D nearest position and back. Afterwards, it was shifted in one step to the closest and then back to the farthest position.

Two test persons had to be excluded from the study. The long eyelashes of one subject partly covered the pupil and inhibited reliable measurements. The other subject was excluded, because her refractive error of 4 D overstrained the refractive buffer of the lens. In addition, three trials of one subject were rejected, because individual calibration was not optimal. The refractive range of the lens did not coincide entirely with the target range.

The other subjects were divided into two groups. A younger group (24–31 years, 4 females/2 males, spherical equivalent [SE] = –0.44 ± 0.44 D) and an elderly group (51–64 years, 5 females/3 males, SE = –0.27 ± 0.7 D). Detailed information on all subjects is listed in the Table. In all subjects, decimal visual acuity was 1.0 (Snellen 6/6) or better. Since the younger subjects still had the full accommodation range, cyclopedia had to be induced in their exposed eye to avoid erroneous accommodation. Then, 1% cyclopentolate was applied two times in each subject of this group. This does not only paralyze accommodation, but also induces an evident, long-lasting dilation of the pupil. The mobility of the other pupil and, therefore, its ability to control the lens still was unimpaired. Two members of the second group were pseudophakic. The others were in an advanced stage of presbyopia. Accepting a possible underperformance, no cyclopedia was applied in this study.

### Table. Data of the Subjects

<table>
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<tr>
<th>Subject</th>
<th>Lens Fixation</th>
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**FIGURE 4.** Evaluation of a single trial. (A) The black curve denotes the target distance and the gray curve shows the focused distance in diopters. The dotted lines display the intervals, in which the target was shifted. (B) The bold curve is the pupil width. The gray, vertical lines mark the intervals, in which the target was shifted. Due to continuous adaptation, the sensitivity of the lens control decreased during the trial, which is reflected by the constrictions at 8 and 185 seconds. Both have nearly the same impact on the control. Nevertheless, the control did not worsen over time. (C) The box plot shows the focusing profile of the trial. Comparable to accommodation in humans, the adjustment of the lens exhibits a lag for near target positions and a lead for farther ones. The dashed, diagonal line marks the equilibrium of focused and target distance.
group. Differences between the groups will be highlighted in detail in the Results section.

RESULTS

The results were analyzed with MATLAB (Mathworks, Natick, MA). The main criterion for the evaluation of the experiment was the defocus. It resulted from the difference of the target position in diopters and the current refractive power of the lens. Representative results of one trial are shown in Figure 4. Figure 4A shows the target distance in diopters (black curve) and the refractive power of the lens (gray curve). The dotted curves indicate the rejected intervals. Figure 4B shows the pupil diameter. The pupil constricted the more, the closer the target came. It is remarkable that the small constriction at 8 seconds has the same impact on the control as the much larger constriction at 185 seconds. As mentioned above, the increase in the measured pupil range changed the sensitivity of the control during the trial. Nevertheless, the subject adapted to these changes and managed to bring all target distances into focus.

Figure 4C shows box plots of the focused distance in relation to the different target distances in diopters. The dashed, diagonal line marks equilibrium of demanded and actual refractive power. Most subjects underadapted the refractive power at close target positions and overadapted it at larger distances. These findings are in good agreement with natural accommodation reactions in humans. Nonetheless, this lack in reaction makes the interpretation of the results difficult, as the success of the focusing reaction can be justified only in comparison with the demanded power. In Figure 5A, the specific defocus histogram of the same trial is shown. The maximum of the distribution is at 0 D. The cumulative defocus histogram is shown in Figure 5B. Over 60% of the time, the subject was able to keep the refractive power in a range of 0.25 D around the target for 60% of the time.

Consequently, the DFI is a value between 0 and 1, with the magnitude increasing with decreasing average difference between the current and required refractive power.

The null hypothesis, \( H_0 \), was that the movement of the lens induced by the subject’s pupil reaction was not related to the target distance, or rather that any correlation of target distance and refractive power of the lens occurs at random. The level of significance was set to \( \alpha = 0.01 \).

To test this hypothesis, the original defocus curves were compared with defocus curves where the original target distances had been permuted. Since there are more than \( 1.3 \times 10^{12} \) possible configurations to change the order of 15 target positions, not all configurations could be checked. A random sample of 1000 permutations was evaluated for each trial. The surrogate target distances equaled the original data except for the temporal correlation.

If the null hypothesis was correct, the original data and surrogate data had to be two samples of the same population. Figure 7 shows the distribution of performance for the original data and the surrogates. Due to the non-Gaussian shape of the original data and the difference in variance, a nonparametric Wilcoxon rank sum test was performed. The probability of both samples belonging to the same population is \( P < 1.8 \times 10^{-18} \). Thus, \( H_0 \) can be rejected. It is significant that the subjects were capable to control the artificial lens by adjustments in pupil diameter.

The rank sum test just revealed the disparity of the entire distributions of the original and random data. Nevertheless, there was no evident correlation between the target position and the movement of the lens in some trials. The individual performance, as can be seen in Figure 7, differed a lot.

To investigate each individual’s capability to control the lens, all trials had to be graded. A DFI limit had to be defined, below which the trials were classified to have failed. The 95%-p-quantile of the DFIs of the surrogate data was chosen as criterion for passing the test (Fig. 7B, light gray line; Fig. 8, horizontal line). On the one hand, this limit means a probability of less than 5% of achieving an equal ranking with other target configurations. This reflects the likelihood to reach this performance by chance, if the subject’s pupil would not have reacted to the defocus.

On the other hand, this limit allows for an appropriate discrimination of valid and random patterns. It was in good agreement with our visual examination of all trials.

Based on this ranking, 31 of 41 trials were completed successfully. Of all subjects, only one was not able to control the lens in any trial. All others passed at least one test (Fig. 8). It was remarkable that all subjects of the first group passed every trial. The subjects with an advanced stage of presbyopia did

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**Figure 5.** Defocus distribution. (A) Shows the defocus histogram of the trial. (B) Shows the cumulative histogram of the magnitude of defocus. This subject was able to keep the refractive power in a range of 0.25 D around the target for 60% of the time.
not perform that well. The performances of the two groups are shown in a box plot (Fig. 9). The second group performed significantly worse ($< \alpha = 0.05$, $P = 0.03$).

The DFI allows for a well-discriminated assessment of the performances. Nevertheless, it does not represent any good benchmark for the usability of the system in daily life tasks. A more descriptive impression of the achieved positioning accuracy is obtained from the median of the magnitude of the defocus time series. This value is more robust to outliers in the distribution than the mean or other quartiles. It denotes the zone within which the subject kept the defocus for half of the time. In all passed trials, this range did not exceed 0.625 D and

![Figure 6](https://iovs.arvojournals.org/pdfaccess.ashx?url=/data/journals/iovs/933470/)

**Figure 6.** Generating the assessment factor. To obtain an objective assessment factor for the trials, the specific defocus histogram was multiplied by a weighting function, namely, a nonstandardized Gaussian function with an SD of 0.5 D. The integral of the product of the functions yields the scalar assessment factor defined as the DFI. The integral decreases with increasing defocus distribution scatter. The DFI reaches its maximum of 1, only if the full distribution of the histogram concentrates at 0 D, which means that the refractive power perfectly matches the target distances.

![Figure 7](https://iovs.arvojournals.org/pdfaccess.ashx?url=/data/journals/iovs/933470/)

**Figure 7.** Comparison of the subjects’ performances with random defocus surrogates. (A) Shows the distribution of the DFI ranking of all trials. For comparison, (B) shows the ranking of defocus curves for a random permutation of distances destroying the temporal relationship of the refractive power and target distances in the original time series of the subjects. This allowed for testing the likelihood of any conformity of target distances and refractive power of the lens being caused by accident. Then, both distributions must be two realizations of the same population. Both distributions differ from each other significantly ($P < 1.8 \times 10^{-5}$). The 95% p-quantile (vertical line) in (B) marks the limit beyond which the likelihood of the subject reaching this ranking by chance is less than 5%. This limit was taken as threshold for passing a trial. Based on this benchmark, 75% of the trials were successful.
in 13 trials, it was less than or equal to 0.5 D. In three trials, the subjects even kept the defocus in a range of 0.25 D for half of the time.

**DISCUSSION**

The experiments proved that humans can control a lens intuitively with their pupils. Despite the fact that the subjects were not used to the experimental conditions, 78% of them were able to control the lens in the very first trial. Although the way to move the lens was unfamiliar, they immediately realized how to control the lens to decrease the defocus to target object. Moreover, the sensitivity of the lens control readapted to an increasing range of the pupil size. The same mean pupil diameter could lead to very different refractive states in the beginning and at the end of the same trial (Figs. 4A, 4B).

Nevertheless, the performance did not worsen over time. This means that the CNS can correct these changes dynamically. This suggests that the pupillary near reflex arc contains a closed-loop sharpening control circuit. These findings contradict the classical opinion that accommodation or vergence circuits exclusively drive the pupil during near vision tasks.3,5,6

Significant differences exist between our two age groups. The two pseudophakic subjects, who cannot accommodate at all, succeeded in the same way as the young ones did (Fig. 8). This indicated that a small range of accommodation might have remained in the presbyopic subjects, which worsened the performance. Also, the age of the subjects might have affected their learning abilities and, hence, impeded the control of the lens. Another reason could be that in the first group the medication induced a mydriasis in the stimulated eye. This lowers the depth of focus and makes the individuals more sensitive to defocus blur. In the second group, the pupils were smaller due to age and lack of medication. Moreover, the active pupil in the stimulated eye still could affect the retinal image, which might have disturbing, contradicting effects on their effort to reduce blur.

The variability of the pupillary signal causes large and fast fluctuations of the lens position (Fig. 4A). This makes it easier for the subjects to change the refractive power of the lens and to realize which reaction causes which lens adjustment. Preliminary investigations reveal that this facilitates learning to regulate the lens. On the other hand, this prevents the target from being kept in focus. Subjects reported a slipping from control once the object became sharp.

There are three options to improve the ability of keeping the lens in place. The first is low pass filtering of the signal. This can suppress the variability of the lens, but it also will decrease its coupling to the pupil movement. This makes the regulation more difficult for the brain. Moreover, it is likely that the quick movements of the pupil are necessary for the focusing process. They could serve for estimating the distance or at least for detecting the adjustment direction of the refractive power. Based on the retinal blur alone, it cannot be determined whether the observed object sharply imaged on the retina lies in front of or behind the plane sharply imaged on the retina. The microfluctuations of the crystalline lens of the eye presumably support the monocular estimation of distance. This means a suppression of pupil fluctuations might inhibit the ability of the CNS to control the lens at all.

The second option is to define a threshold for the minimum change in pupil diameter required to change refraction. The

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**FIGURE 8.** Ranking of the individual trials. The ordinate shows the ranking of the trials by means of the DFI. The abscissa lists the subjects’ IDs. The subjects were divided into two groups: a younger one with full accommodative range and an older group, whose subjects were pseudophakic or suffered from an advanced stage of presbyopia. Remarkably, all trials of group 1 were successful. In contrast to this, many subjects of group two failed at least one trial. The overall performance of the second group was significantly worse.

**FIGURE 9.** Comparison of the groups. The upper and lower edge and the middle band of the boxes mark the quartiles. The whiskers denote the maximum and minimum. The notches depict 95% confidence intervals of the median. Group 1 performed significantly better ($x = 5\%$, $P = 3\%$). It could not be proven unequivocally that worse performance was caused by age. The difference also might be caused by the difference in medication of the groups.
third optimization criterion is the number of refractive states. If the lens positioning steps become larger, the pupil movements would have to be less precise. These arrangements would simplify maintenance of the refractive state of the lens. The disadvantage of the latter two options is that the reaction of the pupil to change the refractive power of the lens has to be larger in return. Therefore, the control settings enabling driving and holding are contrasting. A compromise between positioning accuracy and control reactivity is necessary. The limiting factor is the freedom of movement of the pupil. The results show that the positioning accuracy is reasonably acceptable. The remaining question is whether an optimization of the control leads to a satisfactory reactivity and accuracy.

In addition, the time series will be analyzed. Extraction of features in the pupillary signal allowing for distinguishing between the need to change and maintaining the refractive power would essentially improve the controllability.

Another topic is that disturbances from the autonomous nervous system and the sensitivity of the pupil to light influence the pupil diameter. During our experiments, external influences, such as lighting level, were kept constant. Future experiments will have to show whether it is possible to develop a control that also can deal with changing light conditions and other external disturbances.

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References