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 measurable indicator of the distance of the observed object to determine the demand of accommodation. As the pupil constrains 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 ($P < 1.8 \times 10^{-19}$). 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

The ability to change from far to near vision is crucial to maintaining a sharp image of close objects. Due to aging, the crystalline lens of the eye becomes more and more rigid, until the refractive power of the eye congeals. This usually happens between the age of 55 and 60.1 Moreover, the natural lens often must be replaced by an artificial IOL due to cataract in many people. To restore accommodation, several solutions were conceived. However, so-called “accommodating IOLs” designed to enable true changes in refractive power fell short of expectations. The IOLs are inserted into the capsular bag, which shrinks and stiffens due to fibrosis. This impairs the mobility of those mechanical elements that are to change the refractive power of the lens.1 For this reason, these implants were not sufficient to restore the ability to accommodate in an acceptable range and in a reproducible manner.

The Artificial Accommodation System bypasses the dependence on the ciliary muscle and the flexibility of the capsular bag by including an actuator to change the refractive power of the optics. Consequently, an energy supply is required, as well as a system detecting the demand of accommodation.

A potential concept consists in using the pupil as an indicator of observation distance, as near vision is accompanied by a reflex: the pupillary near vision response.2 The afference of the reflex is the projection via the optic nerve from the retina to the visual cortex.2 In the forebrain, information processing of the perceived image takes place. This process is not yet fully understood.2

The reflex is not inherent, but conditioned. It evolves in early adulthood.2 Due to the complex processing in the cortex and interferences from the autonomic nervous system, the reflex is very unsteady, changes much in shape over the time course,3,4 and sometimes does not occur at all.5,6 Therefore, it is difficult to detect the reflex reliably in the measured signal of the pupil diameter.3 Nevertheless, controlling a lens with the pupil may be feasible, because one possible aim of the reflex might be to sharpen an out-of-focus image by increasing the depth of focus.2 This would require a neural control mechanism, which detects blur and, accordingly, adapts the pupil diameter.

Experiments show that the pupil can be trained to constrict underwater to reach a superior vision.7 Hence, the pupil can adapt to improve perception in uncommon situations. Nevertheless, this adaptation does not happen immediately after the blur stimulus, but develops slowly over a long period of training. It has not yet been confirmed that there is a short-term control circuit of the pupil, which compensates defocus blur.

However, if such a sharpening control circuit of the pupil exists, it can be used to control an artificial lens. It is required simply to design a suitable control for the lens with regard to the mobility of the iris muscles. The central nervous system (CNS) then could control the lens, as it previously controlled the pupil. To investigate feasibility noninvasively, an experimental setup was developed.
The shifting range of the target was 3 m. From the subject’s point of view, the change in refractive power from the farthest to the closest position was 3 diopeters (D). By means of the diopter scale on the rail accurate positioning was achieved. The range of adjustment of refractive power of the lens was approximately 8 D and reached from −3.3 to +4.7 D. The software control restricted this range to 3 D plus an additional range of 0.5 D on both sides of the target range. This was to prevent an object from being brought into focus accidentally, just because the lens reached the end of its range. Thus, the positioning accuracy, including extreme target positions, could be examined. 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.

There were no measurable changes in the pupil diameter of the subjects, although they were familiarizing themselves with the control of the lens. The subjects got between 3 and 82 seconds before the target was brought into focus accurately, just because the lens reached the end of its range. Thus, the positioning accuracy, including extreme target positions, could be examined. 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.

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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...
**FIGURE 2.** Target image. The size of the target image was 8 × 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 ± 0.12 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, cycloplegia 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 cycloplegia was applied in this group.

Table. Data of the Subjects

<table>
<thead>
<tr>
<th>Subject</th>
<th>Lens Fixation</th>
<th>Dominant Eye</th>
<th>Age</th>
<th>Visual Acuity</th>
<th>Sphere</th>
<th>Cylinder</th>
<th>Spherical Equivalent</th>
<th>Mean Pupil Diameter</th>
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<tr>
<td>JS</td>
<td>Iatrogenic cycloplegia</td>
<td>Left</td>
<td>24</td>
<td>1.25</td>
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<td>0 D</td>
<td>0 D</td>
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</tr>
<tr>
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<td></td>
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<td>24</td>
<td>1.25</td>
<td>0 D</td>
<td>0 D</td>
<td>0 D</td>
<td>5.4 ± 0.01 mm</td>
</tr>
<tr>
<td>SS</td>
<td></td>
<td>Right</td>
<td>26</td>
<td>1</td>
<td>0 D</td>
<td>0 D</td>
<td>0 D</td>
<td>4.12 ± 0.04 mm</td>
</tr>
<tr>
<td>ED</td>
<td></td>
<td>Right</td>
<td>26</td>
<td>1</td>
<td>−2.25 D</td>
<td>−0.75 D</td>
<td>−2.625 D</td>
<td>6.41 ± 0.07 mm</td>
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<tr>
<td>PD</td>
<td></td>
<td>Left</td>
<td>28</td>
<td>1.25</td>
<td>0 D</td>
<td>0 D</td>
<td>0 D</td>
<td>4.89 ± 0.08 mm</td>
</tr>
<tr>
<td>JF</td>
<td></td>
<td>Left</td>
<td>31</td>
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<td>0 D</td>
<td>0 D</td>
<td>0 D</td>
<td>5.79 ± 0.04 mm</td>
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<tr>
<td>Mean</td>
<td></td>
<td></td>
<td>26.5 ± 0.25</td>
<td>1.17 ± 0.06</td>
<td>−0.38 ± 0.38</td>
<td>−0.13 ± 0.13</td>
<td>−0.44 ± 0.44</td>
<td>5.31 ± 0.04 mm</td>
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Group 2

<table>
<thead>
<tr>
<th>Subject</th>
<th>Lens Fixation</th>
<th>Dominant Eye</th>
<th>Age</th>
<th>Visual Acuity</th>
<th>Sphere</th>
<th>Cylinder</th>
<th>Spherical Equivalent</th>
<th>Mean Pupil Diameter</th>
</tr>
</thead>
<tbody>
<tr>
<td>EN</td>
<td>Presbyopia</td>
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<td>51</td>
<td>1.6</td>
<td>−1.75 D</td>
<td>0 D</td>
<td>−1.75 D</td>
<td>3.29 ± 0.03 mm</td>
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<tr>
<td>GS</td>
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<td>57</td>
<td>1</td>
<td>0 D</td>
<td>0 D</td>
<td>0 D</td>
<td>4.05 ± 0.15 mm</td>
</tr>
<tr>
<td>TB</td>
<td></td>
<td>Right</td>
<td>57</td>
<td>1.25</td>
<td>0 D</td>
<td>−0.75 D</td>
<td>−0.375 D</td>
<td>4.67 ± 0.06 mm</td>
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<tr>
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<td></td>
<td>Left</td>
<td>62</td>
<td>1</td>
<td>1 D</td>
<td>0 D</td>
<td>1 D</td>
<td>4.02 ± 0.09 mm</td>
</tr>
<tr>
<td>WD</td>
<td></td>
<td>Right</td>
<td>62</td>
<td>1.25</td>
<td>0.5 D</td>
<td>−1 D</td>
<td>0 D</td>
<td>3.92 ± 0.09 mm</td>
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<tr>
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<td>64</td>
<td>1.25</td>
<td>1.75 D</td>
<td>−1.5 D</td>
<td>1 D</td>
<td>5.53 ± 0.09 mm</td>
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<tr>
<td>BW</td>
<td>Pseudophakic subjects</td>
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<td>57</td>
<td>1.2</td>
<td>−2 D</td>
<td>0 D</td>
<td>−2 D</td>
<td>4.58 ± 0.11 mm</td>
</tr>
<tr>
<td>FI</td>
<td></td>
<td>Right</td>
<td>57</td>
<td>1</td>
<td>0 D</td>
<td>0 D</td>
<td>0 D</td>
<td>4.58 ± 0.07 mm</td>
</tr>
<tr>
<td>Mean</td>
<td></td>
<td></td>
<td>58.4 ± 0.74</td>
<td>1.19 ± 0.11</td>
<td>−0.06 ± 0.19</td>
<td>−0.41 ± 0.41</td>
<td>−0.27 ± 0.27</td>
<td>4.33 ± 0.04 mm</td>
</tr>
</tbody>
</table>

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.5 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 diagram is shown in Figure 5B. Over 60% of the time, the subject was able to keep the defocus in a range of 0.25 D around the target for 60% of the time.

For comparison of the trials, a weighting function was developed, which generated a single value from a time series for statistical analysis. The specific histogram function of the defocus curve was multiplied by a Gaussian distribution with a maximum of 1 and a σ of 0.5 D (Fig. 6). Integration of the resulting function yielded an assessment factor, hereinafter called defocus index (DFI). The integral of the specific histogram has to be 1. The maximum of the weighting function is 1 as well. This means that the integral reaches its maximum of 1 only when the current and required refractive power match perfectly. In any other case, the integral decreases with the scatter of the defocus distribution. 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, H0, 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 a = 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 surrogated 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, H0 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 DFI 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 reaching 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.
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

![Defocus histogram](image1)

\[
\int_{-\infty}^{+\infty} h(x) \, dx = 1
\]

**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.

![Weighting function](image2)

\[
g(x, \sigma = 0.5D) = e^{-\frac{x^2}{2\sigma^2}}
\]

**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
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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