AN INVESTIGATION INTO THE RELATIONSHIP BETWEEN PUPIL AND ACCOMMODATION RESPONSES DURING NEAR VISION

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SUMMARY

A Hamamatsu Video Area Analyser has been coupled with a modified Canon IR automatic optometer. This has allowed simultaneous recording of pupil diameter and accommodation response to be made both statically and continuously, a feature not common in previous studies. Experimental work concerned pupil and accommodation responses during near vision tasks under a variety of conditions.

The effects of sustained near vision tasks on accommodation have usually been demonstrated by taking post-task measures under darkroom conditions. The possibility of similar effects on pupil diameter was assessed using static and continuous recordings following a near vision task. Results showed that if luminance levels remained unchanged by using a pre-and post-task bright-empty field then, although accommodation regressed to pre-task levels, pupil diameter remained for several minutes at the constricted level induced by the task.

An investigation into the effect of a sinusoidally-modulated blur-only accommodative stimulus on pupil response demonstrated that response may be reduced or absent despite robust accommodation responses. This suggests that blur-driven accommodation alone may not be sufficient to produce a pupil near response and that the presence of other cues may be necessary.

Pupil response was investigated using a looming stimulus which produced an inferred-proximity cue. It was found that a pupil reponse could be induced which was in synchrony with the stimulus while closed-loop accommodation response was kept constant by the constraints of optical blur.

The pupil diameter of young and elderly subjects undertaking a 5 minute reading task was measured to assess the contribution of pupil constriction to near vision function in terms of depth-of-focus. Results showed that in the young subjects pupil diameter was too large to have a significant effect on depth-of-focus, although it may be increased in the elderly subjects.

Pupil and accommodation reponses to a temporally-modulated stimulus containing all cues present in a normal visual environment was assessed and results showed that as stimulus temporal frequency increased, pupil response showed increasing phase lag relative to closed-loop accommodation.

The results of this study suggest that it may be necessary to change the accepted view of the function of pupil response as part of the near vision triad and that further study would be of benefit in particular to designers of vision aids such as, for example, bifocal contact lenses.

Key words: pupil, accommodation, near vision, pupillometer, optometer.

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GENERAL INTRODUCTION

Previous work in the research group has centred around the recording of accommodation using a modified Canon Autoref R1 objective optometer. The aim has been to further our general understanding of the accommodative system and in particular to study the effects on the system of sustained near vision tasks. It has long been suspected that the habitual undertaking of such tasks may, at least in part, be responsible for the high incidence of myopia in modern western society. Studies have shown that sustained near vision tasks can induce latent changes in accommodative state in some subjects, although there is no known mechanism by which these transient changes could translate into myopia.

Accommodative after-effects following near vision tasks have generally been assessed by monitoring accommodation under post-task conditions of darkness to open the accommodative loop. In darkness the level of accommodation has no effect on retinal image quality and it is considered that the accommodation system thus receives no feedback and is free to adopt or progress towards a resting or tonic position known as tonic accommodation (TA). Any tone in the accommodative system retained after the cessation of the near vision task is reflected in change in the TA position or a slowing of the regression of accommodation from task to TA level.

A natural progression from the work already done was to extend the laboratory facilities to incorporate recording of pupil responses. The initial impetus for this came from the hypothesis that as pupil near response is thought to be accommodation-driven, any changes in accommodative state following a near vision task may have a corollary in the pupil. As recording of pupil responses is considerably easier than recording accommodation, it was thought that study of the pupil may allow easier access to near vision task-induced effects on the oculomotor system. A Video Area Analyser was purchased that is compatible with the camera inside the Canon Autoref R1 which provides an image of the eye under study on a separate TV monitor screen. This is usually used to aid in alignment of the optometer but by taking the output from the camera through the Hamamatsu C3160 Video Area Analyser before it goes on to the monitor, it is possible to carry out simultaneous recording of accommodation and pupil size. As the optometer provides a wide and open field-of view to the subject, it is possible to simultaneously study pupil and accommodation responses under a variety of stimulus conditions. Recordings have been made in this thesis of pupil response alone and pupil and accommodation responses simultaneously using both static and continuous techniques.

The first experiments monitored first statically and then continuously pupil and accommodation responses following a sustained near vision task. Results showed that open-loop accommodation and pupil responses followed quite different courses post-task and therefore pupil response did not reflect any accommodative changes induced by the task. To demonstrate this, post-task recordings of pupil and accommodation responses had to be made under bright-empty-field conditions as the imposition of darkness led to luminance-driven pupil dilation. The dissociation of accommodation and pupil responses was contrary to current thinking on the drive to pupil near response and led to further experiments with the aim of determining the relationship, if any, between accommodation and pupil responses.

Examination of the relevant literature revealed a good deal of inconsistency in the results of experiments attempting to isolate the drive to pupil near response. Drive has been attributed exclusively both to accommodation and to vergence in different studies, although the current consensus seems to be that accommodation is the primary source of drive to the pupil with vergence possibly playing a secondary role.

The experimental work reported in this thesis suggests that blur-driven accommodation alone is insufficient to drive pupil near response and that to ensure response, the presence of cues which give rise to the awareness of the proximity of the fixated target are necessary. Exclusion of all cues but blur takes considerable care and it seems that the pupil is very sensitive to even small amounts of any cue relating to target movement or proximity.

If pupil near response is related to target proximity, this may have a bearing on its role in visual function. It is usually stated that the pupil constriction that accompanies accommodation and convergence during near vision acts to increase the depth-of-focus of the eye and may allow some moderation of accommodative effort. Study of the literature relating to depth-of-focus in the eye showed that for a significant increase in depth-of-focus to take place, pupil diameter would need to be below 3mm during near vision. Very little data exist on the actual pupil size adopted by human subjects under naturalistic near vision conditions and so a study was undertaken to measure pupil diameter in subjects while they undertook a reading task. The results revealed pupil sizes in young subjects that were too large to have a significant effect on depth-of-focus.

The concluding experiment reported in this thesis investigated pupil and accommodation responses to a temporally-modulated accommodative stimulus containing all cues including size change. This study revealed that whereas accommodation reponse was tightly coupled to the stimulus by the blur-derived feedback loop and showed little phase-lag with increase in temporal frequency, pupil response showed increasing phase lag as stimulus temporal frequency increased.

CHAPTER 1

ANATOMY, PHYSIOLOGY AND PHARMACOLOGY RELATING TO PUPIL RESPONSES

1.1 ANATOMY OF THE IRIS

The human iris is a motive, disc-shaped diaphragm around 12mm in diameter which contains a central circular aperture termed the pupil. Pupil size is variable, maximum diameter being around 10mm and minimum around 1mm (Lowenstein and Loewenfeld, 1969). The iris divides the eye into anterior and posterior chambers, its outer periphery being attached to the anterior surface of the ciliary body at the angle of the anterior chamber. The inner, unattached border forming the margin of the pupil is usually slightly to the nasal and inferior of centre and is supported by the anterior surface of the lens. As the pupil margin is anterior to the iris root, viewed three-dimensionally the iris has the shape of a truncated cone. If the lens is missing, as it is in aphakes, the iris becomes flatter and tremulous due to the lack of support at its central margin.

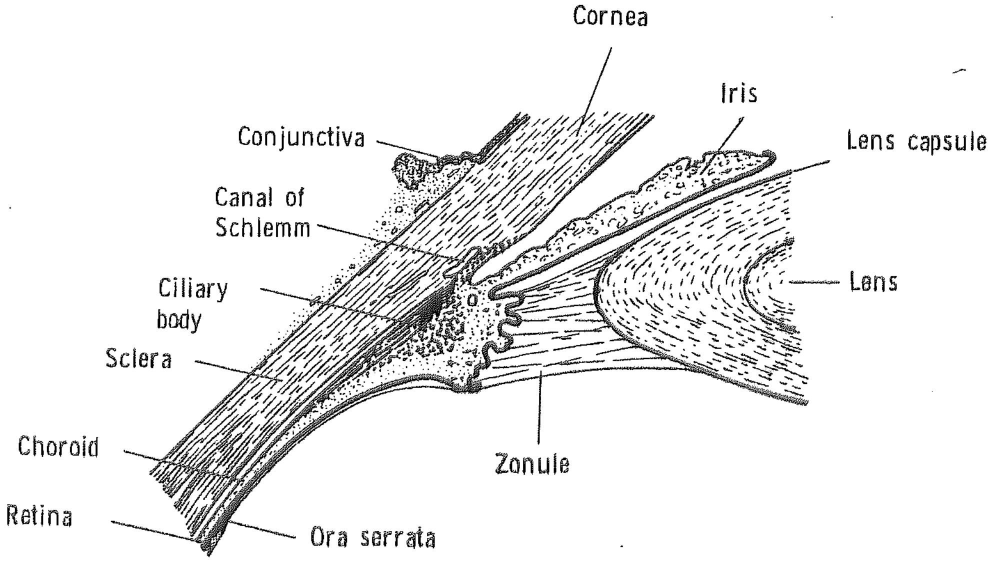


Figure 1.1 Diagram of the angle of the anterior chamber of the eye to show the insertions of the iris and ciliary body (from Fatt, 1978).

The pupil is responsive to many stimuli but the consensus is that its responses serve two main functions:

1. The light reflex regulates retinal illumination to minimise the disabling effects on vision and on retinal adaptation of rapid changes in incident light levels (Woodhouse and Campbell, 1975).

2. The pupil near response results in constriction during fixation of close objects which is believed to contribute to near vision by increasing the depth-of-focus of the optical system of the eye and reducing the detrimental effects of spherical and chromatic aberrations (Lowenstein and Loewenfeld, 1969).

1.1A IRIS MUSCULATURE

Pupil size is controlled by the reciprocal actions of the two smooth muscles of the iris:

1. The Sphincter Pupillae: consists of muscle fibres which run mostly in a circular direction forming a continuous ring about 0.5-1mm wide and 40-80μm thick close to the pupillary margin. Contraction results in constriction of the pupil. Connecting strands bind the sphincter to the surrounding tissue and thus even when the muscle is cut pupil constriction is conserved.

2. The Dilator Pupillae: muscle fibres form a continuous sheet 2μm thick and run radially from an insertion into the ciliary body towards the pupil terminating around 0.3mm short of the pupillary border. Contraction results in dilation of the pupil.

As is characteristic of smooth muscle, the iris is under the involuntary control of the two branches of the autonomic nervous system. Smooth muscle systems, such as the gut and heart, act without conscious awareness to regulate the internal bodily environment whereas the faster-acting skeletal muscles are under voluntary control. Although the ciliary body is also comprised of smooth muscle, there is evidence for some voluntary control of accommodation (see Gilmartin, Gray and Winn, 1991). No evidence exists for voluntary control of pupil responses although it has been reported that it is possible to condition the pupil to constrict or dilate to command (Hudgins, 1933, Borrego and Gardner, 1986).

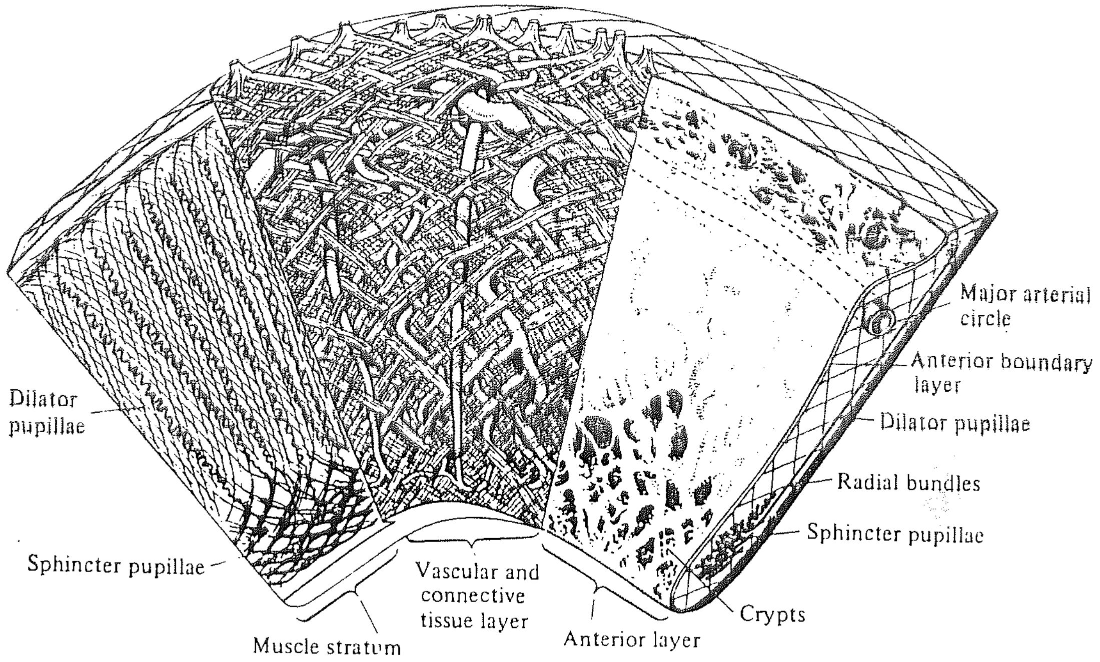


Figure 1.2 The structure of the iris (from Alexandridis, 1985).

The sphincter and dilator pupillae are bound together by connecting strands and as one muscle acts it increasingly stretches the other giving a better mechanical advantage for the antagonistic action. Despite this, it would appear that in pupil reactions to light the sphincter muscle is responsible for most iris movements, dilation being due more to inhibition of innervation to the sphincter than to active innervation of the dilator (Heller *et al*, 1990). The muscles are bound to the surrounding stroma by connective tissue fibres and blood vessels; the stroma or vascular layer consists of loose connective tissue and contains pigmented melanocyte and clump cells which contain the pigment giving the iris its colour.

1.1B BLOOD SUPPLY TO THE IRIS

The blood supply to the iris is derived from the long posterior ciliary and the anterior ciliary arteries which merge and give rise to the major iridic vascular circle in the ciliary body from which vessels radiate towards the pupil margin. At the margin another vascular complex, the minor iridic vascular circle, is formed which is an arteriovenous anastomosis. Iris veins transmit returning blood to the vortex veins. Blood vessels form the bulk of the iris stroma and follow tortuous paths which allow them to adjust to the continuously changing state of the iris.

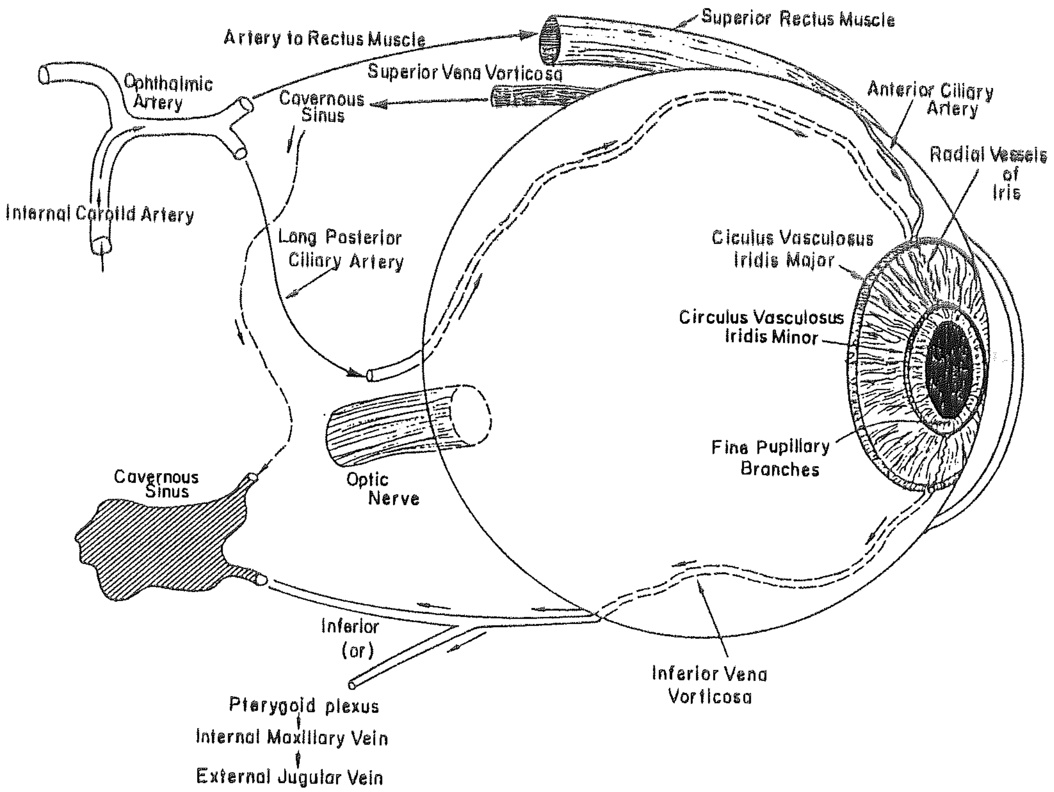


Figure 1.3 Blood supply of the iris (from Zinn, 1972)

1.1C NEURONAL PATHWAYS TO THE IRIS

It has been suggested that the sphincter and the dilator pupillae both receive parasympathetic and sympathetic innervation (Alexandridis, 1985). Active stimulation comes from the parasympathetic to the sphincter and from the sympathetic to the dilator (Lowenstein and Loewenfeld, 1969) and much of the innervational pathways to the pupil are shared with those that serve the ciliary body.

1.1Ci THE PUPIL LIGHT REFLEX PATHWAY

AFFERENT PATHWAY

The afferent pathway begins with the retinal light receptors and continues in the visual pathway to the optic tracts in the midbrain. It is not clear whether pupillomotor impulses are identical to or somehow different to those serving vision, although evidence based on the similarities between pupillomotor and visual functions (see Loewenfeld, 1966, Lowenstein and Loewenfeld, 1969) suggests that the same receptors (both rods and cones) give rise to impulses which serve both as visual and as pupillomotor. From the optic tracts the visual fibres enter the lateral geniculate bodies and then continue via the optic radiations to the visual cortex whilst the pupillomotor fibres remain in the midbrain, branching off via the brachium of the superior colliculus to synapse with the pretectal nuclei located near the posterior commissure. Axons then undergo a further two partial decussations before synapse in the Edinger-Westphal nuclei (E-W nuclei) of the oculomotor nucleus.

EFFERENT PATHWAY

The parasympathetic efferent pathway originates in the midbrain at the E-W nuclei. Axons from the E-W Nuclei exit the brain stem in the IIIrd nerve which also serves accommodation, the upper lid and four of the six extraocular muscles. The nerve divides into several branches, one of which enters the ciliary ganglia in the orbits giving rise to postganglionic fibres which pass to the iris and the ciliary body via the short ciliary nerves.

MIDBRAIN ORGANISATION

Despite extensive investigation, the pupillary light reflex path through the midbrain is still not fully understood (Hultborn, Mori and Tsukahara, 1978) and the issue is complicated by the involvement of the pretectal region in visually guided behaviour (see Sprague, Berlucchi and Rizzolatti, 1973). Investigations using mainly cat and monkey have revealed a fairly consistent midbrain organisation and it is thus thought safe to assume a similar organisation in human. Use of monkey is particularily important as the near vision response triad of accommodation, convergence and pupillary constriction is only found in the highly developed visual system of primates.

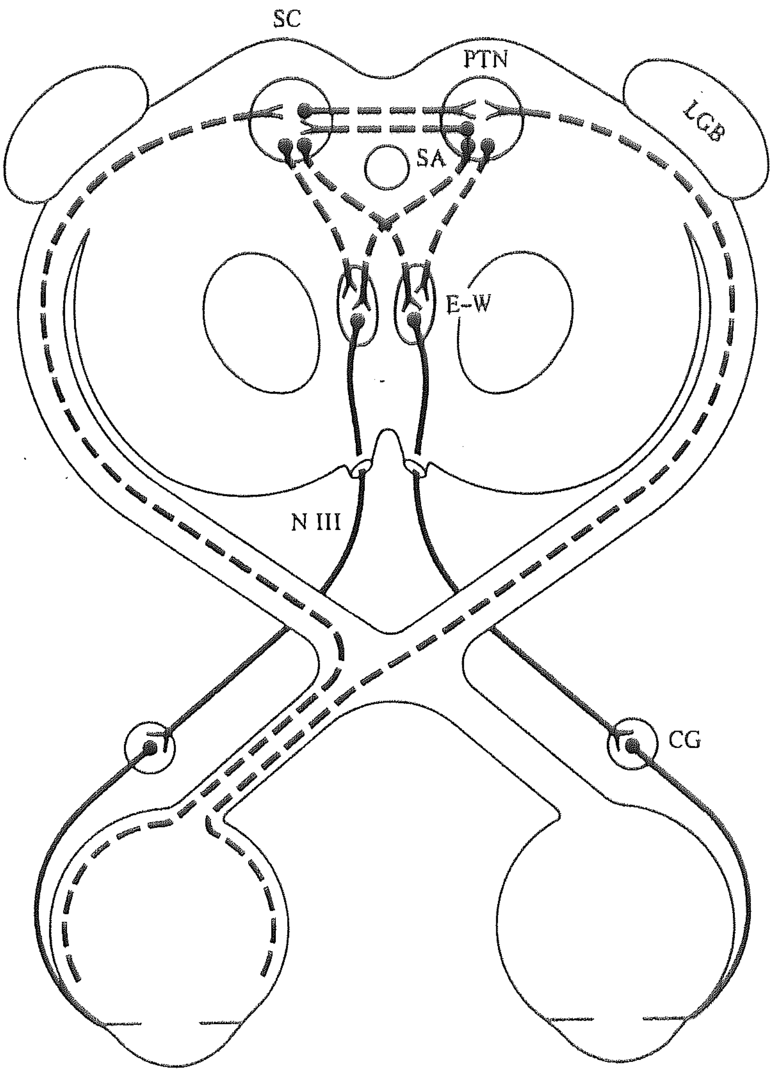


Figure 1.4 Afferent light reflex pathway (dashed lines) and parasympathetic efferent pathway (solid lines) of pupillary light and near responses.(from Alexandridis, 1985). **SC**- superior colliculus; **PTN**- pretectal nuclei; **LGB**- lateral geniculate body; **SA**- sylvian aqueduct; **E-W**- Edinger-Westphal nuclei; **CG**-ciliary ganglion.

The currently accepted pupillary pathway was first mapped out by Ranson and Magoun (1933b) using electrical stimulation of the midbrain in the cat. Pupil constriction was elicited from the brachium of the superior colliculus, the pretectal region, the posterior commissure and fibres emerging from it and continuing around the central grey matter to the oculomotor nucleus. No pupil response was obtained from stimulation of the superior colliculus itself, which clarified conflicting views on the possible contribution of this part of the midbrain to pupil responses. Magoun (1935) further showed that the light reflex in cats remains intact after destruction of the superior colliculus. Ranson and Magoun (1933a) also suggested that pupillary fibres undergo two partial crossings in the midbrain-one in the posterior commissure and a second ventral to the aqueduct. Thus, including the chiasm, pupillary light reflex fibres undergo a total of three partial crossings. Strong evidence that the optic fibres responsible for pupillary constriction synapse on pretectal neurones came from Hare, Magoun and Ranson (1935) who showed that electrical stimulation of the pretectum in cat causes pupil constriction after sectioning of both optic nerves. Latency measurements confirmed the presence of synapses in the pretectal region and the E-W nuclei. Subsequent investigation again using cat (Magoun and Ranson 1935), showed that destruction of the pretectal areas resulted in total, permanent loss of the light reflex. Benjamin (1939) showed by electrical stimulation the importance of the E-W nuclei as pupil constrictor centres in cat and demonstrated anatomically the similarity between the oculomotor nucleus in cat and human. Bender and Weinstein (1943) extended the investigation to monkey obtaining similar results to Benjamin (1939) and also divided up the oculomotor nucleus functionally into separate areas subserving the IIIrd nerve functions of accommodation, pupilllary constriction and eye movements.

Jampel and Mindel (1967) reported accommodation and pupil constriction caused by electrical stimulation in the midbrain oculomotor nucleus of the macaque monkey. They support the view of Warwick (1954) that the E-W nuclei form a continuous mass with the anteromedian nuclei and that both are integral parts of the parasympathetic component of the oculomotor nucleus. Sillito (1969) directly recorded the activity of the light reflex interneurones in the pretectum and demonstrated two types of input: excitatory leading to pupil constriction and inhibitory mediating pupil response to the withdrawal of illumination. Similar results were reported more recently by Inoue and Kiribuchi (1983) by recording in the ciliary nerve of rabbits while electrically stimulating the pretectum. As their results were unchanged by sympathetic blockade, they suggest that the pupillary light reflex is mediated by parasympathetic innervation alone with no contribution from the sympathetic system.

CILIARY GANGLION

Nerve fibres from the E-W nuclei to the iris and ciliary body travel via the ciliary ganglion. Although the presence of synapses for both accommodation and pupillary fibres in the ciliary ganglion has been disputed, Ruskell (1990) in a thorough review of the relevant literature concluded that overall the evidence firmly points to the presence of synapses for both accommodation and pupil. Thus the pathway follows a similar route to the rest of the parasympathetic nervous system in having a synaptic junction between the central control and the effector organ. Warwick (1954) was able to show that in the ciliary ganglion only 3% of cells supply the iris, the remaining 97% serving the ciliary body.

1.1Cii HIGHER CENTRE INVOLVEMENT

The pupil near response is more complex than the light reflex and depends on the integrity of the visual cortex. In cortically-damaged hemianopes, a light reflex can be elicited from the blind hemifield in the absence of any visual sensation (Barbur, Keenleyside and Thompson, 1989). Fibres descending from the visual cortex synapse in the midbrain oculomotor nucleus and the parasympathetic efferent pathways from the E-W nuclei serve to innervate both the pupil near response and the light reflex. The exact pathway between the cortex and the oculomotor nucleus is still unknown. In certain conditions, such as the Argyll-Robertson pupil, the light reflex is abolished whilst the near response remains suggesting that the fibres descending from the cortex synapse more ventrally in the oculomotor nucleus than those involved in the light reflex.

Pupillary constriction was readily obtained from stimulation of the visual cortex in monkey by Schäfer in 1888. In the cat, Barris (1936) was able to elicit bilateral, equal pupil constriction on stimulation of restricted areas of the visual cortex. He was also able to trace fibres from the cortex, along the lateral ventricle wall, over the LGB and into the pretectal area. Imai *et al* (1984) showed in rabbit that pupil constriction could be induced by stimulation of the visual cortex. In the seminal and much cited work of Jampel (1959, 1960) it was reported that accommodation, convergence and pupillary constriction could all be produced by electrical stimulation in areas 19 and 22 of the peristriate cortex in macaque monkey,

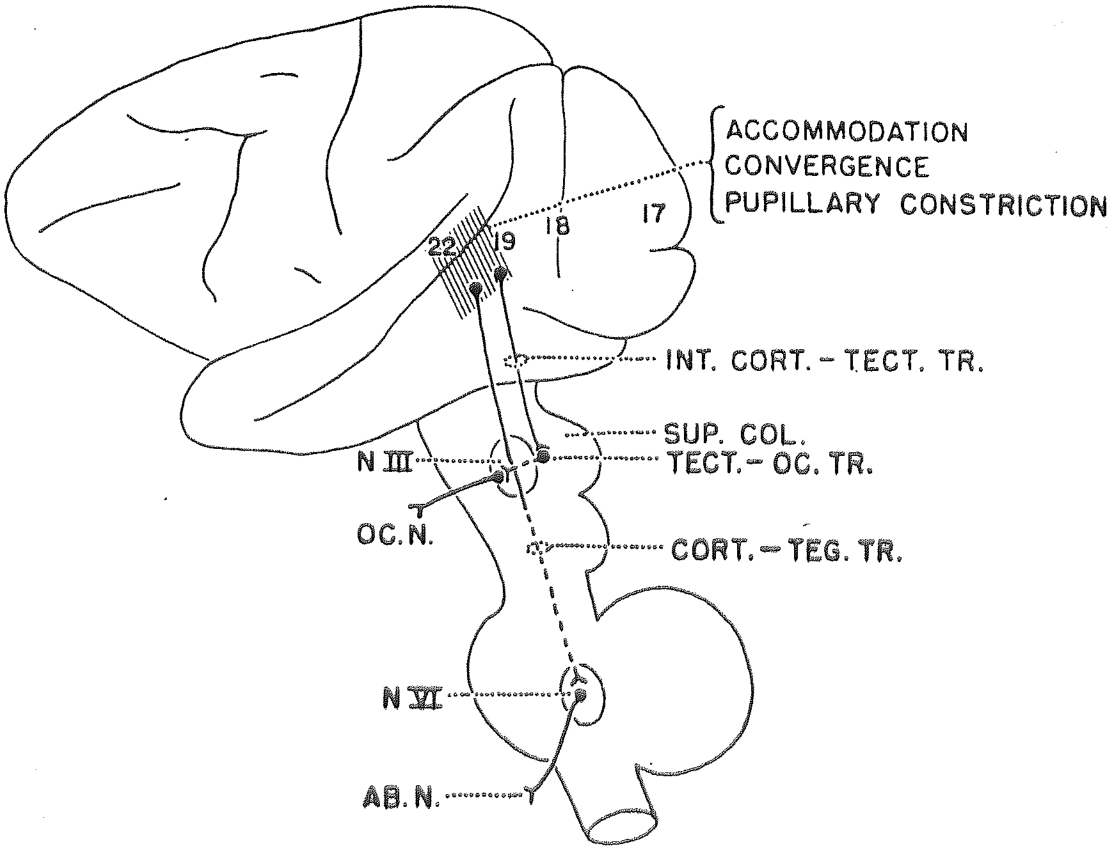


Figure 1.5 diagram from Jampel (1959) showing cortex to midbrain connections in the macaque monkey.

demonstrating that the cerebral cortex is involved in the near response. The pupillary constriction obtained by unilateral stimulation was never more than one third of the original pupillary diameter suggesting that bilateral summation is necessary to elicit a full near response. Jampel (1959) proposed that the near vision response triad is controlled at the highest level of nervous activity, the cerebral cortex, and modified at a lower level, the pretectum and tectum of the midbrain with the oculomotor nucleus acting as a final common pathway to the ciliary bodies, medial recti and sphincter pupillae.

1.1Ciii SYMPATHETIC EFFERENT PATHWAY

The existence of the dilator pupillae and its sympathetic innervation have been the subject of a great deal of disagreement in the literature. Loewenfeld (1958) provides an exhaustive review on this subject and concludes that the evidence overwhelmingly supports the existence of the dilator pupillae and that pupillary dilation, at least to sensory stimuli, is a result of active sympathetic innervation to the dilator pupillae as well as relaxation of the sphincter pupillae caused by inhibition of the midbrain oculomotor nucleus. Recent investigation suggests that in human pupil light reflex, sympathetic innervation plays only a minor role (Heller *et al*, 1990), a situation analogous to that existing in the innervation to accommodation (see Gilmartin,1986). Loewenstein and Loewenfeld (1950), however, state that in monkey the two systems have a more mutual role. The sympathetic pathway consists of three neurons and originates in the posterior hypothalamus from which descending fibres travel to the ciliospinal centre of Budge in the spinal cord (see figure 1.6). The second neuron (preganglionic) travels via the ventral root to the superior cervical ganglia located at the base of the skull where they synapse giving rise to the third neuron which continues to the dilator pupillae and the ciliary muscle via the long ciliary nerves.

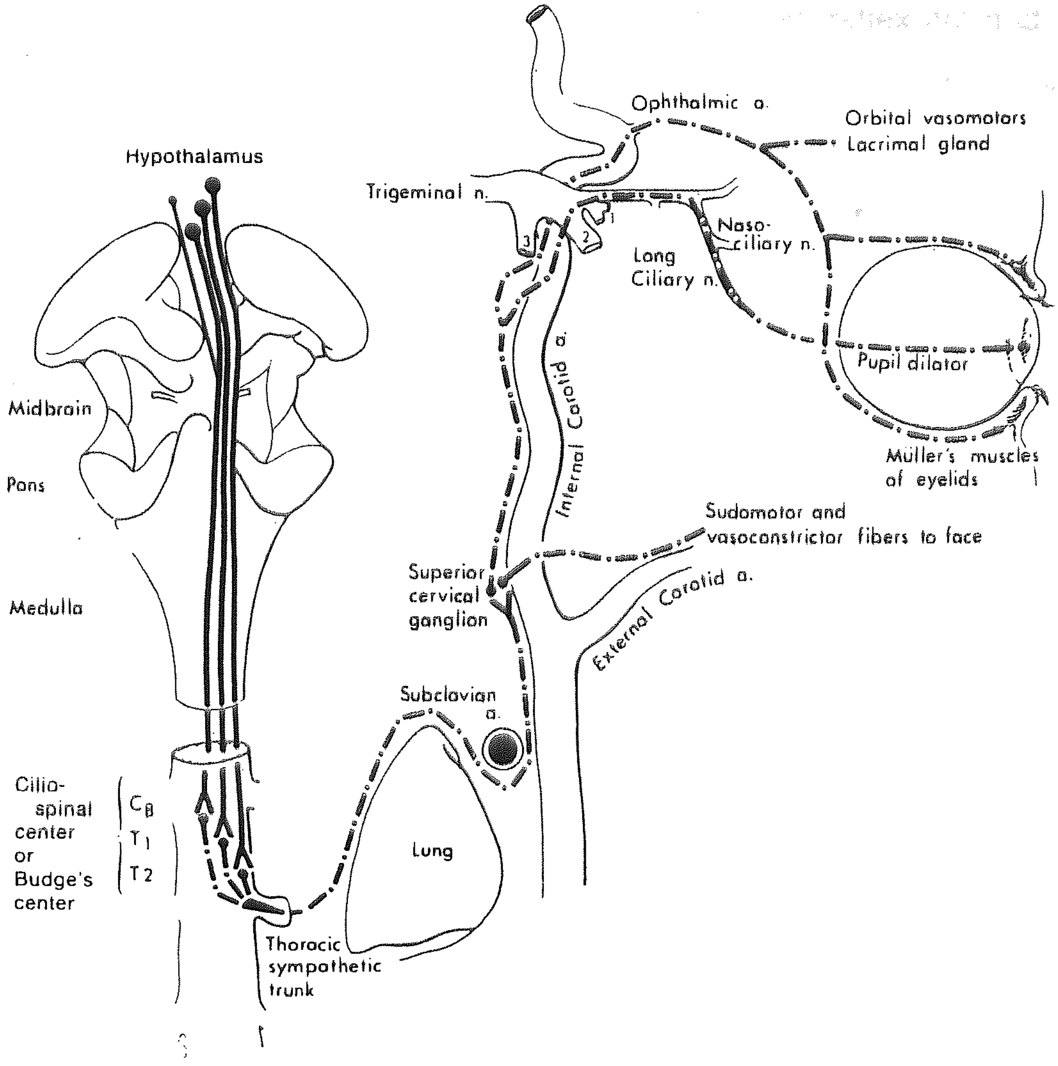


Figure 1.6 Sympathetic pathways to the pupil (from Alexandridis, 1985).

Bilateral dilation of the pupils induced by electrical stimulation of the hypothalamus has been reported in cat (Ranson and Magoun 1933a) and in monkey (Lowenstein and Loewenfeld 1950). Sectioning of the cervical cord has been shown to abolish the pupillary dilation caused by stimulation of the hypothalamus (Beattie, Brow and Long, 1930) thus demonstrating that the hypothalmus forms part of the sympathetic pathway. Although the exact nature of the interconnections is still obscure, the hypothalamus also has connections to the E-W nuclei and the cortex (Lowenstein and Loewenfeld, 1969).

Pupil size and responsiveness at any one time is determined by many, often conflicting, inputs. Most obvious are the inputs via the light reflex arc and those connected with the near response. However, there are also emotional inputs such as arousal which causes pupil dilation (Bender, 1933, Hess and Polt, 1964) and fatigue which causes waves of constriction (Loewenfeld and Lowenstein, 1969).

1.2 PHARMACOLOGY

The principal neurotransmitters of the autonomic nervous system are acetylcholine whose activity is termed cholinergic and noradrenaline whose activity is termed adrenergic. Acetylcholine is the preganglionic transmitter in both branches of the autonomic nervous system. Postganglionic (i.e. at the effector organ) parasympathetic neurons are cholinergic, acting on muscarinic receptors in the target organs. Sympathetic postganglionic neurons are mainly adrenergic acting on either α or β adrenoceptors. Drug actions on organs are classified according to their potency in stimulating or blocking cholinergic and adrenergic transmission.

Acetylcholine receptors are divided into nicotinic and muscarinic subtypes. All muscarinic receptors such as those of the sphincter pupillae and ciliary body are blocked by atropine, a competitive muscarinic antagonist which in the eye causes mydriasis and cycloplegia. Pilocarpine is a muscarinic agonist and in the eye causes miosis and spasm of accommodation (when accommodation is present). Nicotinic receptors occur in autonomic ganglia such as the ciliary ganglion where transmission is first stimulated by nicotine and then blocked as the concentration increases.

Adrenergic receptors are divided into two subtypes- α and β, further divided into α_1, α_2 and β_1, β_2 according to their responses to various agents. The dilator pupillae contains α_1 adrenoceptors which are also present on the sphincter pupillae and ciliary body although their roles are uncertain in these latter two sites. β_2 receptors are predominant in the ciliary body and are mainly involved with the production of aqueous humour. Phenylephrine is an α_1 agonist used in the eye as a mydriatic and has minimal effects on accommodation. Timolol, a β_2 blocker, has no effect on the pupil but reduces aqueous ouflow from the ciliary body.

1.3 HIPPUS

Under conditions of steady illumination and fixation, the pupil can be seen to be in constant motion which, it is believed, will continue indefinitely (Lowenstein and Loewenfeld, 1969). These oscillations have been called pupillary unrest or hippus, although the derivation of the term hippus is obscure and its use is ambiguous between authors. Thompson, Franceschetti and Thompson (1971) report that after meaning nystagmus for 1500-2000 years, hippus came to refer to the pupil around 200 years ago. They further remark on the confusion surrounding hippus which has been considered pathologic in the past and linked to very many diseases, far too many for it to be of any diagnostic significance. It is now accepted that hippus represents a physiological fluctuation in the size of the pupil and can be seen in any normal human subject.

The origin and exact nature of hippus is still obscure. Stark, Campbell and Atwood (1958) put forward the view that hippus is simply noise in the pupillary system and contains no particular rhythm. Recordings showed that the movements of the two pupils are almost perfectly correlated and that therefore hippus originates in the central nervous system and not the iris musculature. In a later paper, Stanten and Stark (1966) proposed that the E-W nuclei are the source of the noise following their finding that the amplitude of hippus increased during active accommodation. The view of hippus as noise containing no dominant frequencies has been supported by Howarth *et al* (1987).

Other investigators have claimed that hippus is rhythmic in nature and has correlations with respiration rate (Daum and Fry 1981, Borgdorff, 1975, Ohtsuka *et al*, 1988) and pulse rate (Daum and Fry, 1982). However, no evidence has been shown of increase in hippus frequency after exercise to raise pulse and respiration rates. Bouma and Baghuis (1971) suggest that hippus is most prevalent in a relaxed subject, has amplitude of 1mm and temporal frequency of around 0.2Hz, shows no correlation with pupil size, heart rate, respiration rate or skin conductance but is suppressed by a mental task. Yoss, Moyer and Hollenhurst (1970a) further confuse the issue by defining hippus as the waves of pupillary contraction that occur in tired subjects.

It would appear that if a number of recordings of pupil size over a certain time period under steady illumination and accommodative level are averaged, then the results suggest hippus to be random noise. Over a short time period, however, rhythmic oscillations in pupil size can certainly be demonstrated (see below).

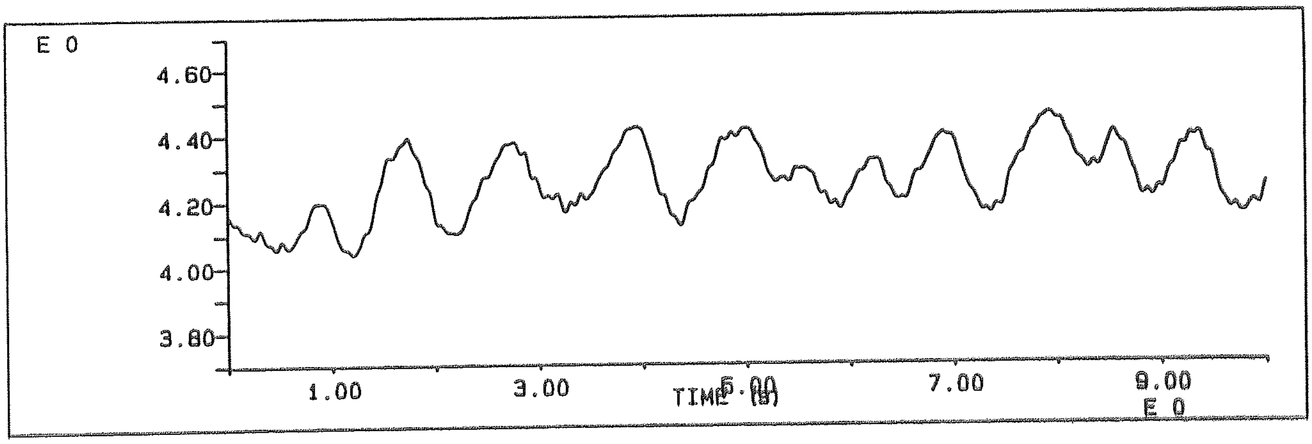


Figure 1.7 continuous recording of pupil diameter (subject BW) under steady illumination (900 cdm^{-2}) over a 10 second period (from Phillips, 1990).

1.4 THE EFFECT OF AGE ON THE PUPIL

It is generally held that pupil size decreases with age although surprisingly little data exist particularly in relation to pupil size under conditions of illumination other than darkness. Most published studies have investigated pupil size in complete darkness presumably because it is the easiest condition of illumination to reproduce. A clear age-related decrease of pupil size in darkness has been found in most studies (Birren, Casperson and Botwinick, 1950, Kadlecova and Peleska 1957, 1958, Said and Sawries, 1972, Loewenfeld, 1979). Birren, Casperson and Botwinick (1950) and Kadlecova and Peleska (1957) both also measured light-adapted pupil size and found that the rate of change of pupil size with age is decreased with increased illumination. Leinhos (1959) and Tyler (1989) both refute any significant correlation between pupil size and age under conditions of bright illumination.

The study by Loewenfeld (see figure 1.8 below), illustrates typical findings in darkness. A clear age trend is seen with the pupil relatively small in infants, reaching a maximum in adolescence and then showing a steady decline with increasing age. At any one age, a wide spread of pupil diameters occurs.

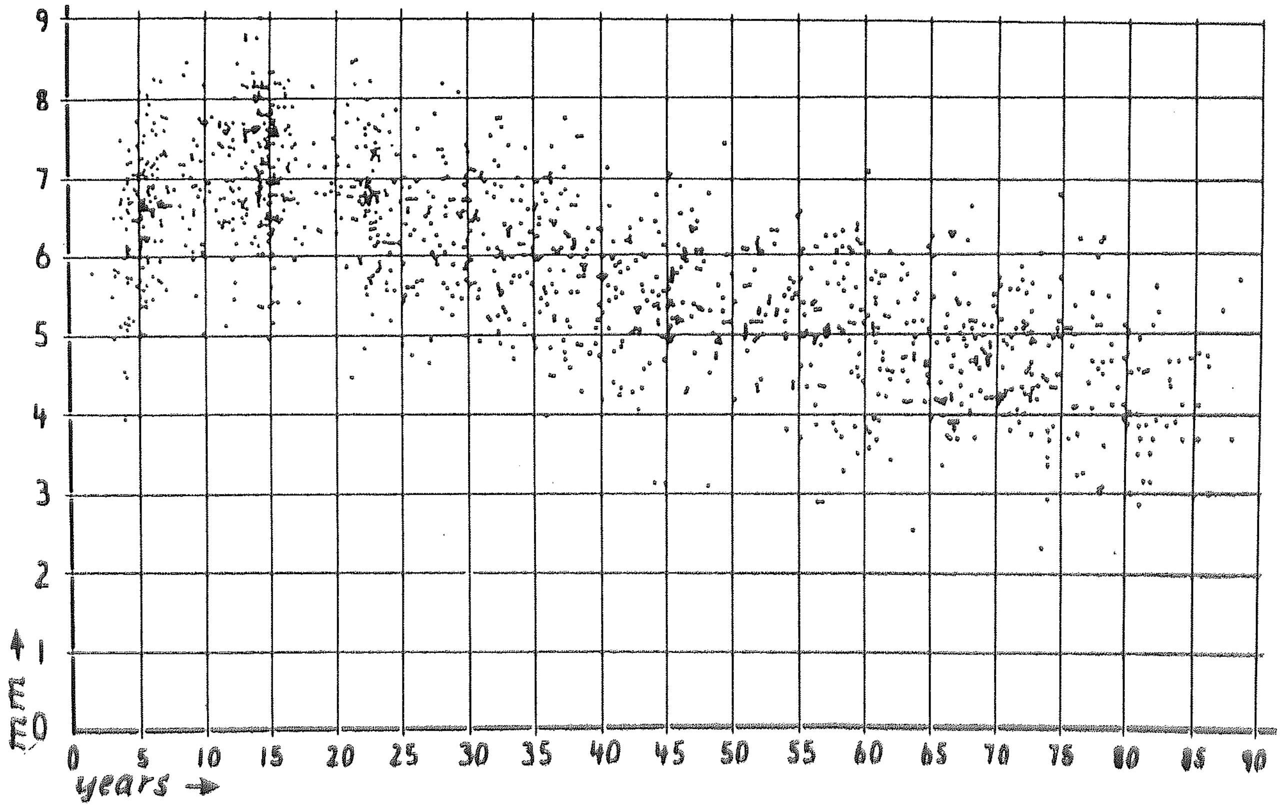


Figure 1.8 Pupillary size in darkness of 1263 subjects (from Loewenfeld, 1979).

It has been shown that various aspects of pupil responsiveness also show a decline with age (Kumnick, 1954, 1956b, 1956d, Loewenfeld, 1979). However, although the amplitude of response may decrease, taken as a proportion of starting size, the aged pupil is equally as responsive to both light and near stimuli as it is in young persons (Birren, Casperson and Botwinick, 1950, Kuminck, 1956a, 1956c, Schäfer and Weale, 1970).

There are no clear reasons for the decline in pupil size with age. Kornzweig (1954) listed atrophy of the dilator muscle, sclerosis of the iris blood vessels and deposition of hyaline substance in the tissue below the sphincter muscle as causes. Schäfer and Weale (1970) suggest progressive dysfunction of the dilator muscle itself. Although these changes may take place, they are unconvincing explanations for senile miosis as the pupils of aged persons dilate well to mydriatic drugs thus ruling out mechanical restriction of dilation. Indeed Korczyn (1976) found a relatively greater magnitude of pupil dilation to phenylephrine (a direct acting α_1 agonist) in elderly patients and achieved an average dilated pupil diameter of 8.21mm compared to 8.28mm in younger subjects. Korczyn (1976) suggested that generalised decreased sympathetic tone in elderly subjects is the cause of reduced pupil diameter. Docherty and O'Malley (1985) state that peripheral α-adrenoceptor responsiveness is generally unchanged or decreased with age except in the eye where it apparently increases. Davis and Byard (1988) demonstrated that a lower concentration of phenylephrine was needed in elderly subjects to produce 1mm pupil dilation than in young subjects and that the concentration of carbachol (a muscarinic agonist having a potency and action similar to that of acetylcholine) necessary to produce 1mm pupil constriction was unchanged. They concluded that senile pupil miosis was therefore not due to decrease in α-adrenergic responsiveness or to increased cholinergic responsiveness but was probably due to a lack of available sympathetic neurotransmitter. However, Buckley *et al* (1987) have shown that if baseline differences in pupil size are first eliminated using thymoxamine, then no difference in responsiveness to phenylephrine is shown between young and elderly subjects.

Loewenfeld (1979) examines the various reasons put forward to explain senile miosis and concludes that the miotic pupil in the elderly resembles that in the young when fatigued except that in the elderly the effects are irreversible. Thus Loewenfeld (1979) considers the miotic elderly pupil to be a result of a form of chronic fatigue and due to reduction in supranuclear inhibition to the sphincter pupillae. Pressman, DiPhillipo and Fry (1986) have compared pupil sizes in normal subjects to those found in age-matched subjects suffering from sleep disorders. They found that dark-adapted pupil size was significantly smaller in the subjects with sleep disorders than in those without and suggested that sleep disorders and daytime sleepiness may contribute to senile miosis.

CHAPTER 2

THE CHARACTERISTICS OF PUPIL RESPONSE

2.1 RESPONSE TO LIGHT

In certain animals, such as the frog, the iris tissue is itself responsive to light (Barr and Alpern, 1963). In human, no such response has been demonstrated and the pupil responses to light are considered to be mediated via the midbrain pupillary pathway and to depend on the retinal light receptors. A large body of literature exists concerning pupil light responses (for a review see Loewenfeld, 1966) and only the main characteristics will be considered here.

Three partial decussations occur in the neuronal pathway subserving the pupillary light reflex in human and as a result, stimulation to one eye causes, in normal individuals, an equal reaction in the two pupils. Although it has been shown (Smith, Ellis and Smith, 1979) that the direct pupil response (i.e. ipsilateral to the stimulus) may be approximately 6% larger than the consensual response (i.e. contralateral to the stimulus) it is generally considered that in humans the direct and consensual responses are effectively equal. This equality of responses between the two eyes also applies to all pupil responses elicited by stimuli other than light.

2.1A PUPIL RESPONSE TO STEADY-STATE LIGHT LEVEL

Pupil diameter varies with steady-state light level (see figure 2.1). Although varying pupil size is the only means available to the eye of controlling retinal illumination, a diameter change between 8mm and 2mm (a reasonable estimate of the operating range of the pupil under normal conditions) will alter retinal illumination only by a factor of 16X, which is negligible when compared to the 10^6X range of light level which may be encountered by the human eye. Hence retinal adaptation accounts for most of the eye's ability to cope with widely varying ambient illumination conditions and thus the function of pupil response to light is not immediately clear. Campbell and Gregory (1960) suggested that the pupil light response acts to maximise acuity across varying luminance levels.

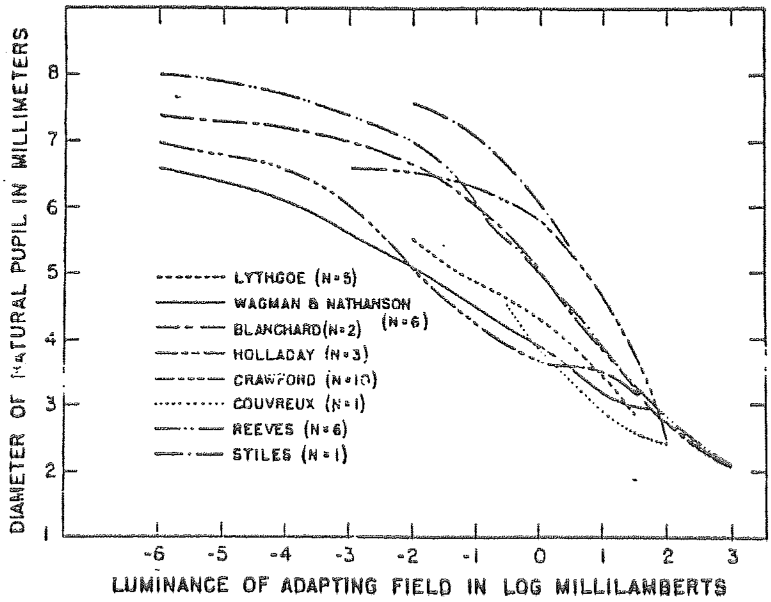


Figure 2.1 The relationship between pupil diameter and steady-state light level compiled from eight studies (from de Groot and Gebhard, 1952).

Woodhouse (1975) showed that this effect is small and that whereas a fixed, constricted pupil would be a great disadvantage at low light levels, a fixed, dilated pupil would only cause problems at high light levels and even then only lead to an 18% loss of resolution. Woodhouse and Campbell (1975) investigated further the possible advantages of a mobile pupil and showed that pupil constriction in bright light minimises light adaptation in readiness for sudden reductions in illumination. The time necessary for dark adaptation to occur may be reduced by as much as 10 minutes compared to that occurring with a fixed, dilated pupil. In dim illumination, the dilated pupil maximises sensitivity by allowing for collection of the maximum possible light energy.

2.1B PUPIL RESPONSE TO CHANGE IN LIGHT LEVEL

2.1Bi THRESHOLD

The stimulus threshold for pupil response is dependent on the level of light adaptation of the retina. In the dark adapted eye, using 1s flashes of light, the pupil reaction threshold is one log unit stimulus intensity higher than that necessary for visual detection (Lowenstein and Loewenfeld, 1958). At threshold the reaction is small in amplitude and has a long latency; as the stimulus step increases, reaction amplitude increases to a maximum diameter change of around 4mm with short latency. Above 7-9 log units over threshold no further increase in reaction occurs and at this level the reaction outlasts a 1s stimulus (Loewenfeld, 1966).

2.1Bii LATENCY

Pupil light response latency (ie the time elapsed betweeen the onset of the stimulus and the beginning of the response) will vary according to the conditions under which it is measured. Young and Biersdorf (1954) investigated latency for constriction and dilation and found mean results of 175 and 180ms respectively for a previously stable pupil. Following pupil activity the latencies were lengthened to 220 and 385ms. Electrical stimulation of the ciliary ganglion in monkey leads to pupil reaction with a latency of around 200ms which shows that most of the latency is caused by the neuromuscular apparatus (Loewenfeld, 1966). In human, the light reflex latency decreases linearly with increasing stimulus intensity from 400-500ms near threshold to approximately 250ms for strong supra-threshold stimuli (Cibis, Campos and Aulhorn, 1977).

2.1Biii PUPILLARY CAPTURE AND ESCAPE

If a fairly dim stimulus light is used, following contraction the pupil may redilate to its original level; this is known as pupillary escape. A stronger light stimulus results in pupillary capture when the pupil remains at its constricted level. Sun and Stark (1983) showed that pupillary escape can only occur with large pupil sizes. With small pupils capture always occurs even with a dim light stimulus.

2.1Biv SUMMATION

Summation in the pupil response to light occurs in various forms. Temporal summation is known to be one form and is reflected both in latency and depth of reaction. Close to threshold, for stimulus durations up to 1s, the pupil responds to the total energy contained within the stimulus so that at those near threshold levels, intensity and duration of the stimulus are interchangeable (Loewenfeld, 1966).

Spatial summation can also occur and the pupil response elicited by a light stimulus depends on the area of retina stimulated. When a small stimulus field is enlarged, the pupillary threshold is reduced and whereas with small stimulus areas pupillary threshold is higher than that for visual detection, when very large stimulus areas are used, the two thresholds are more equal. Thus spatial summation is more pronounced for pupil response than for vision (Loewenfeld, 1966).

Within limits, the afferent impulses from the two eyes summate. Thomson (1947) showed that the pupil constriction resulting from light stimulation of the retina of both eyes is significantly greater than that when only one eye is stimulated and suggested that this summation takes place below cortical level, somewhere in the reflex arc pathway.

2.1Bv INFLUENCE OF STIMULUS FREQUENCY

The pupil shows discrete responses to a light source flickering at up to around 4Hz (see figure 2.2). At higher flicker rates, the pupil can no longer follow the stimulus although it has been reported that the flicker continues to influence mean pupil size up to around 60Hz (Howarth, 1989). The flickering light decreases mean pupil size compared to that when the same light is held constant, even though mean luminance over time is decreased.

2.1Bvi RECEPTORS RESPONSIBLE FOR PUPIL LIGHT RESPONSES

Identification of the receptors responsible for pupil light response has prompted much debate although the evidence now suggests that they are the same receptors as those responsible for vision and that both rods and cones contribute (Loewenfeld, 1966). The pupillomotor threshold lies just above that for vision across the visible spectrum and across all areas of the retina. In the dark-adapted eye pupillary spectral sensitivity shows the same Purkinje shift as visual sensitivity; evidence that both rods and cones contribute to pupil response (Loewenfeld, 1966).

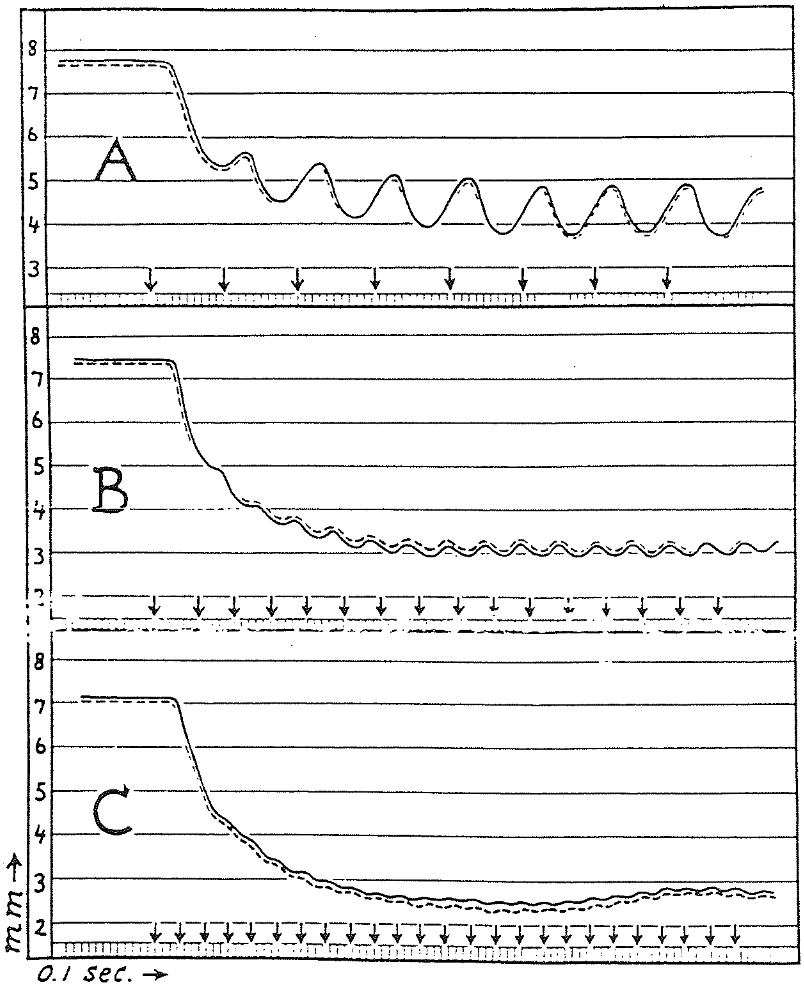


Figure 2.2 Pupil response to a flickering light stimulus (from Loewenfeld, 1966). Pupil response is plotted in mm against time in 0.1 second units. The solid line represents the right pupil and the broken line the left. The small arrows indicate the occurrence of a 5ms white light stimulus at 1Hz (A), 2Hz (B) and 3Hz (C).

It has been shown (Stiles and Crawford, 1933) that light rays entering the eye through the periphery of the pupil have lower luminous efficiency than those entering centrally and it was thought that peripheral rays should therefore be less effective in causing pupil response. Spring and Stiles (1948) showed data suggesting that this was not the case but Alpern and Benson (1953) were able to demonstrate a Stiles-Crawford effect on the pupil using a small central field. They concluded that the differing results were due to field size; over a large field, both rods and cones contribute to pupil response and rods have very little directional sensitivity.

Ten Doesschate and Alpern (1965) were able to demonstrate that cones contribute to steady-state pupil size by using an observer with a rod-free retina. However, in normal observers cone contribution may only be significant for small, central fields and with full hemisphere illumination, the action spectrum of steady state pupillomotor response reflects rod activity alone (Alpern and Ohba, 1972) as the activity of the far greater number of rods in the retina swamps the cone influence.

The consensus is that the receptors responsible for pupil responses to light are the retinal rods and cones. It is not known, however, whether certain rods and cones relay impulses only to the pupil, or if some of the receptors are somehow able to serve both the pupil and the visual system.

2.1Bvii SUPPRESSION

Like visual sensation, the pupil light reflex is suppressed during retinal rivalry (Bárány and Halldén, 1948) and just before and during saccadic eye movements (Zuber, Stark and Lorber, 1966). Response latency was shown to be increased in the amblyopic eye of several amblyopes when compared to the normal eye (Kase *et al*, 1984).

2.2 NEAR RESPONSE

During near fixation in prepresbyopic observers, the 'near vision triad' of accommodation, convergence and pupil constriction occurs. A small degree of cyclorotation of the eyes also accompanies near fixation, although it is usually considered to be of no significance. The pupil constriction occurring during near fixation has attracted less interest than the light reflex and much less literature is available (for a review see Loewenfeld, 1966). Accommodation and convergence have well defined roles in near vision. The accommodation mechanism is driven principally by retinal blur and refocusses the eye by changing the curvature of the lens to produce a clear retinal image. Convergence is driven by retinal disparity and alters the angle between the two visual axes to place the image of the fixated object on the fovea of each eye and to allow fusion of the two retinal images. In contrast, the drive to and the function of pupil near response is not as easily defined. Much of the relevant literature deals with the controversy concerning the drive to pupil near response.

2.2A ROLE OF THE PUPIL NEAR RESPONSE

In many vertebrates the iris plays a large part in near vision (Duke-Elder, 1958). Some make use of highly mobile pupils to increase their effective accommodative range such as the pinhole pupil used by aquatic snakes. In reptiles, turtles and birds the sphincter pupillae is extremely powerful and acts directly on the lens, squeezing it to increase its curvature and consequently accommodative range can be up to 50D. Deformation of the lens only by variation in the elasticity of the lens capsule is a mechanism peculiar to mammals and the efficiency of the mammalian accommodative system is poor compared to other vertebrates. The otter is an exception in which the powerful iris sphincter muscle acts directly on the lens (Duke-Elder, 1958). One recent paper (Crawford, Kaufman and Bito, 1990) suggests that the iris may have a role in accommodation in the rhesus monkey. It was found that after total iridectomy in one eye, the maximum drug-induced accommodation was reduced by 40% in the iridectomised eye compared to the normal eye. However, accommodative level induced by midbrain stimulation was unaffected by iridectomy.

There is no known direct mechanical influence of the iris on accommodation in human and it is usually stated in optometry text-books that the pupil constriction associated with near vision acts to increase the depth-of-focus of the eye. There is however, little evidence to support this statement. Although optical theory predicts a significant effect of pupil size on visual resolution (Westheimer, 1964), most studies show that within its normal operating range, pupil size has little effect on vision or depth-of-focus. Campbell (1957) measured depth-of-field in the human eye and found it larger and less influenced by pupil size than theory would predict. This was attributed to the Stiles-Crawford effect and the presence of chromatic aberrations in the eye. Ogle and Schwartz (1959) showed a linear relationship between pupil size and depth-of-focus although the effect was small-between pupil diameters of 2.5 and 8mm depth-of-focus increased by around 0.12D (ie +/-0.06D) per mm increase in pupil size. Ripps *et al* (1962) showed that at pupil diameters larger than 3mm, accommodation response to a fixed target remained constant thus suggesting no concomitant change in depth-of-focus. Tucker and Charman (1975) measured depth-of-focus using Snellen letters and agreed that with pupil sizes greater than 3mm, increase in pupil size had no effect on depth-of-focus. Charman and Whitefoot (1977) used a laser optometer to provide objective measures of depth-of-field and showed that for pupil diameters above 3mm, depth-of-field remained constant and only increased significantly with pupil diameters below 2mm.

Although Campbell and Green (1965) showed improvement in contrast sensitivity with decreasing pupil size, two later studies showed much less effect. Legge *et al* (1987) found that for a sine wave grating of spatial frequency 3.5 cycles per degree (c/deg), depth-of-focus increased only for pupil diameters below 2.5mm and that for diameters above 3mm, the depth-of-focus remains relatively constant.

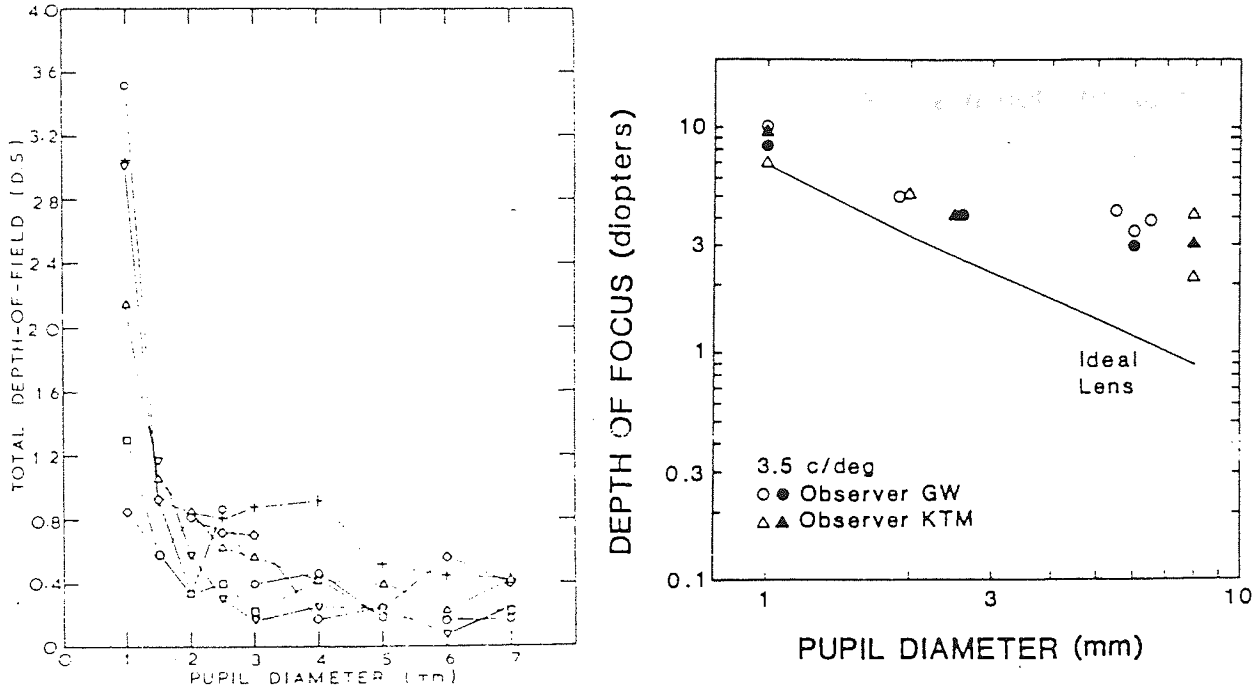


Figure 2.3 The relationship between depth-of-focus and pupil diameter (left plot from Charman and Whitefoot, 1977 (symbols indicate individual results for each of the 6 observers used) and right plot from Legge *et al*, 1987).

They stated: "the depth-of-focus of the human eye becomes relatively insensitive to pupil size at diameters above 3mm and to frequencies above about 4c/deg. In this domain the depth-of-focus lies between 1 and 3D, the former corresponding to the widest pupils and highest spatial frequencies." In considering why depth-of-focus was greater than expected with large pupils, they decided that spherical and other monochromatic aberrations and the Stiles-Crawford effect actually led to greater tolerance to defocus at larger pupil sizes. Kay and Morrison (1987) were able to demonstrate no significant effect on contrast sensitivity between pupil diameters of 6, 3 and 2mm under normal viewing conditions in which the retinal illumination was allowed to vary with pupil size. They suggested that any benefit of a smaller pupil may be outweighed by the reduced retinal illumination that results.

2.2B DRIVE TO THE PUPIL NEAR RESPONSE

It has usually been assumed that the pupil constriction associated with near fixation is driven by accommodation or one or more of the components of convergence, rather than being a separate event in its own right. Loewenfeld is one of the few to suggest otherwise and states: "Accommodation, convergence and pupillary contraction are associated movements, and are not tied to one another in the manner usually referred to by the term 'reflex'. They are controlled, synchronized and associated by supranuclear connections, and are not caused by one another." (Loewenfeld, 1966, p69).

Fry (1945) used a modified haploscope to induce changes in accommodative and vergence demand and concluded that pupil near response is associated with accommodation, accommodative convergence and possibly fusional convergence. Knoll (1949) modified Fry's techniques and used infra-red (IR) photography to record the pupil. Subjects fixated targets presented at a variety of distances in order to determine the effects of different levels of accommodation. Knoll found pupil constriction associated with accommodation and accommodative convergence in all 10 of his subjects and with fusional convergence "in at least some" (Knoll, 1949, p356).

Marg and Morgan (1949) review early literature relating to the drive to pupil near response finding the evidence presented contradictory but suggest that overall the consensus was that pupil near response is more closely associated with convergence than with accommodation. Their own studies (Marg and Morgan 1949,1950a) suggested that accommodation elicits a pupil response in all subjects and fusional convergence a lesser response in about half. Marg and Morgan (1949, 1950a) report a linear relationship between accommodative level and pupil diameter and also between accommodative convergence and pupil diameter. On average they found pupil constriction of 0.48mm per dioptre of accommodative stimulus change and also investigated the influence of target proximity by having subjects fixate targets at varying distances and equating the accommodative demand using lenses. From this they concluded that awareness of target proximity played no part in pupil response in 6 out of their 7 subjects. Marg and Morgan (1950b) further report that any pupil reflex apparently caused by interruption or resumption of fusion alone is an artefact caused by lack of control of accommodation, convergence and illumination.

Renard and Massonnet-Naux (1951) proposed that pupillary near response represents a synergy with convergence and is not associated with accommodation. An investigation into the effect of fusional vergence on the pupil was carried out by Backer and Ogle (1964) using prisms to induce disparity. Using an electronic IR pupillograph to monitor the LE, they found in all their subjects that pupil constriction occurred for convergent disparities and dilation for divergent disparities. Whichever direction of disparity was introduced, an initial transient pupil constriction occurred.

Jones (1989), reported that pupil constriction is associated with blur-driven accommodation but not with fusional vergence. Accommodation was driven with negative lenses while vergence and pupil responses were open-loop (using monocular viewing through a 3mm pupil). Fusional vergence was induced using prisms while accommodation and pupil responses were open-loop (using binocular pinhole viewing). Accommodation, vergence and pupil size were measured simultaneously using IR recording devices. He attributed reports of convergence-driven pupil response to the fact that accommodation was not open-loop in earlier experiments.

Myers and Stark (1990) state that the synkinetic relationship between accommodation and vergence is relatively well understood and attempted to determine how pupil response fits into the near vision triad. They compared the latencies of accommodation, vergence and pupil responses to a blur-only stimulus to those obtained using a blur plus disparity stimulus. As the addition of disparity to blur resulted in greater reductions in the latencies of accommodation and vergence than of pupil, they concluded that pupil near reponse results from an asymmetric drive from accommodation and vergence.

Recently, Stakenburg (1991) reported that if experimental conditions are very carefully controlled to minimize visual cues, then a blur-only accommodative stimulus may produce no concomitant pupil response at all. Subjects viewed two superimposed targets of equal angular subtense through semi-silvered mirrors and an accommodative step stimulus was created by switching illumination from the far (0.40D) to the near (2.78D) target. Accommodation response was presumed from the consistent vergence response of the unstimulated eye. When the step from far to near target was accomplished with no apparent lateral movement, complete absence of pupil response was shown in two out of the three subjects used. When lateral target displacement was introduced, an increase in pupil responsiveness was observed. Tsuchiya, Ukai and Ishikawa (1989) have also demonstrated accommodative change without pupillary constriction in a paper in which they report that following a sustained near vision task, pupillary redilation may lag behind change in accommodative level.

Unlike the literature relating to other pupil reactions, the literature relating to the drive to pupil near response is confusing and contradictory. It seems that pupil response can be found to be associated with accommodation and one or more aspects of vergence or can be absent depending on experimental conditions. This suggests that other factors may be involved and further, carefully-controlled experiments will be necessary before pupil near response is fully understood.

2.2C LATENCY

The latency of the pupil near response is longer than that for the light response. This is taken to be due to the longer neuronal pathways involved because of cortical involvement. Figures given vary; O'Neill and Stark (1968) give latencies of 430ms for far to near (5-8D step) and 400ms for near to far (8-5D) and for the same stimuli accommodation latencies were 100ms shorter in each case. Myers and Stark (1990) give 331ms as mean latency for pupil near response to a blur accommodative stimulus and to the same stimulus accommodative latency is given as 50ms longer.

2.3 EFFECT OF SPATIALLY MODULATED STIMULI

Much interest has been shown in recent years in the finding that pupil constriction can be elicited by reversal of patterns such as gratings or checkerboards even though mean luminance levels remain constant. van der Kraats, Smit and Slooter (1977) described pupil contractions to alternating checkerboard stimuli, the amplitude of the response being dependent on the check size presented and it was therefore thought that an objective measure of acuity could be obtained using the pupil. Slooter and van Norren (1980) continued this work and showed a high correlation between 'pupil acuity' obtained using checkerboards and that obtained using conventional methods. Ukai (1985) argued that the responses to alternating checkerboards were due either to local luminance changes or to small accommodative changes. Barbur and Forsyth (1986) report pupil constriction to appearance of a spatially modulated pattern and that this response was absent in the blind hemifield of a cortically damaged hemianope despite the presence of the light reflex. The response was present in the normal hemifield and thus the response to the stimulus appeared to be cortically mediated. Amplitude of response was shown to vary with spatial frequency. Tobimatsu *et al* (1990) conversely report pupil dilation to a grating stimulus and suggest that the difference between their results and other reports may be due to the use of different stimulus parameters.

2.4 EFFECT OF EMOTION ON THE PUPIL

Changing emotional states are capable of both diminishing pupil responses to extraneous stimuli and eliciting internally mediated responses (Loewenfeld, 1966). For review of effects of emotion on the pupil see Goldwater (1972). Strong emotion such as anxiety has been shown to be capable of diminishing pupil reflexes to light (Bakes, Bradshaw and Szabadi, 1990) possibly as a result of supranuclear inhibition and pain can have the same effect (Bender, 1933). Schneider *et al* (1987) showed that resting pupil size is larger in subjects with higher arousal levels (Type A subjects defined as those displaying characterisitics of time urgency and hostility) than in their more relaxed subjects (Type B subjects defined as those displaying absence of Type A characteristics) and suggested that this was due to increased sympathetic tone.

Cognitive tasks have also been shown to affect the pupil. Hess and Polt (1964) showed that when subjects were given a mental task to perform, the pupil dilated and only returned to base level once the task was completed. The amplitude of dilation was found to be correlated with the difficulty of the task. Matthews *et al* (1991) demonstrated similar effects and postulated that the effect was mediated by the parasympathetic system as topical instillation of an alpha-1 adrenergic antagonist (thymoxamine HCl) did not diminish the effect.

2.5 EFFECT OF PUPIL SIZE

Loewenfeld and Newsome (1971) have demonstrated that the pupil shows fairly linear responses to stimuli which are limited as the pupil approaches extreme dilation or constriction due to mechanical factors. Semmlow, Hansmann and Stark (1975) investigated the variation in responsiveness of the pupil to accommodative and light stimuli over a range of pupil diameters. They found that the pupil was most responsive at mid-range sizes, although in the diameter range 3.5-6.0mm, variation in responsiveness was limited to +/-10%.

CHAPTER THREE

ELECTRONIC PUPILLOMETRY AND ITS APPLICATIONS

3.1 INSTRUMENTATION

Interest has been shown in pupillary reactions for many centuries (Lowenstein and Loewenfeld, 1958) although early studies were hampered by the lack of any precise stimulus generation and pupil response recording apparatus. Accurate observations of dynamic pupil responses cannot be made with the naked eye due to the rapidity of the responses and their variability. Only during this century has technology advanced sufficiently to allow accurate control of stimulus parameters and recording of pupil responses.

Otto Lowenstein introduced and developed pupillography from the 1920s onward (Lowenstein, 1956, Lowenstein and Loewenfeld, 1958). His original technique consisted of making motion picture recordings of the two pupils just before and following controlled stimuli. In 1935, Lowenstein introduced infra-red (IR) photography under IR illumination which allowed for the first time recording of the pupils under conditions of darkness (Lowenstein and Loewenfeld, 1958). To obtain a pupillogram, the recorded negative film images were enlarged by projection and the maximum pupil diameter measured by hand frame-by-frame and plotted against time. As each clinical film required up to 4000 measurements (Lowenstein and Loewenfeld, 1958), this was a time-consuming process. In 1947, Lowenstein introduced an automated process for taking pupil measurements from the film. Again the negative film images were projected onto a screen and these were scanned by a rotating mirror over a slit mask covering a photocell. The time taken for the pupil portion of each image to scan over the photocell was recorded as an indirect measure of pupil size. Although precise, this method was complex and expensive due to the large quantities of IR sensitive film needed and so during the years 1953-1957 a binocular, electronic, IR, direct-recording pupillometer was developed.

For details of the instrument devised see Lowenstein and Loewenfeld (1958). The principle used was to scan the two pupils in a repeating vertical series of 9 narrow horizontal sweeps using a small slit of IR light. An IR sensitive photocell was set to receive the reflected light. During each horizontal sweep, as the slit passed over the iris a certain amount of IR light would be reflected compared with almost none as the slit passed over the pupil. Monitoring the voltage output from the photocell allowed a picture of the pupil to be built up on an oscilloscope screen. Pupil diameter was recorded indirectly as the maximum voltage output obtained during a complete scan. The instrument gave binocular recordings of pupil diameter with high resolution (0.025mm), calibration for absolute values being achieved using artificial pupils of known diameter.

All electronic pupillometers subsequently developed whether binocular or monocular use essentially the same principle i.e. they all utilise IR illumination and distinguish between the non-reflective pupil and the reflective iris, although the method of achieving this varies from one instrument to another. Electronic IR pupillometers of varying designs are described by Borgdorff and van Mill (1979), Saini and Cohen (1979), Smith, Jones and Taylor (1984), Reulen *et al* (1988) and Alexandridis, Leendertz and Barbur (1991).

3.2 APPLICATIONS

3.2i CLINICAL

Lowenstein and Loewenfeld (1958) considered continuous, simultaneous, binocular recording of the pupils desirable for use in ophthalmology and neurology as an aid to detection and localisation of pathology affecting the pupillary system. Using their pupillometer, they were able to demonstrate modifications of the normal pupillary reflexes which were characteristic of specific disease processes. Binocular pupillometry is necessary to demonstrate the disruption of the normal symmetry in responses between the two eyes caused by some conditions. Lowenstein and Loewenfeld (1958) felt that pupillometry had the potential to become a useful diagnostic tool in neuro-opthalmology and in other branches of medicine, although it would appear that pupillometry is not now as widely used as they had hoped.

A further suggested clinical application of pupillometry has been the objective evaluation of fatigue (Lowenstein, Feinberg and Loewenfeld, 1963) which is difficult to quantify and to measure. Pupil responses reflect the balance of the autonomic nervous system and are outside voluntary control and may therefore alter according to fatigue levels. Lowenstein, Feinberg and Loewenfeld (1963) recorded the pupils of subjects sitting in conditions of darkness for around 15 minutes. Healthy, young, alert subjects demonstrated large, around 7mm, stable pupils. In similar, tired subjects, after a few minutes in darkness the pupils became smaller and oscillated in size as the subject relaxed. Prior to falling asleep, the pupils are reported to be have been small, although a sudden stimulus such as a loud noise could awaken the subject and restore the pupils to their original diameter. Chronically tired subjects show an exaggerated form of normal tiredness, which Lowenstein, Feinberg and Loewenfeld (1963) suggest can be assessed by pupillometry. This concept was extended to a study of patients suffering from narcolepsy (a condition characterised by more or less constant drowsiness and attacks of sleep) by Yoss, Moyer and Ogle (1969). Having found that the pupil movements were largely hidden by eyelid closure as the subjects became drowsy, a second study (Yoss, Moyer and Hollenhorst, 1970b) made use of a lid crutch to study the behaviour of one pupil even during sleep. They studied 156 narcoleptic subjects and the authors concluded that pupillometry is a sensitive and objective indicator of decreased wakefulness in narcoleptics and proved useful in evaluating the efficacy of prescribed medication.

The presence of pupillary abnormalities of mainly neuropathic origin (Smith *et al*, 1978, Smith and Smith, 1983) in diabetes has led to interest from clinicians in the possibility of using pupillometry both in diagnosis and monitoring of the disease. Smith *et al* (1978) state that diabetics with neuropathy often have abnormally small pupils that fail to dilate in darkness. Smith and Smith (1983) used phenylephrine (a sympathomimetic which dilates the pupil by acting directly on ∞_1-adrenoceptors in the dilator pupillae) and hydroxyamphetamine (an indirect sympathomimetic which dilates the pupil by releasing noradrenaline from the sympathetic nerve terminals) to investigate the cause of the reduced pupil size. They demonstrated that the small pupil in diabetics is supersensitive to phenylephrine but reacts normally to hydroxamphetamine, evidence that the damage is of neuropathic, rather than myopathic, origin. Alio *et al* (1989) attempted to establish the significance and characterisitics of pupil reactivity in diabetics. Their results suggested that pupil abnormalities due to sympathetic denervation may be an early sign of systemic autonomic neuropathy in diabetics. To assess the value of pupillometry in diagnosis of diabetes, Kuroda *et al* (1989) compared the light reflex of borderline diabetics with non-insulin-dependent diabetics and with normals. They report that the borderline diabetics had autonomic neuropathy indicated by pupillary abnormalities before the actual disease became overt and that therefore pupillometry may have a function in early detection and in management of diabetes. The use of pupillometry is supported by Papakostopoulos, Dean Hart and Corral (1991) who suggest that pupil reactivity is a sensitive index of autonomic dysfunction in diabetics.

3.2ii PHARMACOLOGICAL APPLICATIONS

Loewenfeld (1963) states that the iris has enjoyed great popularity as an indicator of drug effects although many investigations have failed to use accurate pupillometry. In particular, the pupil has been used to investigate cholinergic and adrenergic drug mechanisms and these are now understood sufficiently to allow the observation of drug effects on the pupil to be used to test the integrity of the sympathetic and parasympathetic innervation to the eye (Thompson, 1972). A comparison of the effects of physostigmine and pilocarpine on pupil reflexes

(Loewenfeld, 1963) showed how pupillometry can be used to elucidate the effects of drugs that act on the pupil but demonstrates the importance of accurate, preferably binocular, pupillometry. Although both drugs constrict the pupil and so may appear to have similar effects, dynamic recording of the pupil responses to light showed that the two drugs act on the pupil in different ways.

Pupillometry is attractive because it is a non-invasive method of investigating both the local and systemic pharmacological effects of new or existing drugs on human subjects (Millson, 1991). Further, pupillometry can be useful in defining the dose and dosage intervals necessary for administration of a particular drug (Millson, 1991). Kergoat, Lovasik and Doughty (1989) report on the use of IR pupillometry in the evaluation of a newly-introduced mydriatic drug combination (phenylephrine HCl 5% and tropicamide 0.8%). Their results using pupillometry showed that although the drug combination acted as an effective mydriatic, it had no demonstrable advantage over tropicamide 1% alone.

3.2iii PSYCHOLOGICAL APPLICATIONS

The pupil is responsive to many inputs including emotional change (see Goldwater, 1972, Hess and Goodwin, 1974) and psychologists have recognised that it may be possible to use pupillometry to objectively assess emotional state. Sturgeon, Cooper and Howell (1989) report on the use of pupillometry as an objective measure of arousal during the treatment of snake phobics. They found that pupil reponses correlated well with fear levels and that the pupil responses were modified according to the reduction of fear achieved in treatment. Lavie (1972) used pupillometry to measure ultradian rhythms in human subjects. Pupil size, light reflex and motility were measured every 15 minutes for 10 continuous hours in young subjects. Results showed rhythmic variations in the measured parameters with periodicity of 75 to 125 minutes and may reflect underlying rhythms in the CNS.

3.2iv COMMERCIAL APPLICATIONS

Several commercial applications of pupil response to psychological inputs have been suggested. Krugman (1964) discusses the possible applications of pupillometry in advertising as an objective means of testing responses to new products and designs. It was hoped that pupillometry could provide a means of objectively assessing reactions and bypassing the normal problems with language barriers and reluctance to reveal true feelings. It would appear that the technique has not found widespread acceptance and this may be partly due to the difficulty in eliminating light reflex effects when viewing visual stimuli. This difficulty was pointed out by Goldwater (1972) who advises caution in any commercial application of pupillometry but concludes that it may have use in research applications as an indicator of states of arousal.

Geacintov and Peavler (1974), following the work of Lowenstein, Feinberg and Loewenfeld (1963) who showed decrease in pupil diameter with increasing fatigue, attempted to use pupillometry to assess levels of fatigue in telephone operators. Although the results were not entirely conclusive, it was felt that pupillometry had some potential as an objective indicator of fatigue. A further industrial application is reported by Metalis and Hess (1986) who used pupillometry to assess the cognitive loads imposed by reading in different varieties of video screen fonts. They reported that the pupil was consistently larger during reading in the more cognitively demanding font.

3.2v OBJECTIVE PERIMETRY

Measurement of visual fields is a time-consuming process and relies on accurate subjective responses from an alert patient. Mapping the visual fields by recording pupil responses to small spot stimuli similar to those used in standard perimetry is attractive due to its objectivity. Bresky and Charles (1969) attempted to correlate the thresholds for pupillary response and visual sensation in normal and abnormal subjects. They concluded that the pupillomotor field parallels the standard visual field whether the cause of defects was pre- or post-chiasmal as far as the occipital cortex. This finding cannot be explained using the accepted version of the pupillary light reflex pathway in which the cortex plays no part. Cibis, Campos and Aulhorn (1975) investigated 'pupillary hemiakinesia' i.e. the lack of a pupillary reaction in the blind part of a visual field while it is maintained in the seeing portion. This phenomenon should occur only in pre-geniculate defects and therefore be a useful diagnostic test between pre- and post-geniculate lesions. However, their results showed absence of pupil response to light in the blind areas of 5 subjects who all had cortical lesions.

Cibis, Campos and Aulhorn (1977) suggest using pupillometry to measure the latency of the pupillary light reflex at varying locations across the retina. Since light reflex latency was shown to be inversely proportional to log stimulus intensity, variation in latency across the retina to a constant stimulus should reflect differences in sensitivity and thus allow mapping of a pupil field.

Kardon, Kirkali and Thompson (1991) and Kardon *et al* (1992) have linked a computerized IR pupillometer with a Humphrey Field Analyzer. They report that pupil perimetry has several advantages over standard visual threshold perimetry. It is less stressfull for the patient, fixation loss is less of a problem and it is objective. However, patients must be able to control blinking and have resting pupil diameter ideally 3.5mm or above. In their system, rather than determining a pupil threshold, they use suprathreshold stimuli and determine the amplitude of response at each stimulus location which gives information about the depth of responsiveness at each location tested. They further suggest that comparing the latency of pupil responses at each location may also be a useful method of assessing sensitivity. In the majority of patients tested, the 'pupillary defect' closely resembled the visual field defect although in a few cases the two were remarkably different. Further investigation using pupil perimetry may improve the usefulness of the technique and furnish more information concerning the pathways serving vision and pupil responses. Another combination of automated perimetry and pupillometry has been described by Fankhauser and Flammer (1990).

3.2vi OBJECTIVE ACUITY

In 1977, van der Kraats, Smit and Slooter described pupil contractions in response to alternating checkerboard stimuli. The amplitude of the responses showed a monotonic dependence on the check size used suggesting that the response was not a simple light reflex mediated by the midbrain pupil pathway but demonstrated involvement of higher centres. From this finding, it was suggested that pupil response to gratings could be used to objectively determine visual acuity. Slooter and van Norren (1980) investigated further and measured pupil responses to checkerboard stimuli in normal subjects. To minimise any light reflex effects, they used appearing/disappearing checkerboards of the same mean luminance as the blank screen. Pupil acuity was found to have a very high correlation with the subjectively determined acuity using the same stimuli. The technique was applied to visually abnormal subjects by Slooter (1981), who again found good correlation between the objective acuity determined from pupil responses and standard, subjectively-determined acuity. The determination of objective pupil acuity proved particularly useful in malingerers.

In 1987 Barbur and Thomson investigated the possible use of pupil response as an objective measure of visual acuity. Using sinusoidal gratings they found that the gratings caused pupil response of amplitudes that varied systematically with spatial frequency. Maximum pupil response amplitudes were elicited by gratings in the spatial frequency range 1-5 c/deg. They compared the effects of defocus and eccentric fixation on both the pupil response function and the subjectively-determined contrast sensitivity function and found that the effect on both was essentially the same. Further confirmation of the validity of pupil acuity has come from Cocker and Moseley (1991, 1992). An objective means of measuring acuity has an obvious application in young infants. This has been investigated by Cocker *et al* (1992) who report that a pupil grating response can be reliably elicited in human infants as young as 1 month of age.

It has also been suggested that pupillometry may be of use in assessing other aspects of central visual processing (Barbur and Forsyth, 1986, Barbur, Keenleyside and Thomson, 1989). Convincing evidence is provided that the pupil responses elicited by spatial stimuli do indeed reflect central processing. Pupil grating responses were tested in two observers with homonymous hemianopia caused by well defined cortical defects. Both observers showed pupil responses to gratings presented in their normal hemifields but absence of response in their blind hemifields. Pupil light reflex, however, could be demonstrated in both the normal and blind hemifields thus demonstrating the integrity of the midbrain pupil pathways in these subjects and showing that these pathways are not responsible for the pupil response to the gratings. As a further control for light reflex effects, Barbur (1991) reports pupil responses to the appearance of a grating in which the mean luminance was set such that the bright areas of the grating were of same luminance as the background when the grating was not present i.e. no luminance increase occurred at any point on the retina. In addition, Barbur, Harlow and Sahraie (1992) report that pupil constriction can also be elicited by the onset of coherent movement in a dynamic random dot pattern. Replacing an achromatic grating with an isoluminant red-green grating also elicits a pupil grating response but of longer latency than that caused by the achromatic grating. Barbur, Thomson and Forsyth (1987) and Barbur, Harlow and Sahraie (1992) hypothesize that the onset of sudden changes in neural activity in the visual cortex is reflected in pupil constriction due to a transient weakening of inhibitory input to the pupillomotor nucleus.

3.2vii MODELLING OCULOMOTOR RESPONSES

Biomedical engineers have been attracted to the study of human pupil responses both by the availability of instruments allowing objective and non-invasive pupil recording and by the response of the pupil to easily-quantifiable stimuli. They have attempted to model the system according to control engineering principles (Webster, 1971). Pupillometry has allowed study of dynamic responses of the pupil both under steady-state conditions and in response to light and to near vision as part of the near vision triad. The development of dynamic IR devices to record accommodation and vergence of the eyes has allowed study of these components of the near vision triad to be studied in detail. For a useful review of methods and instrumentation used in studying and modelling the near vision response see Hung, Semmlow and Ciuffreda (1984). As pointed out in the review, the part played by pupil constriction in the near vision response has received very little attention and pupil constriction associated with near vision is considered by Hung, Semmlow and Ciuffreda (1984) to be essentially an open-loop response.

Simultaneous, continuous recording of accommodative, vergence and pupil responses using IR recording devices (O'Neill and Stark, 1968) have been used by Myers and Stark (1990) in an attempt to model the topology of the near response triad. To account for pupil behaviour, they had to postulate asymmetric drives to the pupil from accommodation and convergence although suggested that this could vary between individuals.

Tsuchiya, Ukai and Ishikawa (1989) have used a combined IR optometer and pupillometer to study the effects on pupil and accommodation of sustained near vision tasks. They report that the pupil may remain constricted following a near vision task even in the presence of a reduction in accommodative level. Also, they found that an accommodative response could be elicited in one subject without concomitant pupil constriction. The authors propose that monitoring pupillary changes may be of value in assessing the effects of near vision tasks on the visual system. Stark *et al* (1984) suggest that monitoring of dynamic accommodation and pupil responses can be useful in subjects with abnormal near vision responses.

Hung and Sun (1988) used an IR pupillometer to record pupil responses to change in light level at a range of velocities. They aimed to reveal the basic control properties of the system and were able to demonstrate ramp responses for low velocities of light intensity change and an increasing incidence of step responses as velocity increased. These results suggest that the system samples the change in light level over a short period of time and responds accordingly. Similar patterns of response have been demonstrated in accommodation (Hung and Ciuffreda, 1988) and vergence (Hung, Semmlow and Ciuffreda, 1986).

3.2viii USE OF THE PUPIL AS AN INDICATOR OF BIOLOGICAL AGE

The average age of the population of the western world is currently increasing. By the year 2050, the number of persons aged 65 and over is expected to be double what it is now (Werner, Peterzell and Scheetz, 1990). Hence, there is a great deal of interest both in the ageing process itself and in methods of monitoring the effects of ageing. Of particular interest is the measurement of biological as opposed to chronological age (Ludwig and Smoke, 1980) i.e. a person's age expressed in terms of health and function rather than simply as the number of years a person has been alive. Several aspects of vision are known to change predictably with age, one of which is pupil diameter. Sekuler (1982) regards pupil diameter as a promising indicator of biological aging due to its ease of measurement compared to other factors such as, for example, lenticular density. Sekuler and Owsley (1983) conclude that pupil size as a measure of ageing is attractive because it is non-invasive but point to its variability as a disadvantage. It has also been reported that light reflex latency increases with age (Feinberg and

Podolak, 1965, Hasegawa and Ishikawa, 1989) as does light reflex contraction time while light reflex amplitude decreases (Micieli *et al*, 1987).

A large pupil has always been associated with youth and vitality and a constricted pupil with age and boredom (Thompson, 1972). Further investigation may increase the usefulness of pupillometry in monitoring vitality levels as a measure of biological age.

CHAPTER 4

INSTRUMENTATION

4.1 THE CANON AUTOREF R1

The instrumentation in the laboratory is centred around a Canon Autoref R1, an infrared (IR) automated optometer introduced in 1981 by Canon Europa to provide objective measures of refractive error in a clinical setting. The Autoref R1 operates on the grating focus principle (see Matsumura *et al*, 1983) and its accuracy has been demonstrated in several studies (Matsumura *et al*, 1983, McBrien and Millodot, 1985). A reliable operating range of +/-15D sphere and +/-7D cylinder is claimed by the manufacturer and the optometer gives power readings in increments of 0.12D and cylinder axes in 1 degree steps. The Autoref R1 offers two particular advantages over other commercially-available automated IR optometers:

1) The subject whose refraction is being measured has, through a large semi-silvered mirror, an open, binocular field-of-view (18 x 50 deg) which reduces instrument myopia (Hennessy, 1975) and allows the selected fixation target to be viewed at any distance.

2) An internal IR camera provides an image of the eye being measured on a separate TV monitor screen which makes alignment of the instrument easy and allows the subject's fixation to be assessed visually by the operator.

These features make the instrument particularly useful as a research tool and several studies have made use of the Canon Autoref R1 to measure static accommodative level under a variety of conditions (Gilmartin and Bullimore, 1987, Winn *et al*, 1987, Ward, 1987). In order to extend the use of the Autoref R1 to the study of accommodation dynamics, it has been modified to allow continuous recording of accommodative state (Pugh and Winn, 1988, 1989, Winn *et al*, 1989).

4.1A MODIFICATION OF THE CANON AUTOREF R1 OPTOMETER FOR CONTINUOUS RECORDING OF ACCOMMODATION

In its original, static-measurement mode of operation, the Autoref R1 detects the focus of an IR grating projected onto the subject's retina in each of three meridians separated by 60 degrees. This is achieved by driving a set of focusing lenses along the optic axis of the instrument during a 0.2s measurement cycle (Matsumura *et al* 1983) and recording the level of IR light reflected back from the retina using 3 photodetectors (see figures 4.1 and 4.2). During the measurement cycle, the position of best focus for each meridian is marked by peaks in the level of light reflected from the eye and the instrument uses the *location* of the peak in each of the three meridians to compute the refraction (see Matsumura *et al*, 1983, McBrien and Millodot, 1985, see Pugh and Winn, 1988 for further details).

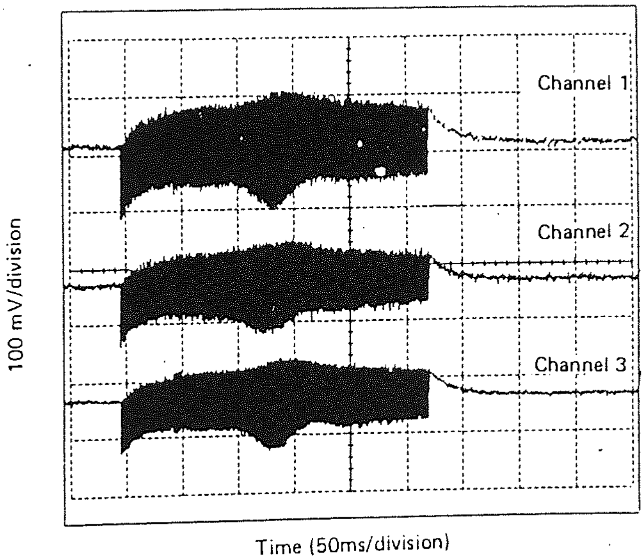


Figure 4.1 Output signals from the 3 photodetectors as the Canon Autoref R1 performs a static measurement of refractive error (from Pugh and Winn, 1988).

Pugh and Winn (1988, 1989) have modified the Autoref R1 for use as a continuously recording IR optometer by disabling the automatic drive to the focusing lenses and recording the voltage output from a single photodetector.

With the focusing lenses stationary, the photodetector output amplitude varies according to the refractive level of the eye and so can be used as a measure of accommodation. The modification involved disabling the lens drive mechanism to allow the focusing lenses to be manually adjusted using an installed gear wheel. The signal from each of the photodetectors is processed electronically and then the signal from one of the photodetectors (any one of the 3 can be used) is fed into a digital storage oscilloscope. Pugh and Winn (1988) have verified that the modified Autoref R1 is capable of measuring accommodation dynamics using both a model eye (see figure 4.4) and a human eye.

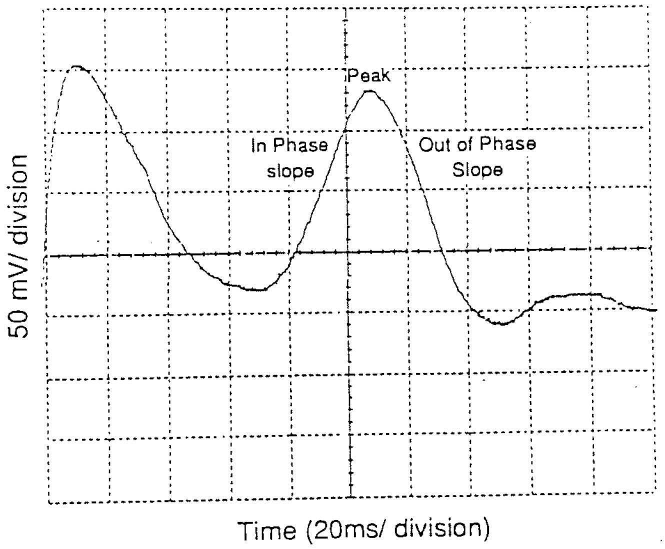


Figure 4.2 Output from a single photodiode as the Autoref R1 performs a static measurement of refractive error. The signal has been processed electronically (as it would be during continuous recording) to facilitate location of peak output and the in and out of phase slopes to each side of the peak (from Pugh and Winn, 1989).

In operation, an oscilloscope is used to view the photodetector output voltage and with an aligned subject fixating a steady target, the focusing lenses can be manually set to give just off peak photodetector output. Any change in the subject's accommodative level then produces a change in the voltage output from the photodetector and this output can be recorded as a measure of accommodative level (see figure 4.3). The change in voltage output will be either an increase or a decrease depending on the direction of accommodation and the side of peak output on which the focusing lenses are set. If the lenses are set to peak output, then a change in accommodation in either direction will always result in a decrease in voltage output and the instrument is then of no use in recording accommodation dynamics (see figure 4.4). A particular feature of the modification is that it has been carried out such that the instrument's ability to record static single-shot measures of refractive error remains unaltered and changing between the two modes of operation can be quickly and easily carried out (for further details of the modification see Pugh and Winn, 1988, 1989).

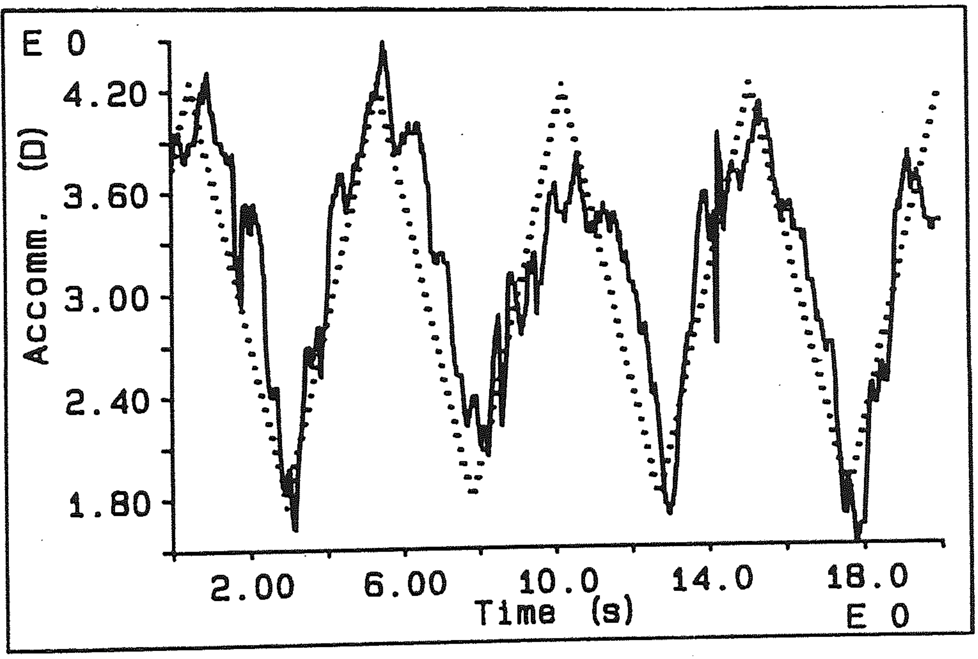


Figure 4.3 Continuous recording of accommodation using the modified Canon Autoref R1. The stimulus waveform is shown by the dotted plot and represents a 2.5D accommodative stimulus temporally modulated at 0.2Hz using a triangular waveform.

4.1Ai THE EFFECT OF PUPIL SIZE ON ACCOMMODATION MEASUREMENTS

All IR optometers have a limiting pupil diameter below which the signal returning from the eye becomes too attenuated to allow the reliable calculation of refractive error to take place. When this happens, the Autoref R1 is unable to accurately locate the peak in the photodetector output and is therefore unable to calculate refractive error. This limit is usually in the range 2.5-3.0mm and the manufacturers state that limiting pupil diameter is 2.9mm for the Autoref R1 in its static mode of

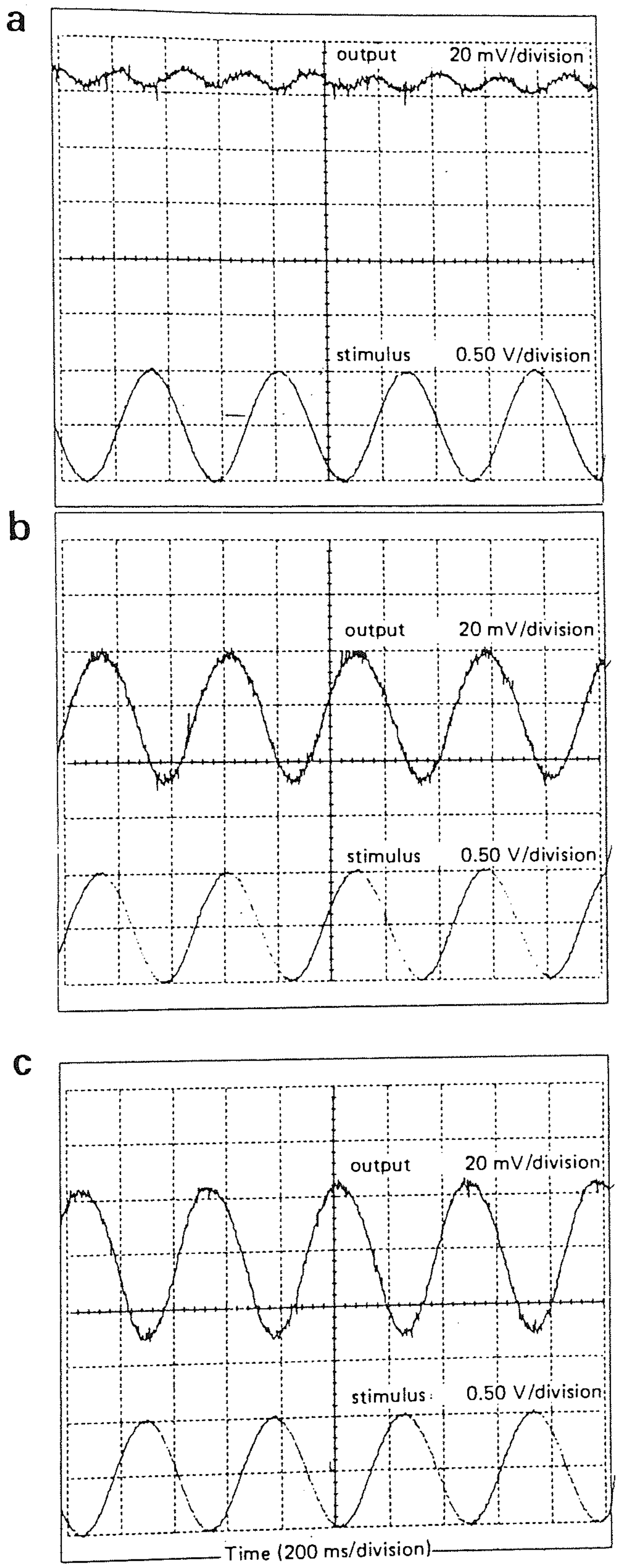


Figure 4.4 Output waveforms obtained using the modified Autoref R1 in continuous mode to record from a dynamic model eye driven at 2Hz to simulate periodic accommodative change. Results show the effect of setting the focusing lenses a) on the peak, b) on the positive slope giving response in phase with the stimulus and c) on the negative slope giving response 180 deg out of phase to the stimulus (from Pugh and Winn, 1988).

operation (Winn *et al*, 1989). With pupil diameters above 2.9mm, the instrument is pupil independent as it uses the *location* of the peak photodetector output to calculate refraction rather than signal amplitude. Winn *et al* (1989) have investigated the limiting pupil size for the modified optometer and demonstrated that for continuous recording of accommodation, a minimum apparent pupil diameter of 3.9mm is necessary and this seems to correspond to the area over which the optometer collects the light reflected from the retina. Below this pupil size, the amplitude of the photodetector output varies with pupil size and thus for continuous recording the instrument is no longer pupil-independent. This has important implications in the study of accommodation dynamics because it limits the demand of near vision tasks that can be imposed on subjects. However, providing pupil diameter can be maintained above 3.9mm by careful subject selection and manipulation of accommodative demand and lighting levels, then continuous recordings of accommodation can be made without the need to instil mydriatic drugs into the eye. The use of mydriatic drugs is undesirable because of their unpredictable effects on accommodation and because their use would rule out the simultaneous recording of pupil and accommodation responses.

4.2 THE HAMAMATSU C3160 PERCEPT SCOPE VIDEO AREA ANALYSER

To allow continuous recording of pupil size, a Hamamatsu C3160 Percept Scope Video Area Analyser has been coupled with the modified Autoref R1. The Percept Scope is a video measuring unit that measures the dimensions of objects 60 times per second (i.e. at mains voltage frequency) from their image taken with a TV camera. It was developed by Hamamatsu Photonics for use in factory automation and academic research and is designed to be compatible with a wide variety of cameras. Compatibilty with the IR sensitive TV camera inside the Autoref R1 has allowed simultaneous continuous recording of pupil size and accommodation responses by taking the signal from the TV camera through the Percept Scope before the signal continues on to the TV monitor.

Under IR illumination, the iris reflects a large amount of the incident light compared to that reflected back from the fundus through the pupil. The Percept Scope discriminates between the reflective iris and the apparently non-reflective pupil area. As pointed out by Lowenstein and Loewenfeld (1958), the amount of light reflected from the iris will depend on the level of iris pigmentation (i.e. eye colour) and so an instrument relying solely on the amplitude of reflected light would give differing pupil sizes according to iris colour, leading to errors of up to 60% (Lowenstein and Loewenfeld, 1958). This problem is overcome in the Percept Scope by utilising what the manufacturers describe as binary detection (see figure 4.5) rather than relying on reflected light amplitude. A variable threshold level must be set and the instrument then divides the image into those portions brighter than the threshold level (i.e. the iris) and those portions darker than the threshold level (i.e. the pupil).

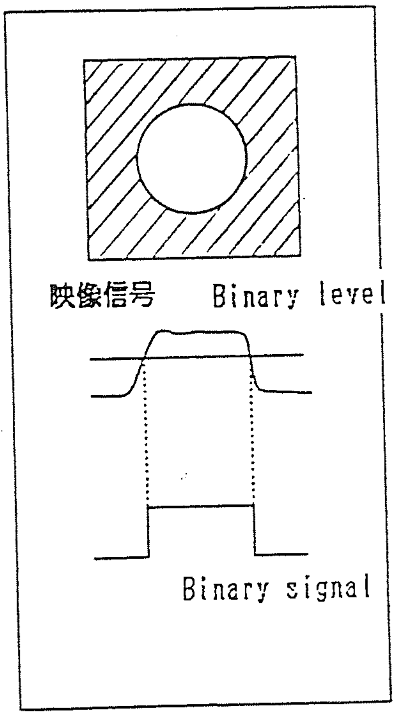


Figure 4.5 Schematic diagram representing binary detection of a video image to discriminate areas of above-threshold brightness from those of below-threshold brightness (taken from the handbook supplied with the Percept Scope).

4.2A ILLUMINATION

IR illumination of the eye for the TV camera inside the Autoref R1 is provided by two IR light sources which are separate to the IR system used for the measurement of refraction. The two light sources produce Purkinje images which can be seen on the TV monitor and the two bright 1st corneal Purkinje images are used to aid in alignment of the eye to facilitate accurate measurement of refraction. Unfortunately, these images interfere with the measurement of pupil size as the Percept Scope cannot distinguish them from the iris and so they had to be removed by covering over the light sources. To provide the IR illumination necessary for the camera, a separate illumination system was devised and installed by Dr Kazuhiko Ukai (Visiting Research Fellow in the Department of Vision Sciences at Aston University on an exchange arranged by The Royal Society and The Japanese Society for the Promotion of Science) using fibre optic cables to direct light to the eye from a standard slide projector. The ends of the cables are covered with Wratten 87 IR filter which transmits light only in the non-visible IR part of the light spectrum. A bundle of five cables was used, affixed to the optometer at an angle such that the Purkinje images appear on the superior part of the cornea, outside of the window selected for pupil diameter measurement. Although this illumination system is not ideal, later attempts to improve the illumination using more cables and varying configurations did not improve the results obtained. The Autoref R1 can still be aligned for accommodation measurement using the stationary alignment circle that appears in the centre of the TV monitor and by ensuring steady subject fixation.

4.2B SETUP PROGRAMME

As the Percept Scope is intended for a variety of uses, a number of setup parameters must be input each time the instrument is used for pupil measurement. These set parameters such as the type of measurement to be made and the method of discrimination to be used. To simplify this procedure, a computer program was written by Dr Ukai on an Epson XT IBM-clone desktop computer and running this program allows the Percept Scope to be set to the parameters required for pupil measurement in a very short time.

4.2C OPERATION OF THE PERCEPT SCOPE

In operation, once all the required parameters have been set, a 'window' appears on the TV monitor screen connected to the Autoref R1. The window can be set to any desired size and delineates the area over which measurement takes place. Within the window, the instrument discriminates between the reflective iris which has brightness above the set threshold level and the non-reflective pupil which has brightness below the set threshold level. On the screen, areas of below threshold brightness are indicated by coalescence of the screen pixels into an opaque white area. The adjustable threshold level must be set to give as good a level of discrimination of the pupil border as possible which can be seen both on the TV monitor (see photo figure 4.6) where the pupil appears filled white as the screen pixels coalesce (ideally with a clean border at the pupil margin), and also on the oscilloscope where a correct threshold level gives a clean signal with low noise level . A measurement is given in figures on the monitor screen and is the *maximum* width of the filled white area, i.e. the pupil, in pixels.

4.2D CALIBRATION

The Percept Scope records the dimension selected for measurement (width, height or area) in screen pixel units. Width measurement was selected to record horizontal pupil diameter because it is the least likely to be influenced by lid artefacts or small eye movements and allowed the Purkinje images caused by the illumination system to be positioned above the measurement window. It is generally considered safe to assume that the pupil is circular and its reactions symmetrical, and that therefore measurement of horizontal diameter is adequate to record pupil size and responses (Terry, Guillon and Chissadon, 1992).

Figure 4.6 Photo showing the appearance on the TV monitor with the Percept Scope threshold optimally set for the measurement of pupil diameter.

An initial task was to calibrate the instrument to read in mm rather than pixels. To achieve this, the screen magnification factor had to be found and so a 300mm ruler was attached to the headrest of the optometer and the ruler was imaged on the monitor screen. Several length increments were measured from the image on the screen with electronic calipers (with a resolution of 0.01mm) and compared to actual length giving a result of 8.2X magnification (i.e. a 10cm increment on the ruler measured 82cm when imaged on the screen). Then, using the Percept Scope, a range of measurement window widths was created on the screen and the Percept Scope threshold level set such that a measure of the entire window width was given in the form of a readout in pixels on the screen. The pixel values were recorded and plotted against window size in mm (divided by 8.2) measured from the screen with the electronic calipers (see figure 4.7). This gave a conversion factor of 52.38 pixels per mm actual size which was entered into the Percept Scope to allow direct readout on the screen of pupil diameter in mm. It should be noted that this calibration affects only the figures displayed on the TV monitor and has no effect on the output voltage. As the instrument resolution is one pixel unit, the maximum resolution possible for pupil diameter is thus slightly better than 0.02mm.

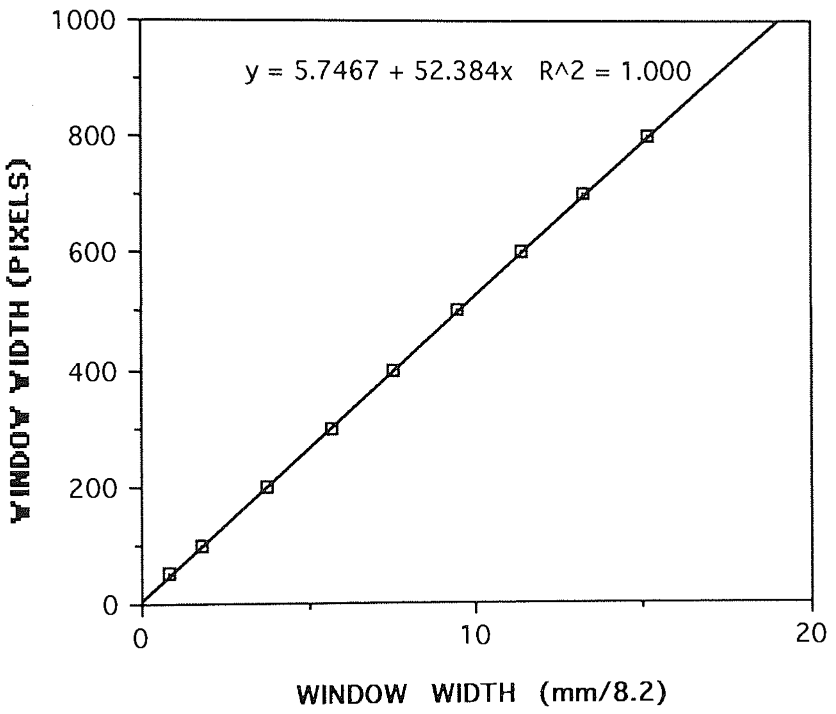


Figure 4.7 1st calibration graph for the Percept Scope.

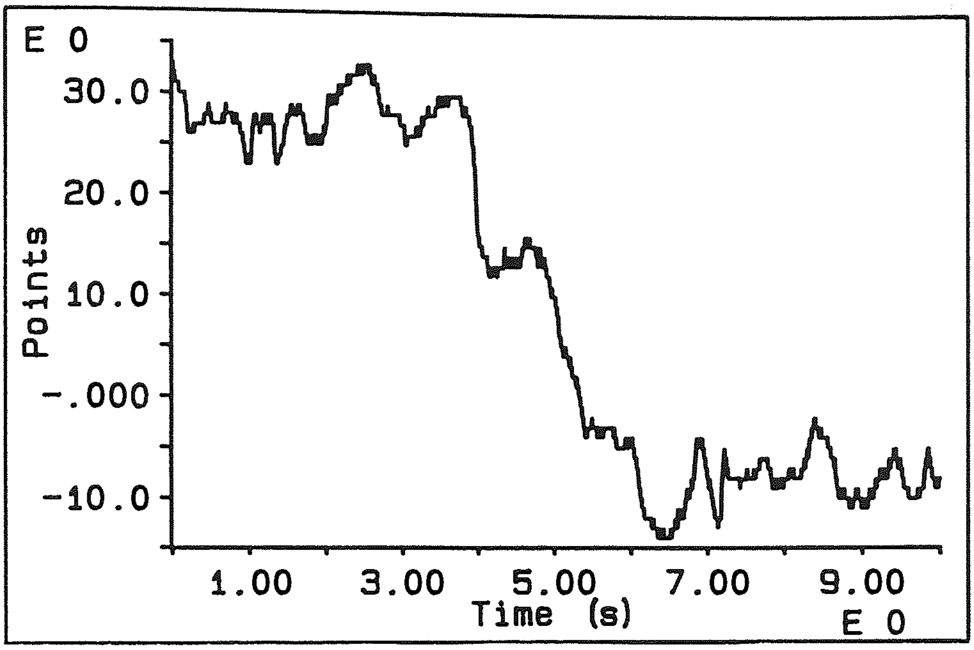
4.3 ANCILLARY EQUIPMENT

The continuous voltage outputs from the modified Autoref R1 and from the Percept Scope are fed into two channels of a Gould 1604 four-channel digital storage oscilloscope via an IEEE-488 interface bus. The outputs are displayed in analogue form as traces on the oscilloscope screen during experiments and, when required, stored digitally in one of the oscilloscope's 50 memories. The oscilloscope is controlled by, and data later transferred to, an Epson XT IBM-clone desktop computer using *Asystant* software which has been customised by Professor John Pugh of Glasgow Polytechnic to allow the instantaneous and simultaneous recording of the traces displayed on 1, 2 or 3 oscilloscope channels. Recorded traces can then be analysed and displayed utilising the Asystant functions and plotted using an on-line Hewlett-Packard ColorPro plotter.

The oscilloscope screen can be considered as a matrix of points, 1024 points across and 248 points high. When a displayed trace is recorded, it enters the memory as a stream of 1024 points each with a value of between -124 and +124 (zero being the horizontal midline of the screen). The gain and sampling rate of the recording varies according to the sensitivity and time base set on the oscilloscope. As accommodation and pupil outputs are recorded as a stream of point values, further calibrations must take place to convert the traces to accommodation level in dioptres (D) and pupil diameter in mm.

4.3A ACCOMMODATION CALIBRATION

To calibrate accommodation, a step response of known static accommodative magnitude must be continuously recorded. Using the Autoref R1 in its original mode of operation, static measures of accommodative level are taken with the subject viewing targets set at two distances first at far and then at near, aligned along the optic axis of the subject. 5 readings are taken for each fixation distance and averaged to give mean sphere power + 1/2 mean cylinder power. Then, with the instrument switched to continuous recording, the subject is asked to fixate first the far and then the near target and the voltage output recorded (see figure 4.8) and transferred to the computer for analysis. Averaging the point levels recorded with the subject fixating at far and at near and calculating the difference between the two gives the change in point level for a known dioptric step and therefore simple division yields a points per dioptre conversion factor. Recorded accommodation traces can thus be converted to change in accommodation



Mean point level of first 2 secs (far fixation)	27.02
Mean point level of last 2 secs (near fixation)	-7.65
Change in point level	34.67
Dioptric step from far to near	2.35D
Conversion factor	34.67/2.35 **=14.75 points/Dioptre**

Figure 4.8 Continuous recording of a step change from far to near for accommodation calibration purposes and calculation of conversion factor.

although not absolute level. However, for most purposes absolute accommodative level is not critical.

4.3B PUPIL CALIBRATION

For pupil recordings, a further calibration had to be made to convert the recorded oscilloscope traces to diameter in mm. To achieve this, a range of window widths was again created on the monitor and with the discrimination threshold set to measure the entire window width, the width of the window in mm shown on the TV monitor was recorded and the corresponding trace on the oscilloscope stored, transferred to the computer and the average point level determined and recorded. As oscilloscope screen zero is the horizontal midline, a zero width was first set up and the corresponding oscilloscope trace set at the bottom of the oscilloscope screen. The negative point value corresponding to zero width was then subtracted from all subsequent point levels making them all positive with the base of the screen equating to 0mm pupil diameter. Plotting the scope screen point level (minus the zero recorded) against window width readout in mm gave a points per mm calibration (see figure 4.9 below). This value of 22.683 points per mm was used in all subsequent recordings with the necesssary zero level being recorded and subtracted from all point values each time. The use of a zero level in each set of recordings allows the calculation of absolute pupil diameter. It should be noted that this calibration factor is only correct when the gain on the oscilloscope is set to 0.5 volts per division (V/D) for the channel used in pupil recording. This gain allows a range of around 8mm pupil change to be recorded which is more than adequate to record human pupil responses. As the previous value of 50 pixels/mm is now compressed to 22 points/mm, resolution is correspondingly reduced from 0.02mm to approximately 0.04mm.

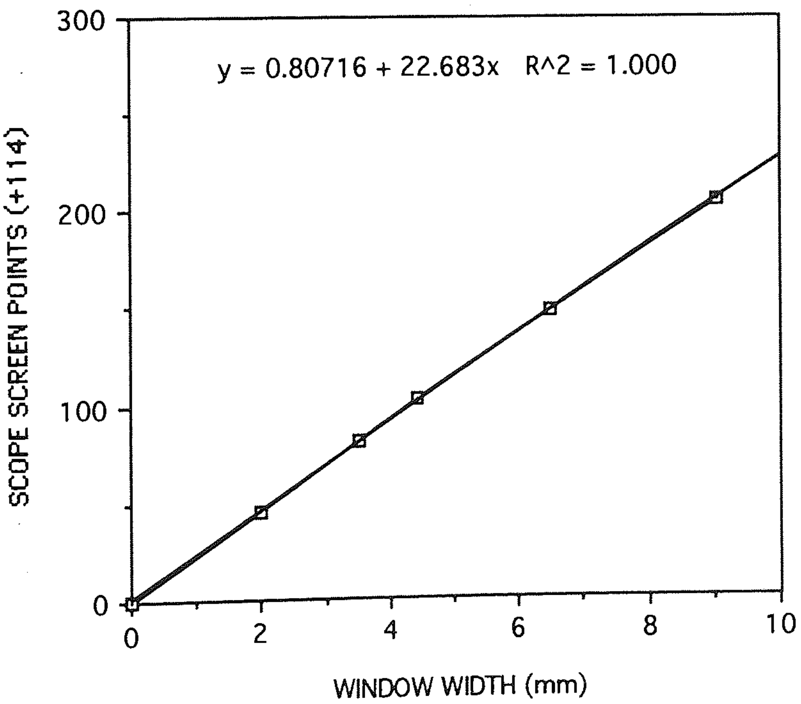


Figure 4.9 2nd pupil calibration graph.

4.4 SUMMARY

The equipment described allows simultaneous, continuous recording of accommodation and pupil responses to a variety of stimuli (see figure 4.10 for schematic diagram of the apparatus). Large quantities of data can be collected in a relatively short time and stored for later analysis. In some experiments, a third oscilloscope channel is used to record stimulus waveform or mark events along with pupil and accommodation responses. During continuous accommodation recordings, subjects must be kept aligned and as steady as possible to avoid movement artefacts. This is achieved using a chin rest, head restraint and dental bite, individual dental bites being made for each subject using dental wax. To keep the instrument free from any vibrations, the headrest has been separated from the body of the optometer and firmly attached to the wall and laboratory bench. As the system allows viewing of the accommodation and pupil response traces on the oscilloscope during experiments, any data containing unwanted artefacts can be rejected.

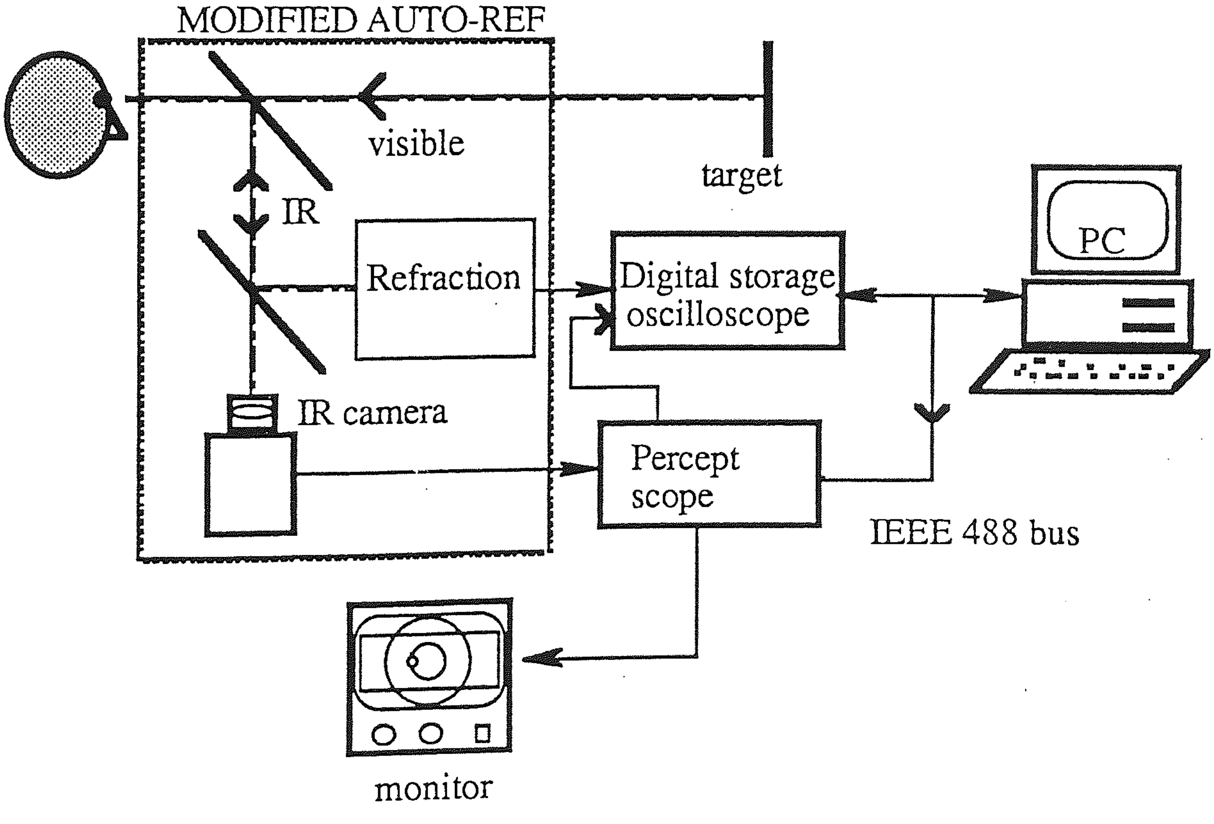


Figure 4.10 Schematic diagram of the laboratory apparatus (drawn by Dr Ukai).

SUPPORTING PUBLICATIONS

Phillips, N. J., Winn, B., Gilmartin, B. and Ukai, K. Simultaneous recording of accommodation and pupil responses: some preliminary investigations. *Ophthal. Physiol. Opt.* **10**, 412 (1990).

CHAPTER 5

PUPIL AFTER-EFFECTS FOLLOWING A NEAR VISION TASK DEMONSTRATED USING QUASI-STATIC MEASUREMENT OF PUPIL AND ACCOMMODATION RESPONSES

5.1 INTRODUCTION

In the absence of a visual stimulus, the accommodation system assumes a resting position, not at infinity focus but at an intermediate position which varies according to the subject and the measurement technique used. This is known as the resting focus of accommodation or tonic accommodation (TA) (Heath, 1956, Westheimer, 1957, Leibowitz and Owens, 1975a, 1975b). TA can be measured in darkness, in a bright empty field or using a 0.5mm pinhole to produce a large depth-of-focus. All three conditions result in open-loop accommodation i.e. there is no feedback to accommodation as the level of accommodation does not affect the quality of the retinal image. Values of TA normally fall in the range -0.5 to -2D (Heath, 1956) although Leibowitz and Owens (1978) recorded values ranging from +0.50D to -4.00D with a mean of 1.52D and a standard deviation of 0.77D using a laser optometer. It has been proposed that TA represents in an individual the resting balance point of the parasympathetic and sympathetic components of the autonomic nervous system supplying the ciliary muscle (Toates, 1972). McBrien and Millodot (1987) have shown that average TA levels differ between refractive groups.

A number of studies have demonstrated that a sustained near vision task can induce transient changes in post-task accommodative state (Ebenholtz, 1983, 1991, Erlich, 1987, Fisher, Ciuffreda and Levine, 1987, McBrien and Millodot, 1988, Gilmartin and Bullimore, 1987, 1991), sometimes known as accommodative hysteresis, which are thought to represent adaptation of the accommodation mechanism to the dioptric demand of the task. The origin of accommodative adaptation following a near vision task is uncertain and the size and duration of the effects varies between subjects, between refractive groups and according to the stimulus and measurement system used. Adaptational effects can be recorded either as a change in TA level or as a slowing of the post-task regression of accommodation to pre-task TA level following a near vision task and are often assessed by measuring post-task accommodation levels under conditions of darkness (Ebenholtz, 1983, 1991, Gilmartin and Bullimore, 1987, 1991, McBrien and Millodot, 1988, Rosenfield and Gilmartin, 1988).

Some studies have reported that adaptation effects on TA may be masked in darkness (Schor, Kotulak and Tsuetaki, 1986, Wolfe and O'Connel, 1987) and only become manifest under the presence of a light stimulus. Wolfe and O'Connel (1987) suggested that the accommodative system rests only in darkness and maintains a more vigilant state when any light is present.

Adaptation effects have also been demonstrated in the vergence system (Owens and Leibowitz, 1980, Schor, 1988). Owens and Leibowitz (1980) showed that the adaptation positions of accommodation and vergence are different and that therefore the adaptation of the two systems following a near vision task is relatively independent.

The reported time course of adaptive effects on accommodation and vergence varies widely. Wolf, Ciuffreda and Jacobs (1987) report that changes in TA and tonic vergence are transient and decay back to baseline levels within 3 minutes following a 45 minute reading task at -5D vergence. Gilmartin and Bullimore (1987) recorded post-task changes in TA levels in 15 emmetropes following a 10 minute counting task located at -5D and showed that pre-task levels were reached within around 30s in darkness. McBrien and Millodot (1988) used a similar methodology and showed that post-task changes in TA vary according to refractive group. They reported increased TA level lasting for more than 15 minutes in late onset myopes (LOMs- subjects whose myopia first developed after the age of 15 years and whose myopia may have at least in part an environmental aetiology) whereas little effect occurred with the other refractive groups. Ebenholtz (1983) demonstrated shifts in TA lasting for more than 16 minutes in emmetropes following an 8 minute near task and Tan and O'Leary (1986) report adaptive changes in TA lasting for over 6 hours.

Pupil constriction accompanying near fixation is a well established phenomenon (Hung, Semmlow and Ciuffreda, 1984, Jones, 1989, Myers and Stark, 1990) and it would be reasonable to infer that any adaptation effects in accommodation or vergence might have a corollary in adaptation of pupil size. To date, only one study (Tsuchiya, Ukai and Ishikawa, 1989) has investigated the possibility of pupil adaptation following a near vision task. Tsuchiya, Ukai and Ishikawa (1989) report that following a strong (up to 10D), short (typically 2 minutes) near vision task, a proportion of subjects demonstrate retained pupillary constriction, lasting in some cases for more than 15 minutes. They recorded accommodation and pupil responses by a 'quasistatic' method (Ukai, Ishii and Ishikawa, 1986) and demonstrated that some degree of pupil constriction was retained following the near vision task in 33% of their subjects (8 out of 24), while adaptive changes in TA levels were found in only 17%. Changes in pupil and TA together were found in only 8% of subjects and therefore adaptation of the two systems was usually independent. Tsuchiya, Ukai and Ishikawa (1989) called the retention of pupillary constriction following a near vision task an after-effect rather than adaptation, as adaptation did not seem to them to possess '*active meaning*' when applied to the pupil. They carried out an additional experiment on one subject and concluded that the pupil after-effect is not masked by darkness despite the presence of a strong luminance drive to the pupil.

This experiment aimed to further investigate the incidence and time course of pupil after-effects following a near vision task. Of particular interest was the presence or absence of masking of any after-effect in darkness given the additional presence of the luminance drive to the pupil. Pupil diameter and accommodative level were recorded simultaneously every 3s by a quasistatic method under three experimental conditions.

5.2 METHODS

5 visually normal subjects were used in the study, 4 were emmetropic and 1 was an early onset myope of -5D who was corrected with a soft contact lens. Details are shown in table 5.1.

SUBJECT	AGE	SEX	IRIS COLOUR	REFRACTION
KY	36	F	DARK BROWN	EMM
KZ	38	M	DARK BROWN	EOM (-5D)
NP	28	M	BROWN	EMM
FE	28	M	BLUE	EMM
RD	24	M	GREEN	EMM

Table 5.1 Details of subjects used in the study (EMM=emmetrope, EOM=early -onset myope).

Accommodation was measured using a modified Canon Autoref R1 automated optometer in static single-shot mode (see Chapter 4 for details). The output from one of the three photodiodes was displayed on a four channel digital storage oscilloscope (see figure 4.2 in Chapter 4) and then transferred to an Epson PCe-XT IBM-clone desktop computer. A Hamamatsu C3160 Percept Scope Video Area Analyser connected to the TV camera of the optometer was used to measure horizontal pupil diameter. Output from the Percept Scope was also displayed on the oscilloscope and then transferred to the computer. A measurement programme written by Dr Ukai for the computer was used to automatically calculate refractive level from the location of the peak in the optometer photodiode output and pupil diameter from the Percept Scope output and store the two sets of data. Accommodative level and pupil diameter readings were made and stored every 3 seconds, the time needed for the calculation and storage procedures to take place. A pre-set trigger level on the oscilloscope prevented erroneous data (e.g. blinks) from being transferred to the computer. Use of the optometer in its static mode of operation was ideal for this experiment as it allows accommodation recording with pupil diameters down to 2.9mm and was suitable for the long time course of the experiment. A photodiode was connected to a third channel of the oscilloscope and served to indicate the light level and mark the points during experiments when the light level changed. During experiments, subjects were kept steady using chin rest and dental bite. All recordings were made from the RE only and the LE was occluded.

Each subject took part in three measurement conditions consisting of recording for 2 minutes pre-task, 2 minutes during the task and 10 minutes post-task. A minimum of 24hrs was allowed for each subject between trials. The three measurement conditions were as follows:

A (Near-Far)

Pre-task: the subject viewed a far target consisting of a black dot of angular subtense 0.5 degrees surrounded by a light (32 cdm^{-2}) area (5 degree square) located at the TA position of the subject (previously measured with the optometer after 10 minutes in darkness).

Task: the subject viewed for 2 minutes a maltese cross located at approximately 3D (again determined using the optometer) above TA level. The luminance and subtense of the near target was the same as the pre-task far target.

Post-task: identical to pre-task.

B (Near-Dark)

Pre- task: the subject was in darkness with a dim green LED located at the TA position acting as a fixation target (it had previously been ascertained that the green LED did not act as a stimulus to accommodation- see Owens, 1991). Prior to this experimental condition, subjects were dark adapted for 10 minutes.

Task: the subject viewed for 2 minutes the maltese cross target (luminance 32cdm^{-2}) at 3D above TA.

Post-task: identical to pre-task.

C (Light-Far)

Pre-task: the subject viewed for 2 minutes the far target (as in condition A pre-task, luminance 32cdm^{-2}) at TA position.

Task: viewing the same far target at TA position but with an increase in luminance to 50cdm^{-2}, designed to give a similar amplitude of pupil constriction as the near task it replaced.

Post-task: identical to pre-task.

5.3 RESULTS

The experimental conditions were designed to give approximately equal amplitudes of pupil constriction during the task in all three conditions and an accommodative response only in conditions A (Near-Far) and B (Near-Dark). The averaged sizes of the responses are summarised in table 5.2.

PUPIL in mm	NEAR-FAR	NEAR-DARK	LIGHT-FAR
PRE-TASK	5.79(SD 0.52)	6.53(SD 0.53)	5.65(SD 0.64)
TASK	3.83(SD 0.74)	4.24(SD 0.78)	4.01(SD 0.58)
DIFFERENCE	1.96(SD 0.43)	2.29(SD 0.73)	1.64(SD 0.39)
ACC in D			
PRE-TASK	1.16(SD 0.33)	2.02(SD 0.65)	1.05(SD 0.36)
TASK	3.85(SD 0.39)	4.20(SD 0.58)	0.96(SD 0.39)
DIFFERENCE	2.70(SD 0.16)	2.18(SD 0.69)	-0.10(SD 0.11)

Table 5.2 Mean amplitude and SD of the responses induced in each condition.

The data shown in figure 1 a), 1 b) and 1 c) is for subject KY and represents two complete sets of the three experimental trials to demonstrate the repeatability of the data. In the figures accommodative level in dioptres and horizontal pupil diameter in mm have been averaged over 30s periods post-task (0 to 10 mins) and over the entire 2 minute pre- (-4 to -2 mins) and inter-task (-2 to 0 mins) periods.

The results were essentially similar for all subjects, representative data for subject KY is shown in figure 5.1 a), b) and c). All 5 subjects demonstrated retained pupillary constriction following the near task in condition A (Near-Far) which did not occur following pupil constriction induced by an increase in light level in condition C (Light-Far). In 4 subjects the after-effect was masked completely in the post-task darkness of condition B (Near-Dark) and in one subject (FE see figure 5.2) the masking was partial.

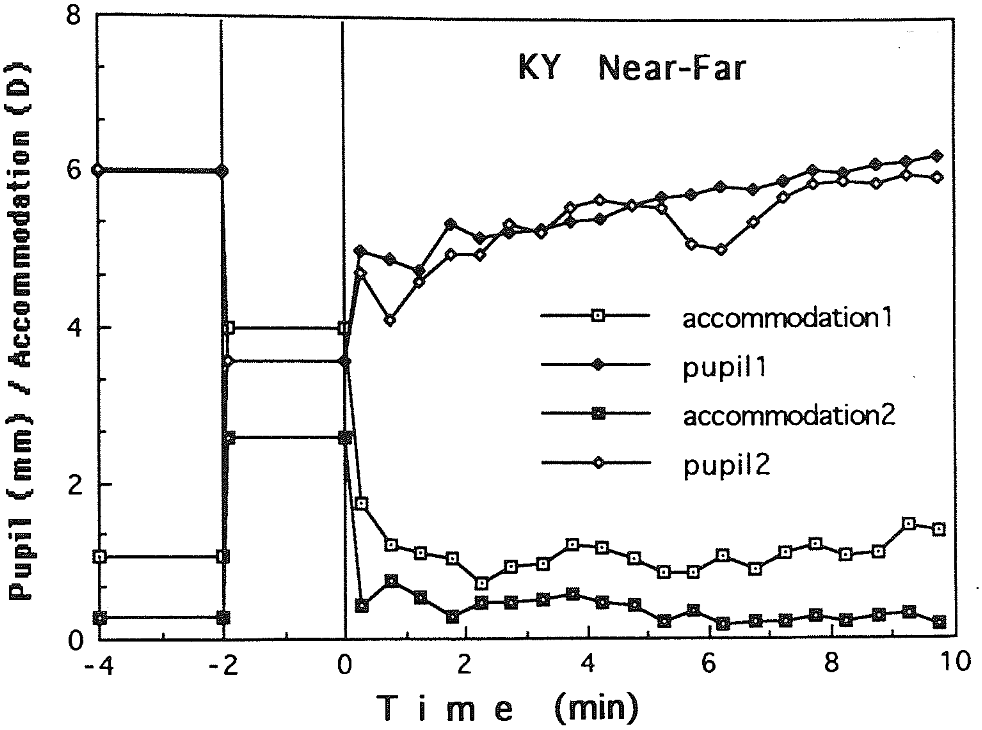


Figure 5.1a) Condition A (Near-Far). The near task induced an increase in accommodative level of just under 3D and pupil constriction of around 2.5mm. Following the task, accommodation regressed to pre-task level within 45s, whereas the pupil redilated slowly, taking around 8 minutes to reach pre-task levels i.e. a pupil after-effect is demonstrated in the absence of any lasting adaptation in accommodation.

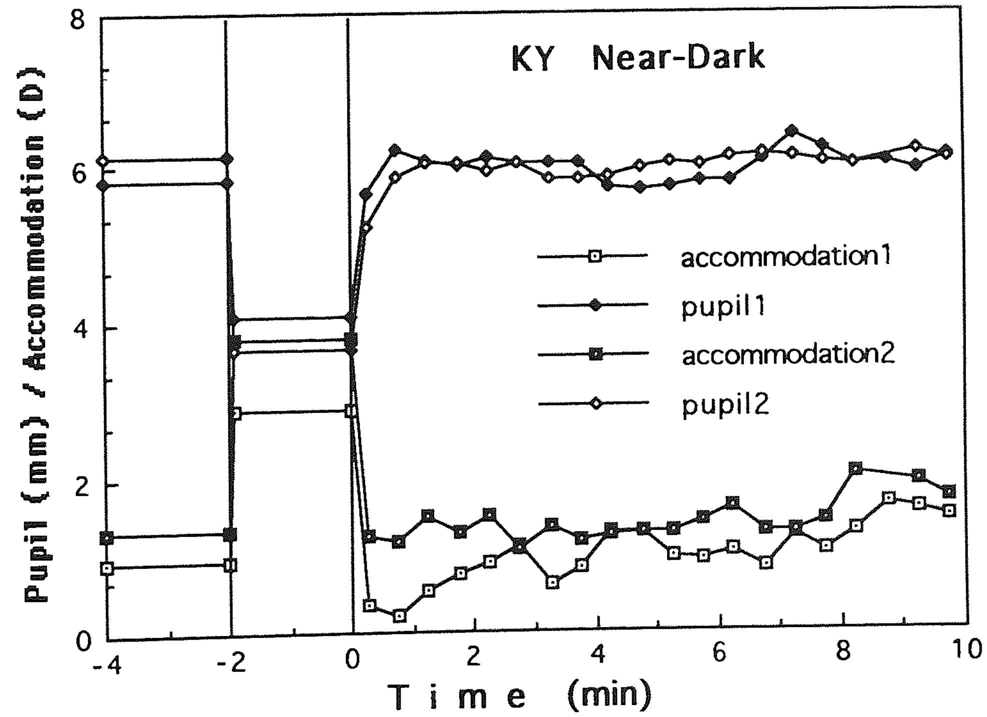


Figure 5.1 b) Condition B (Near-dark). During the task accommodative change and pupil constriction were of similar amplitudes to those recorded in condition A (Near-Far) (see figure 5.1a). Following the task, both pupil diameter and accommodation returned to pre-task levels within 30s i.e. the pupil after effect is masked by darkness due to the rapid response to the luminance change and no adaptation of accommodation can be demonstrated.

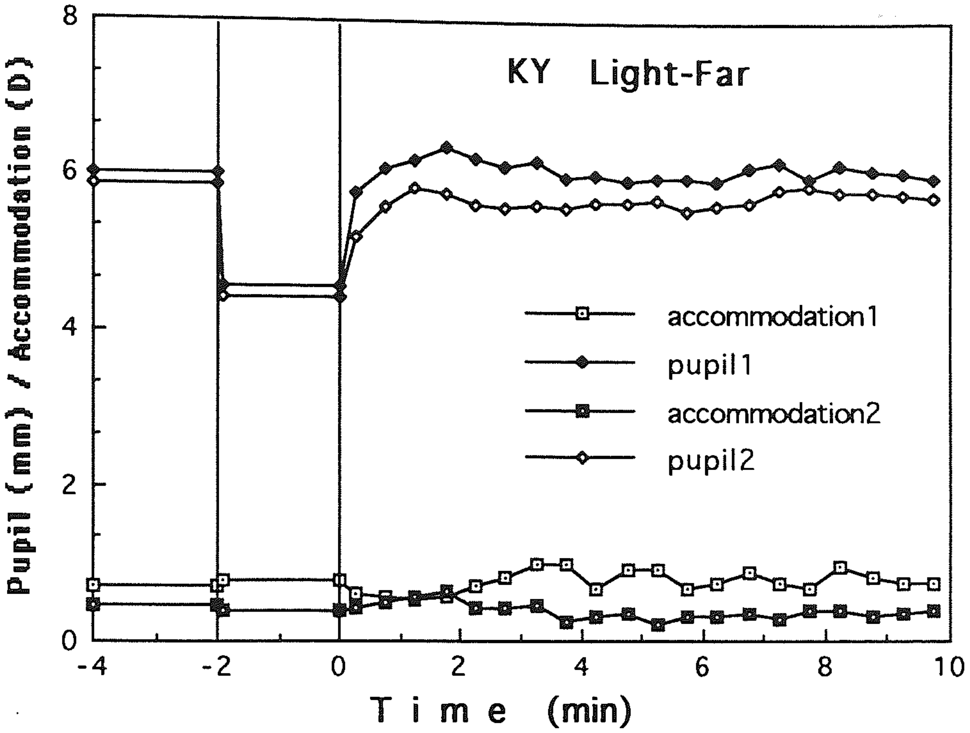


Figure 5.1c) C (Light-Far). Due to pupillary escape (Sun and Stark, 1983), the averaged pupillary constriction (around 1.5mm) in this condition was less than that induced by the near task. Accommodation level remained unchanged throughout this experimental trial. Following the light increment task, the pupil redilated quickly to pre-task levels i.e. no pupil after effect was demonstrated.

Figure 5.2a), b) and c) shows the data obtained under the three measurement conditions for subject FE and shows partial masking only of the pupil after-effect in darkness (see figure 5.2b). Adaptation of accommodation is also demonstrated in darkness for this subject, accommodation taking around 2 minutes to return to pre-task level.

Figure 5.3 a), b) and c) shows the mean data for the 5 subjects and has been normalised to percentage values- 100% represents pre-task values and 0% represents inter-task values of accommodative level and pupil diameter. Thus 100% recovery means a return to pre-task values. Error bars represent +/-1SD of

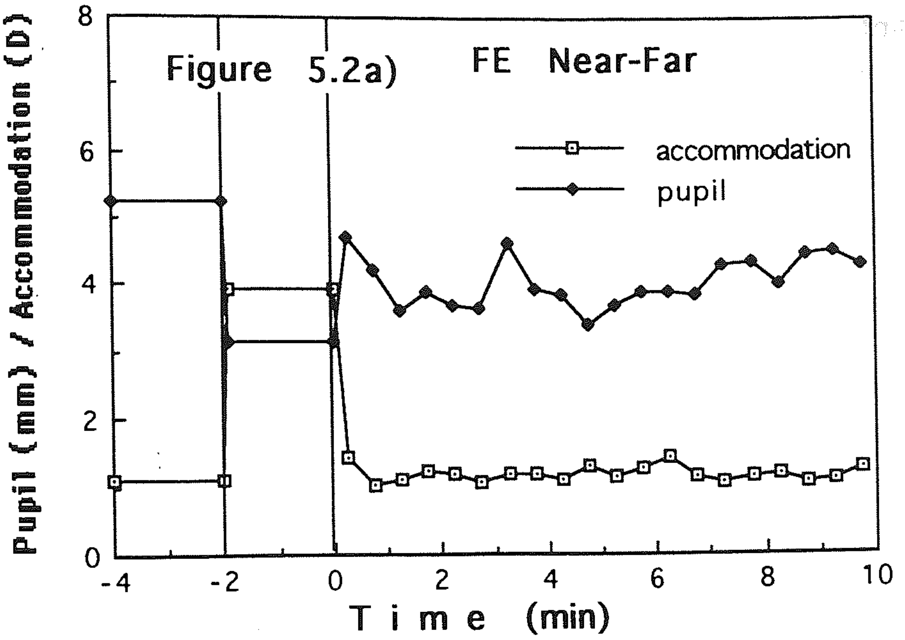


Figure 5.2a)
FE Near-Far
accommodation
pupil
Pupil (mm) / Accommodation (D)
0
2
4
6
8
-4
-2
0
2
4
6
8
10
T i m e (min)

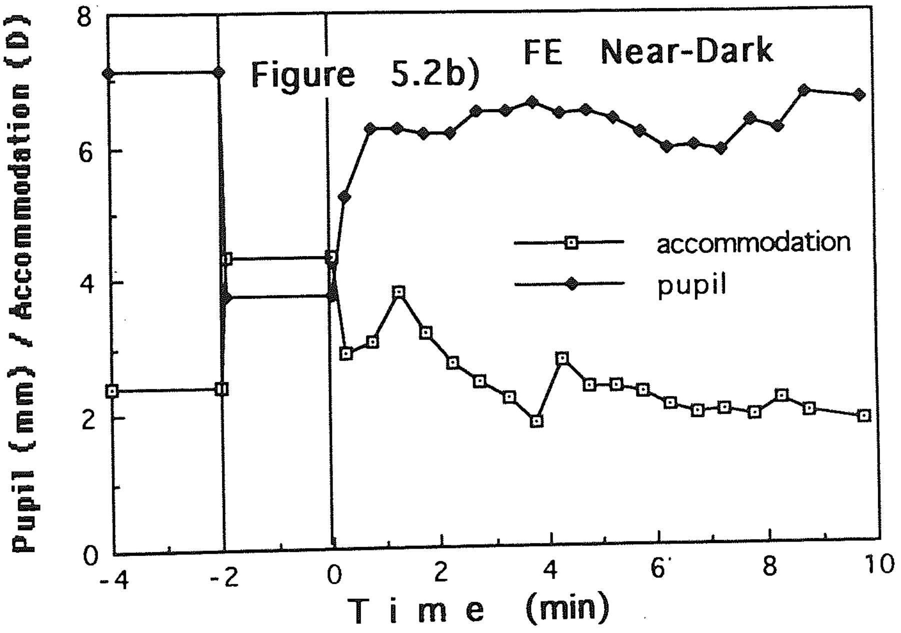


Figure 5.2b)
FE Near-Dark
accommodation
pupil
Pupil (mm) / Accommodation (D)
0
2
4
6
8
-4
-2
0
2
4
6
8
10
T i m e (min)

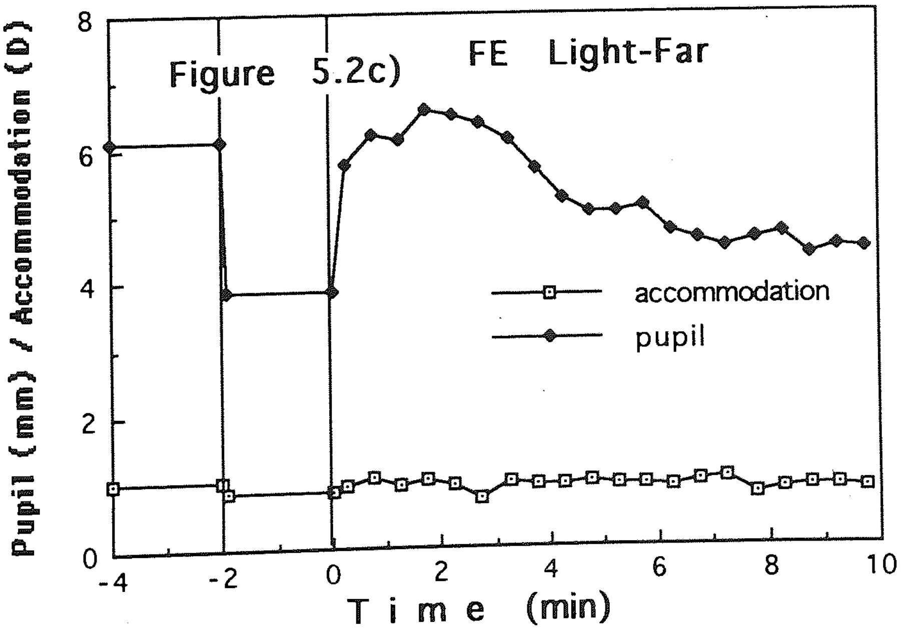


Figure 5.2c)
FE Light-Far
accommodation
pupil
Pupil (mm) / Accommodation (D)
0
2
4
6
8
-4
-2
0
2
4
6
8
10
T i m e (min)

the mean. Figure 5.3a) shows the mean pupil after-effect in condition A (Near-Far) which is masked in darkness in condition B (Near-Dark). In figure 5.3b) it can be seen that no pupil after-effect is induced by the pupil constriction caused by the light stimulus (Light-Far) in the absence of any accommodative change. Figure 5.3c) shows the lack of any overall accommodative adaptation demonstrated.

All subjects showed variations in pupil diameter during the post task recording period (see figure 5.4). These reconstrictions were not linked to changes in accommodative or light level and may represent the effects of fatigue (Lowenstein Feinberg and Loewenfeld, 1963).

5.4 DISCUSSION

The results of this experiment confirm the findings of Tsuchiya, Ukai and Ishikawa (1989) that pupil constriction may be retained following a near vision task. There are two alternative hypotheses to explain this pupil after-effect:

1: The retained pupil constriction following the near vision task in condition A represents adaptation of the pupil to the demand of the near vision task. This adaptation can take place in the absence of any lasting accommodative adaptation and lasts for several minutes. The absence of pupil adaptation in condition B shows that it is masked by darkness in a manner analogous to accommodative adaptation (Schor, Kotulak and Tsuetaki, 1986). The absence of adaptation in condition C shows that pupil adaptation is not simply a result of constriction itself, but requires the presence of active accommodative effort.

2: The pupil constriction following the near vision task in condition A is retained because following the task there is insufficient stimulus to drive pupil redilation. In the absence of any luminance change and in an empty-field condition, the pupil may have no stimulus to change. This would suggest that the change in

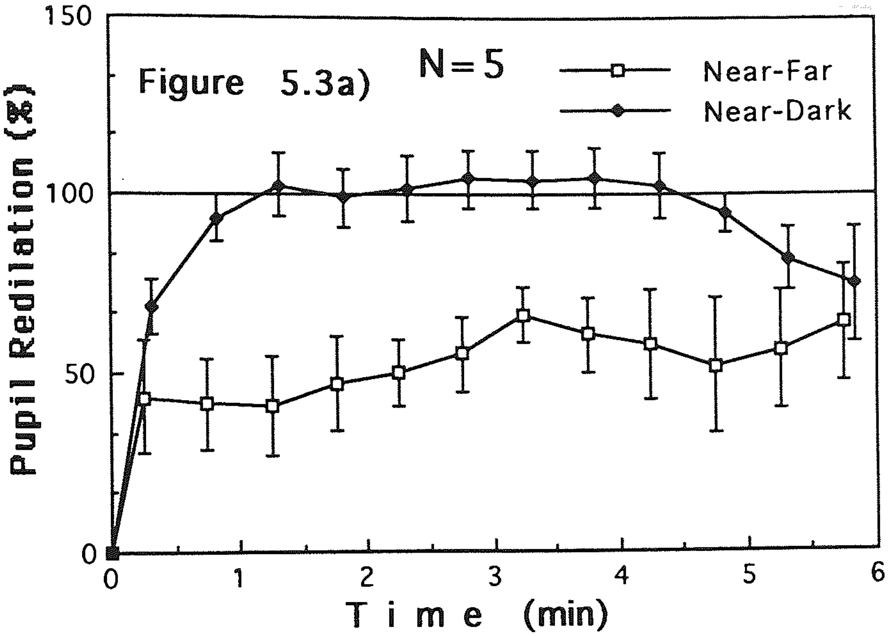


Figure 5.3a)

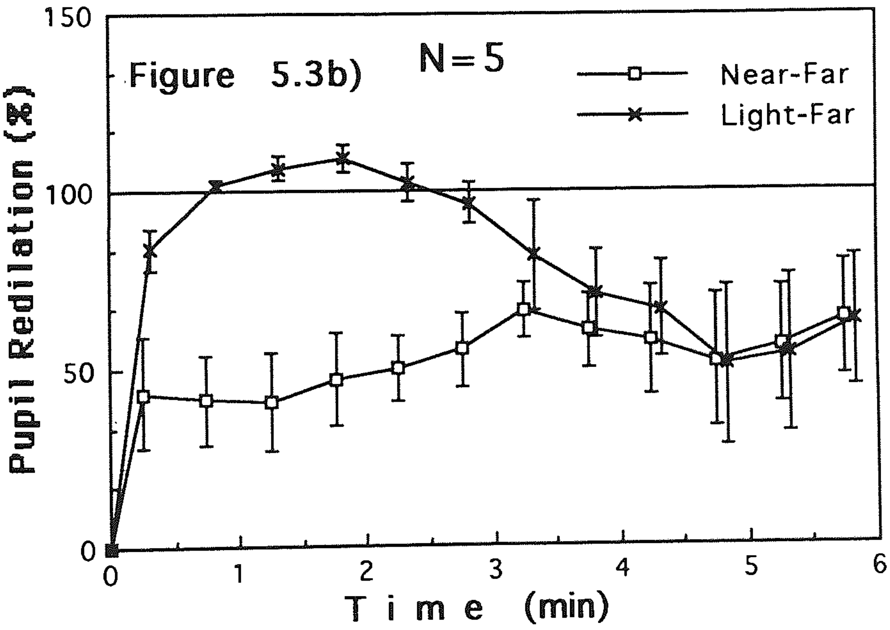


Figure 5.3b)

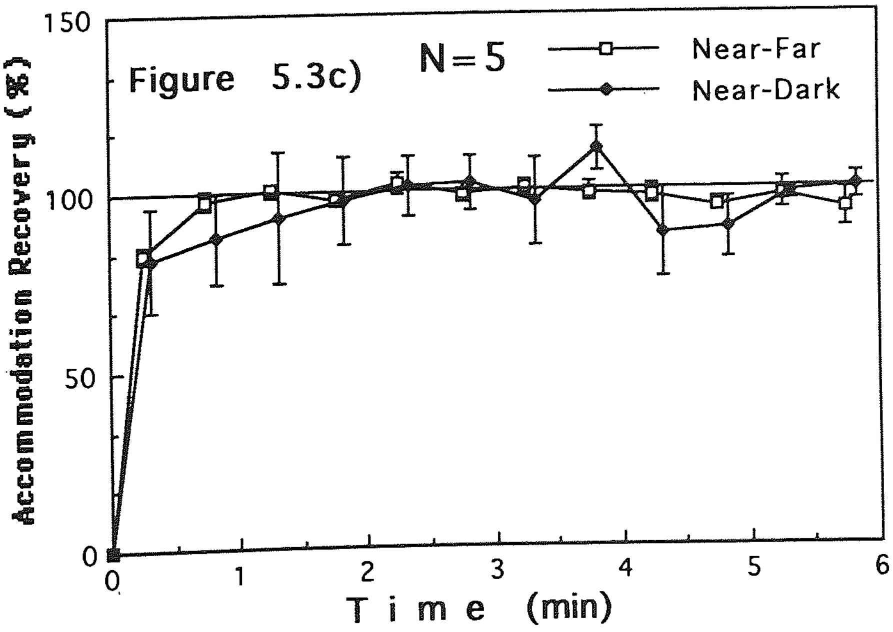


Figure 5.3c)

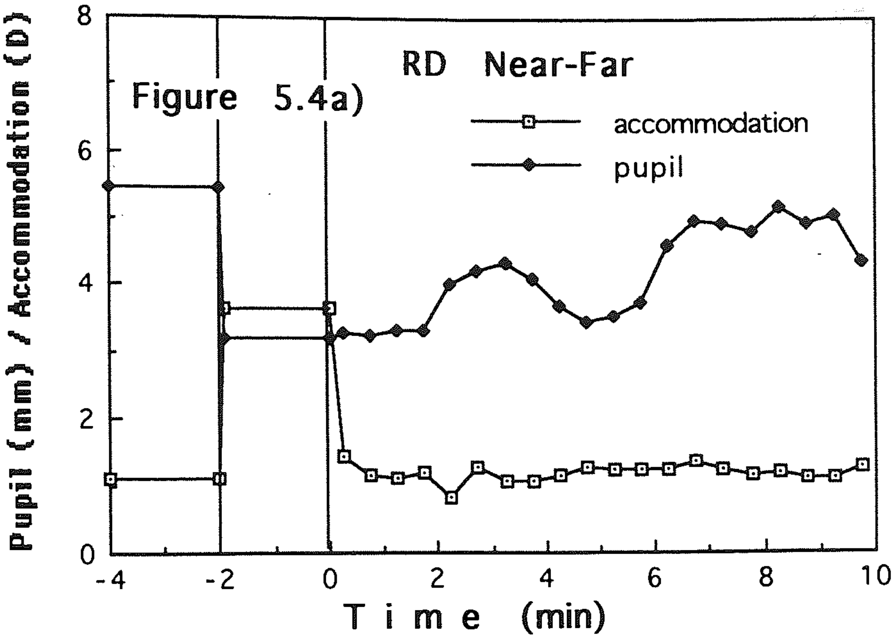


Figure 5.4a)

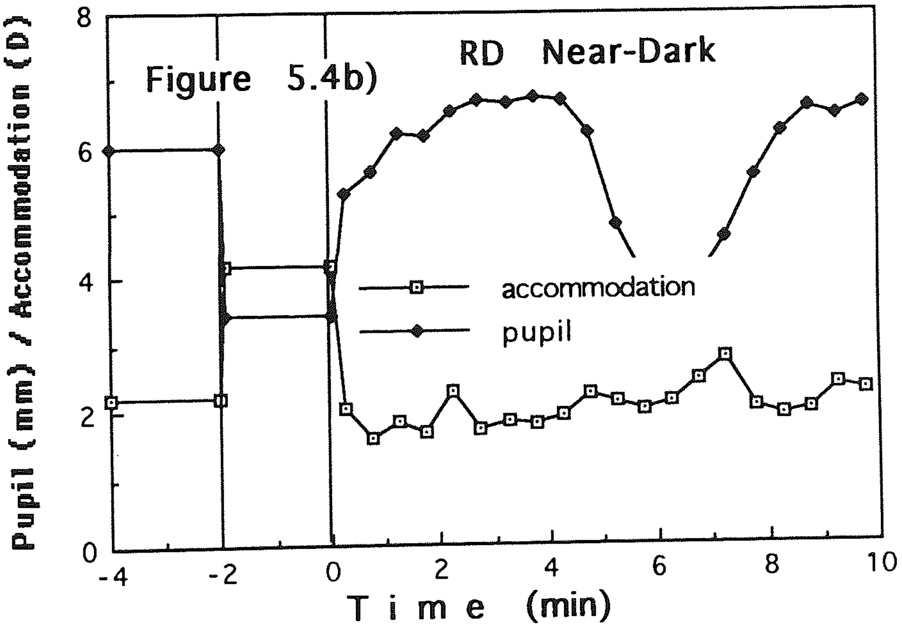


Figure 5.4b)

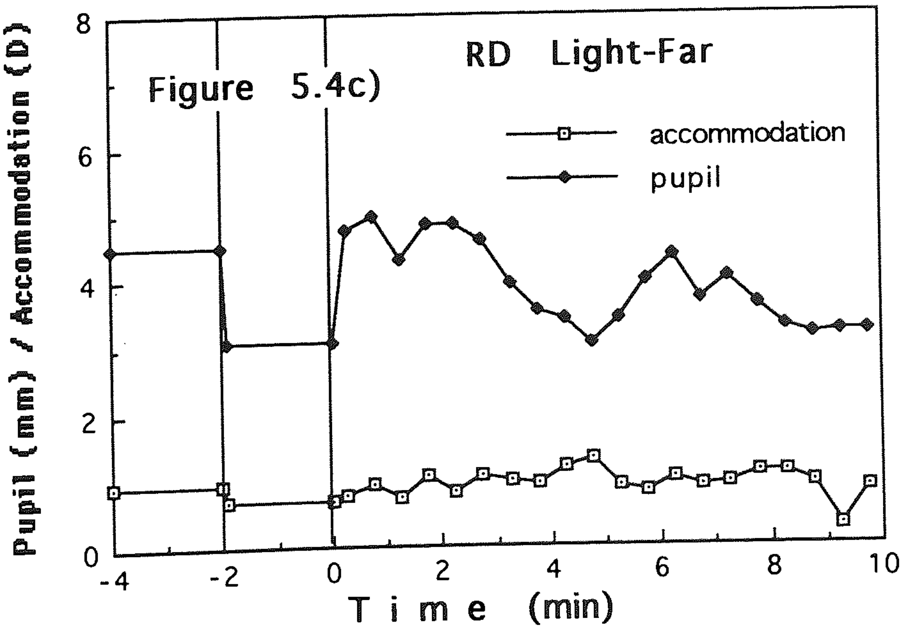


Figure 5.4c)

accommodation alone is not sufficient to cause pupil redilation and that the redilation in conditions B and C is simply luminance driven.

Future experiments will need to investigate further the pupil after-effect and also the relationship between accommodation and pupil responses during near fixation. The pupil reconstriction effects which often occurred after around 4 minutes post-task in this study suggests that future experiments should have a shorter time course to avoid data contamination due to fatigue effects. Investigations of pupil after-effects following near-vision tasks must maintain constant luminance levels to avoid masking of pupil effects by the luminance drive.

SUPPORTING PUBLICATIONS

Ukai, K., Phillips, N. J., Winn, B. and Gilmartin, B. Pupillary adaptation following near vision is masked by darkness. 8th International Neuro-Ophthalmology Symposium Abstracts, **M008** (1990).

Ukai, K., Gilmartin, B., Phillips, N. J. and Winn, B. Pupillary adaptation following near vision is masked by darkness. (In preparation).

ACKNOWLEDGEMENT

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CHAPTER 6

PUPIL AFTER-EFFECTS FOLLOWING A NEAR VISION TASK DEMONSTRATED USING CONTINUOUS MEASUREMENT OF PUPIL AND ACCOMMODATION RESPONSES

6.1 INTRODUCTION

A recent study (Gilmartin *et al*, 1989, 1990) has used a modified Canon Autoref R1 (see Chapter 4 for instrument details) to make continuous recordings of the regression of accommodation back to pre-task levels in darkness following sustained visual tasks. The study demonstrated different regression rates between individuals and it was hypothesized that delayed regression is caused by a deficit in sympathetic innervation to accommodation which may indicate predisposition to the development of late-onset myopia. The coupling of a Hamamatsu C3160 Percept Scope Video Area Analyser to the Autoref R1 allows continuous recording of pupil size to be made from the image of the eye provided by the IR video camera within the optometer. This study was carried out to investigate the possibility that a corollary to the accommodative after-effects demonstrated by Gilmartin *et al* (1989, 1990) may occur in pupil response and also to assess the feasibility of carrying out simultaneous, continuous recording of accommodation and pupil responses. If pupil after-effects could be shown to correlate with accommodation after-effects, then continuous recordings of pupil response could supplement or be used as an alternative to accommodation recording which would have several advantages. Continuous recording of accommodation responses is dependent on retinal reflectivity which does vary between subjects, cannot give absolute values of accommodative level and requires that pupil diameter be at least 3.9mm for reliable recording. These factors limit both the subjects that can be selected for study and the strength and duration of near vision task that can be applied without the use of mydriatic drugs. Pupil size recording is not subject to the same limitations and hence if pupil recording could be used to assess the effects of near vision tasks on the oculomotor system, it would make investigations of hysteresis effects (i.e. delay between the removal of a stimulus and the dissipation of the effect of the stimulus on the system being studied) much quicker and easier and extend the range of subjects and tasks that could be used.

Retained pupillary constriction following a near-vision task has been reported by Tsuchiya, Ukai and Ishikawa (1989) and was also demonstrated in the experiment described in the previous chapter. In both studies, quasistatic recording methods were used over long time bases and showed little, if any, correlation between pupillary and accommodative after-effects. The present investigation used continuous recording of pupil and accommodation responses over a short time scale to give a higher sampling rate and to show in more detail the responses during the first 45 seconds following removal of the near vision task. Studies using IR optometers (Gilmartin and Bullimore, 1987, 1991, Rosenfield and Gilmartin, 1989) have shown that accommodative after-effects have usually dissipated within the first 60 second post-task period and thus a high sampling rate during this early post-task period should reveal the relationship between any induced pupillary and accommodative after-effects.

6.2 METHODS

Pupil diameter was measured using a Hamamatsu C3160 Percept Scope Video Area Analyser connected to the TV camera of a modified Canon Autoref R1 optometer (see Chapter 4 for details). The modified Autoref R1 was used to record continuously accommodation responses along a single meridian. Outputs from the Percept Scope and the Autoref R1 were fed simultaneously into two channels of a four channel digital storage oscilloscope for storage and later transfer via an IEEE-488 interface bus to the Epson PCe-XT IBM-clone desktop computer. A photodiode connected to a third channel on the oscilloscope was used as an event marker and the time from the beginning of the recording to cessation of the task was calculated from the original traces using a remote control cursor. Recordings were made over a 100 second recording period giving a sampling rate of 10.24 points per second.

Four subjects were used and recordings were made under 4 experimental conditions. Subjects were allowed at least 5 minutes looking around the room between conditions. Prior to experimental trials, as described in Chapter 4, an accommodative step of known magnitude was recorded to enable conversion of accommodation recordings to dioptric change and a pupil zero level recorded to allow plotting of absolute pupil diameter. Subject details are shown in table 6.1.

SUBJECT	AGE	SEX	IRIS COLOUR
PI	20	M	DARK BROWN
NP	28	M	BROWN
FE	28	M	BLUE
JH	20	F	BLUE

Table 6.1 Details of the subjects used in the study. All 4 were emmetropic.

All recordings were made from the RE with the LE occluded. Subjects fixated through the centre of a Badal lens surrounded by a circular aperture and were carefully aligned and kept steady during recordings using chin rest and dental bite. Prior to the experiment, tonic accommodation (TA) levels were measured for each subject following 5 minutes in darkness and 5 minutes in a bright empty field (BEF) using the Autoref R1 in static single-shot mode (see table 6.2). The BEF was created using a back-illuminated ($32cdm^{-2}$) translucent white plastic sheet which was blurred by placing it beyond the range of the Badal lens. Subjects were instructed not to make any attempt to bring the aperture surrounding the Badal lens into focus. The back-illuminated sheet also provided the illumination when required during trials. Target positions during trials were set to give the required accommodative response using the optometer in static single-shot mode.

4 experimental conditions were used as follows:

1) **TA+3D-Dark**. Subjects viewed a high contrast photopic maltese cross target for 3 minutes set at 3D above dark TA level. The task was then removed and the subject placed in complete darkness with only a dim, green light for fixation (it had previously been ascertained that the dim green light provided no stimulus to accommodation in darkness- see Owens, 1991).
Aim: to assess any retention of task-induced pupillary constriction under post-task conditions of darkness.

2) **TA+3D-BEF.** Subjects viewed the same high contrast photopic maltese cross target for 3 minutes set at 3D above BEF TA level. The task was then removed leaving the subject under BEF conditions (no luminance change). In order to maintain the BEF, no fixation target could be used and subjects were asked to maintain primary eye position as accurately as possible.
Aim: to determine if the drop in blur-driven accommodation following cessation of the near vision task caused an increase in pupil diameter.

3) **TA-DARK.** Subjects viewed the high contrast maltese cross target set at the dark TA position for 3 minutes and then the task was removed and the subject placed in darkness with a dim green light present for fixation (luminance change only).
Aim: to assess post-task pupil size in darkness when no accommodative effort had been made and compare it to that size achieved in darkness following accommodative effort in condition 1.

4) **TA-BEF.** Subjects viewed the high contrast maltese cross target set at the BEF TA position for 3 minutes and then the task was removed leaving the subject under bright empty field conditions (no change in luminance or accommodative stimulus level).

Aim: to check for the presence of any artefacts in pupil or accommodation responses caused by the removal of the task.

Recordings were made for at least the last 5 seconds during the task and for at least fifty seconds following removal of the task. In figures. 6.1, 6.2 and 6.3, removal of the task is shown as at time T=0 and plots show 5 seconds prior to task removal and 45 seconds following task removal. Accommodation levels have been normalised to TA and so 0D on the accommodation plots represents the TA level.

6.3 RESULTS

Results were similar for all 4 subjects and representative recordings taken using subject PI are shown in figures 6.1, 6.2 and 6.3.

SUBJECT	TA DARK	TA BEF
PI	0.61 (0.12)	0.82 (0.22)
NP	0.73 (0.20)	0.08 (0.23)
FE	1.24 (0.12)	1.05 (0.13)
JH	1.60 (0.21)	1.53 (0.12)

Table 6.2 TA levels (in D) for the 4 subjects used in the study. Each figure represents the mean of 10 measurements and is followed in brackets by the standard deviation.

1) TA+3D-DARK

Pupil (see figure 6.1): all subjects demonstrated rapid pupillary dilation in darkness following the removal of the TA+3D task. A steady pupil diameter was achieved which matched the level achieved in darkness when no near vision task had been undertaken (in condition 3, TA-DARK). Therefore no pupillary after-effect was demonstrated in darkness.

Accommodation (see figure 6.2): results were variable with 3 subjects regressing rapidly to TA levels within 10 secs of task removal whilst 1 subject (PI) held a higher level for around 30 secs. This retention of task accommodative level did not influence pupil diameter.

2) **TA+3D-BEF**

Pupil (see figure 6.1): all subjects demonstrated retained pupillary constriction following removal of the TA+3D task. Pupil diameter remained constant for at least the 45 second post-task recording period.

Accommodation (see figure 6.2) : regressed to TA levels within 10 secs in 3 subjects. Pupil diameter in subject FE dropped below 4mm in the BEF conditions interfering with the accommodation recordings for this subject.

3) **TA-DARK**

Pupil (see figure 6.1): all subjects demonstrated rapid pupillary dilation following removal of the task at TA position, achieving approximately the same post-task diameters as achieved in condition 1 (TA+3D-DARK).

Accommodative levels remained unchanged throughout the trial (see figure 6.3).

4) **TA-BEF**

Both accommodative and pupillary levels remained unchanged throughout this condition, demonstrating that the action of removing the task produced no artefact in pupil or accommodation responses (see figures 6.1 and 6.3).

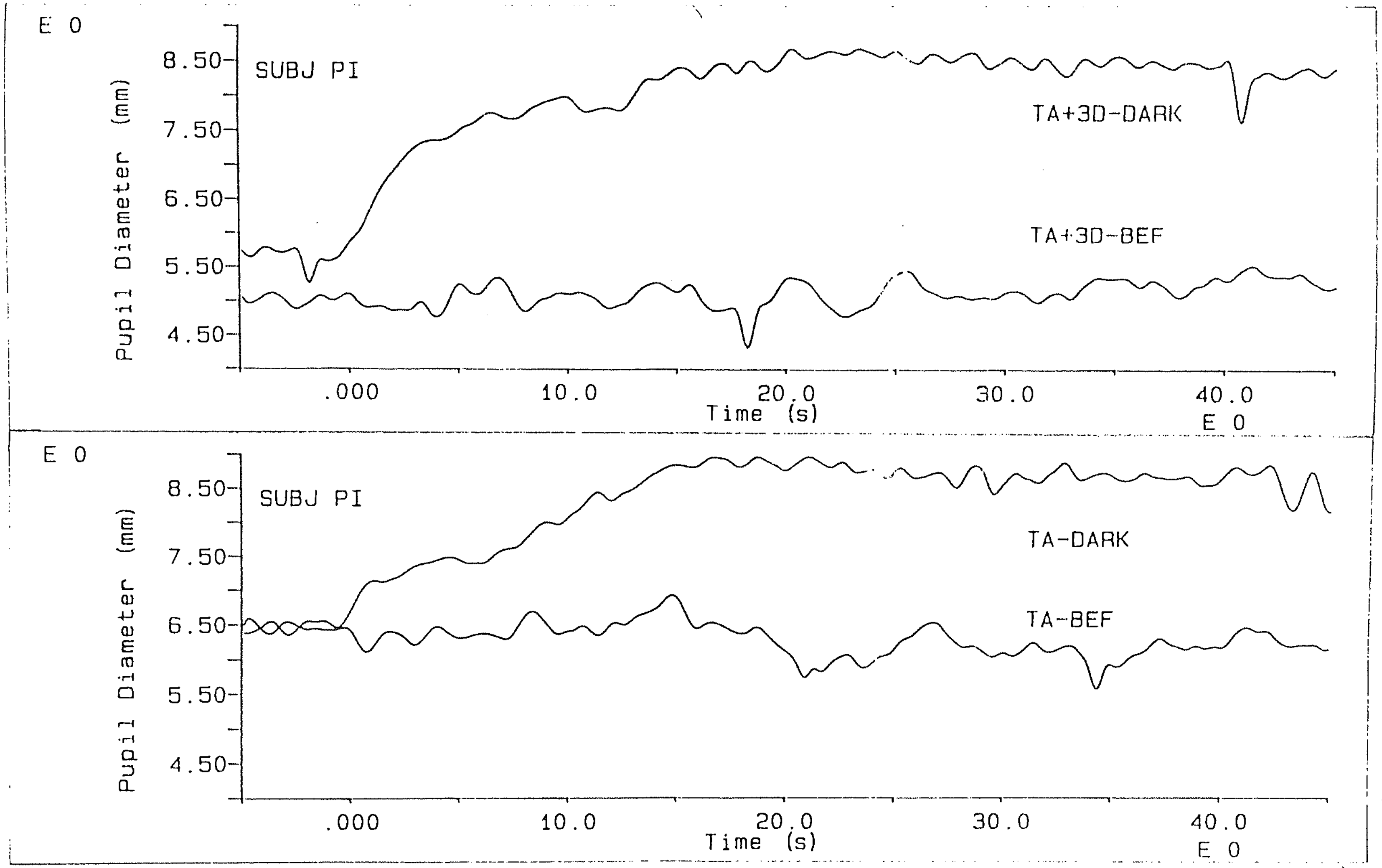


Figure 6.1 Pupil diameter recordings using subject PI under the 4 experimental conditions described in the text and as labelled. Time 0 indicates cessation of the task. Traces have been smoothed to 2Hz.

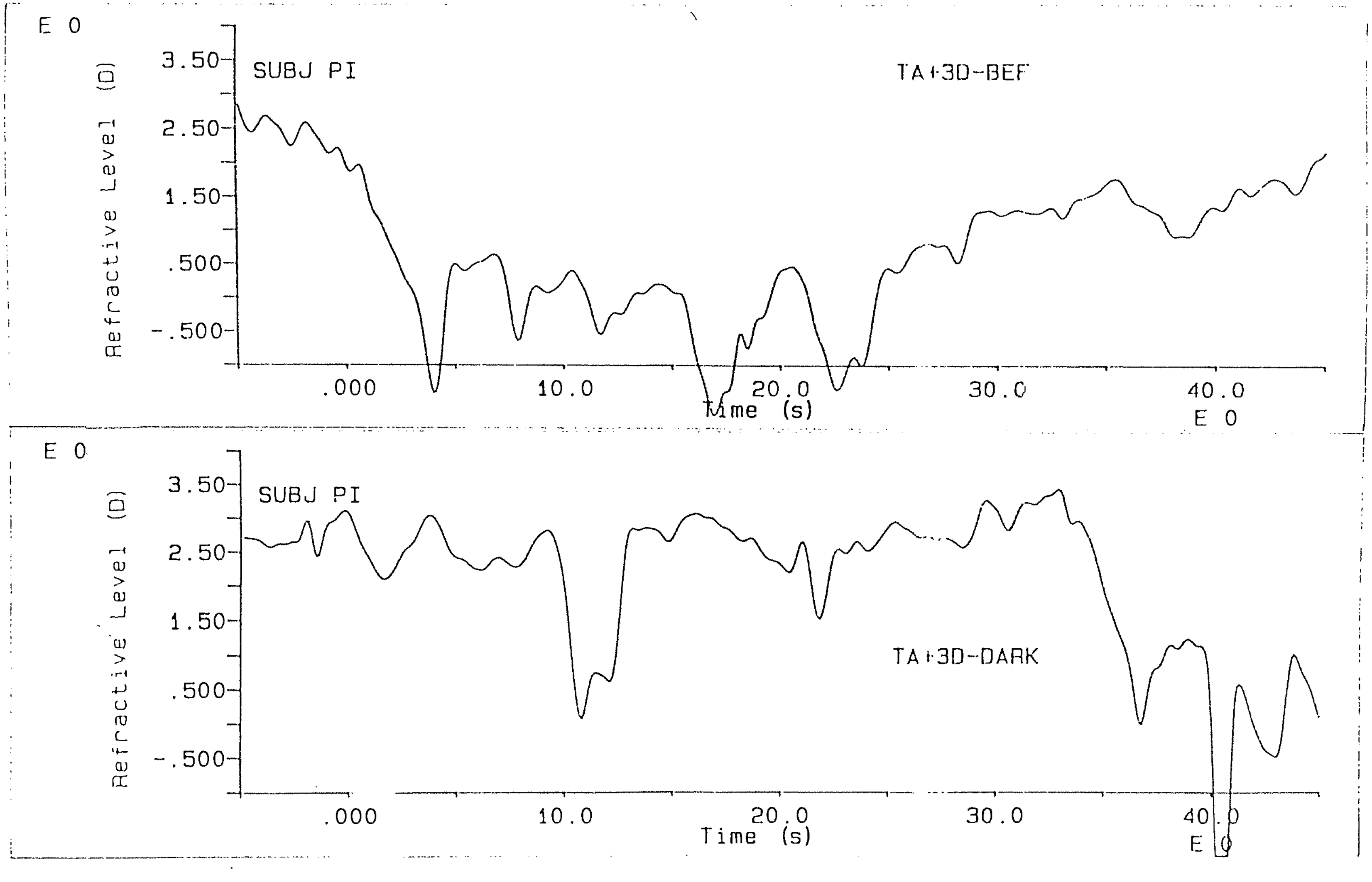


Figure 6.2 Accommodative level recordings using subject PI under the 1st and 2nd experimental conditions described in the text and as labelled. Time 0 indicates cessation of the task. Traces have been smoothed to 2Hz.

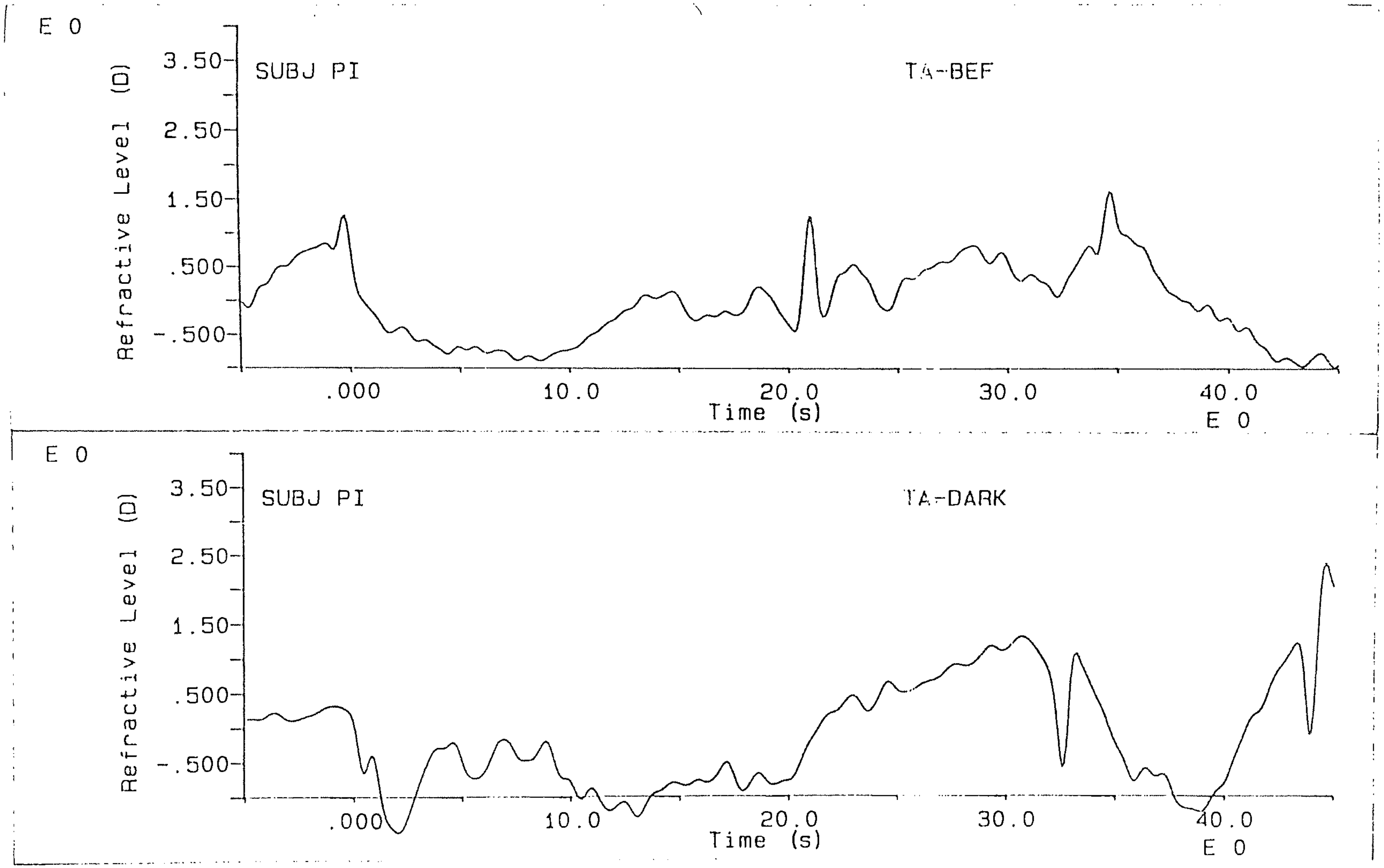


Figure 6.3 Accommodative level recordings using subject PI under the 3rd and 4th experimental conditions described in the text and as labelled. Time 0 indicates cessation of the task. Traces have been smoothed to 2Hz.

6.4 DISCUSSION

The results of this experiment support the findings of Tsuchiya, Ukai and Ishikawa (1989) and those reported in Chapter 5. That is, in the absence of visual stimulus and luminance change, the pupil may fail to redilate on cessation of a near vision task even in the presence of change in accommodative level. The luminance drive to the pupil was isolated in condition 3 (TA-DARK) and proved to be capable of redilating the pupil to the same level as that which was attained in condition 1 (TA+3D-DARK) when a drop in accommodative level was also present. Therefore no pupillary after-effects could be demonstrated in darkness and were either not induced or were masked in darkness as demonstrated in the previous experiment. Tsuchiya, Ukai and Ishikawa (1989) reported that pupil after-effects are not masked in darkness, although results were shown for only one subject.

The results demonstrate that post-task changes in pupillary and accommodative levels are uncoupled in the absence of a visual stimulus. Hence the pupil after-effect is not a corollary of accommodative after-effect and pupil reponse recording cannot be substituted for accommodation recording in the study of oculomotor hysteresis effects.

The exact nature of pupil after-effects still remains unclear. If a true adaptation had taken place following the near vision task, it might reasonably be assumed that post-task in darkness the pupil should be smaller following the task in condition 1 (TA+3D-DARK) than it was when no task was undertaken in condition 3 (TA-DARK). However, this did not occur in any of the subjects and it therefore seems likely that genuine adaptation has not occurred. Rather, it seems that in the absence of luminance change, the drop in blur-driven accommodation does not feed through to the pupil and the pupil fails to redilate. This is contrary to the many reports (Fry, 1945, Knoll, 1949, Marg and Morgan, 1949, 1950, Jones, 1989, Myers and Stark, 1990) that pupil response is driven by accommodation.

If pupil after effects are to be demonstrated then luminance change must be avoided. A problem in experiments utilising a sustained near vision task is that the pupil may constrict below 3.9mm, making continuous recordings of accommodation response unreliable with the modified Autoref R1. This is clearly more likely to be a problem if luminance is to be kept constant. Previous studies (Gilmartin *et al* 1989, 1990) have measured post-task accommodation regression patterns in darkness which acts to dilate the pupil. Despite this, simultaneous, continuous recording of pupil and accommodation responses can be made and promises to be a powerful research tool. Further experiments in this thesis will attempt to investigate the relationship between blur-driven accommodation responses and pupil near response without using sustained near vision tasks in order to maintain sufficiently large pupil diameters to allow satisfactory recording of pupil and accommodation responses.

SUPPORTING PUBLICATIONS

Gilmartin, B., Ukai, K., Phillips, N. J. and Winn, B. Accommodative adaptation to near-vision: is there a pupil corollary? *Ophthal. Physiol. Opt.* **10**, 109 (1990).

Gilmartin, B., Ukai, K., Phillips, N. J. and Winn, B. Accommodative adaptation to near-vision: is there a pupil corollary? Transactions of the 2nd International Conference of the British College of Optometrists, London (1990).

CHAPTER 7

THE EFFECT OF PERIODIC VARIATIONS IN TARGET VERGENCE ON PUPIL RESPONSE

7.1 INTRODUCTION

In Chapter 2, the literature relating to the cause of the pupil constriction associated with near fixation was discussed. It was concluded that the pupil near response is usually considered to be driven by the accommodation and/or the convergence mechanisms rather than occurring as a separate response in its own right.

Jones (1989) concluded from 2 experimental measurement conditions that pupil near response is associated with blur-driven accommodation but not with fusional vergence. In the first trial, negative lenses were used to drive accommodation while subjects monocularly viewed a target through a 3mm pupil to open-loop pupil and vergence responses. In the second trial, accommodation and pupil responses were then held open-loop using binocular pinhole viewing while fusional vergence was induced using prisms. Accommodation, vergence and pupil responses were measured simultaneously using IR recording devices. He suggested that previous reports of convergence-driven pupil response were due to accommodation not being open-loop in earlier experiments. Myers and Stark (1990) recorded the latencies of accommodation, vergence and pupil responses to a variety of stimuli in an attempt to identify the links between pupil response and the other two components of the near vision triad. They proposed that drive to the pupil arises from an '*asymmetric dual interaction*' between accommodation and vergence and that the relative weighting of each component varies between individuals.

Tsuchiya, Ukai and Ishikawa (1989) reported retained pupillary constriction following a near vision task and showed changes in accommodative level that were not reflected in concomitant changes in pupil diameter. This finding is supported by the results of the experiments reported in Chapters 5 and 6 of this thesis. Stakenburg (1991) reported that under carefully-controlled experimental conditions, a blur-only accommodative stimulus may not give rise to pupil constriction. In his study, subjects viewed 2 superimposed targets of equal angular subtense and luminance. By using semi-silvered mirrors, the targets could be alternately illuminated to provide an accommodative stimulus of 2.38D. When change from the far target to the near target was accomplished with no apparent lateral target displacement, then no pupil response occurred in 2 out of the 3 subjects used. Accommodation response was presumed from observation of the vergence response of the unstimulated eye. As lateral target displacement was introduced, pupil responsiveness increased.

The lack of pupil response to even large changes in accommodative level reported by Tsuchiya, Ukai and Ishikawa (1989), Stakenburg (1991) and in Chapters 5 and 6 of this thesis is difficult to explain using the currently held view that accommodation or vergence provide the drive to pupil near response. Due to the strong synkinetic link between accommodation and vergence (Myers and Stark, 1990), it is difficult to separate the effects of these two components and it is likely that in any experiment in which accommodation is stimulated both accommodation and vergence will respond. The present experiment aimed to test the proposal that pupil response may vary with the rate of accommodative change and that a threshold rate of change may need to be reached to trigger pupil response.

7.2 METHODS

Initially a group of 10 young, healthy, visually normal subjects (mean age 22.9 yrs, SD 3.1, 6 male (M), 4 female (F)) was used to investigate pupil response to a sinusoidally modulated accommodative stimulus. The target used was a high-contrast, photopic ($20cdm^{-2}$) maltese cross viewed through a 3-lens Badal stimulus optometer (see figure 7.1), the central lens of which was mounted on the pen-drive bar of an X-Y plotter connected to a frequency generator. Movement of the central lens altered the accommodative demand of the target without changing apparent target size or retinal illuminance. The frequency generator was used to provide a sinusoidal waveform which drove the X-Y plotter and hence the central lens to modulate the accommodative demand over a 2D accommodative stimulus range. Horizontal pupil diameter was measured using a Hamamatsu C3160 Percept Scope Video Area Analyser connected to the TV camera of a modified Canon Autoref R1 IR optometer. Outputs from the Percept Scope and the frequency generator were fed into 2 channels of a 4-channel digital storage oscilloscope controlled by an Epson PCe-XT IBM-clone computer via an IEEE-488 interface bus and using *Asystant* software (see Chapter 4 for further details). The accommodative stimulus was sinusoidally-modulated at frequencies of 0.05, 0.1, 0.2, 0.3, 0.4, 0.5 and 0.6Hz and pupil diameter and stimulus waveform were simultaneously recorded. The duration of recordings

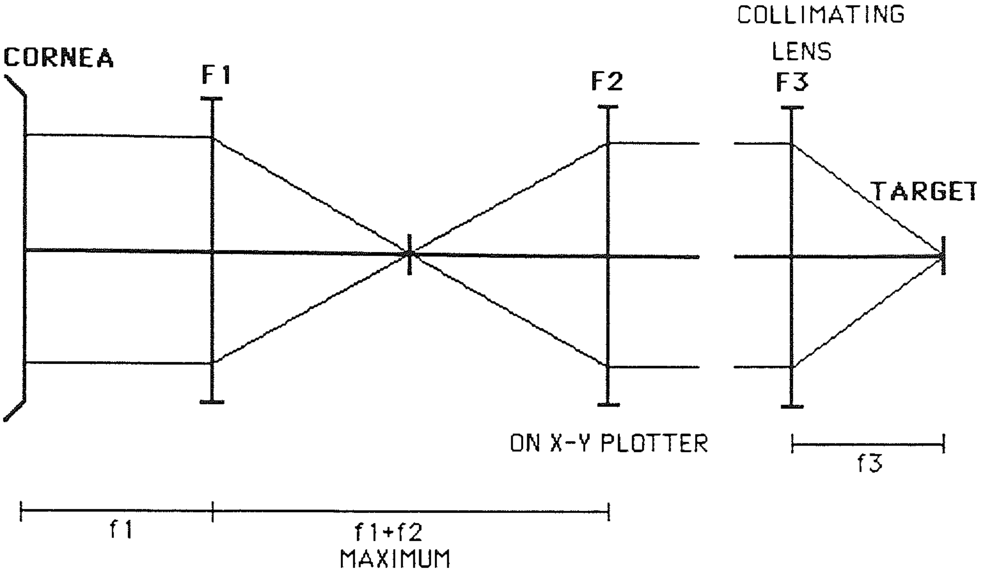


Figure 7.1 Schematic diagram of the Badal stimulus optometer. Lens F2 was varied in position to vary accommodative demand. In the position of F2 shown above, accommodative demand is 0D.

was varied by altering the time base on the oscilloscope to ensure the capture of at least 2 complete stimulus cycles at each temporal frequency.

From the initial group of 10 subjects, 3 emmetropes were selected (NP, M 29, BE, M 27 and GR, F 24) who displayed good fixation and low blink rate. The experiment was repeated incorporating simultaneous recording of accommodation and extended to 3 accommodative stimulus ranges. Following the report by Stakenburg (1991) on the importance of target alignment, the stimulus optometer was further refined by aligning the optical centres of the component lenses along a laser beam directed from the centre of the target to the position occupied by the centre of the subject's cornea during recordings. Subjects were kept steady using chin rest and dental bite. Prior to recording, subjects viewed the moving target and were asked to make small head movements until all lateral and vertical target displacement disappeared. Once this was achieved, the target generally appeared stationary and occasional questioning showed that subjects were not reliably aware of the direction of stimulus movement.

Outputs from the Percept Scope and optometer and the stimulus waveform were fed into 3 channels of the oscilloscope for recording and later transfer to the computer. The accommodative demand was sinusoidally modulated at frequencies of 0.05 to 0.6Hz over stimulus ranges of 1, 2.25 and 3D. The limits of lens movements necessary to achieve these ranges were set individually for each subject using the optometer to record static accommodative reponse. One subject (NP) took part in further recordings in which a triangular waveform was substituted for the sine wave.

The stimulus was designed to provide a reliable accommodative response and previous studies (Campbell and Westheimer, 1960, Kruger and Pola, 1983, 1985, 1986, 1987, McLin, Schor and Kruger, 1988) have shown that repetitive,

Figure 7.2 Photograph of the laboratory

predictable stimuli elicit periodic accommodative reponses, the amplitude of which decreases with increasing stimulus temporal frequency (see figure 7.3).

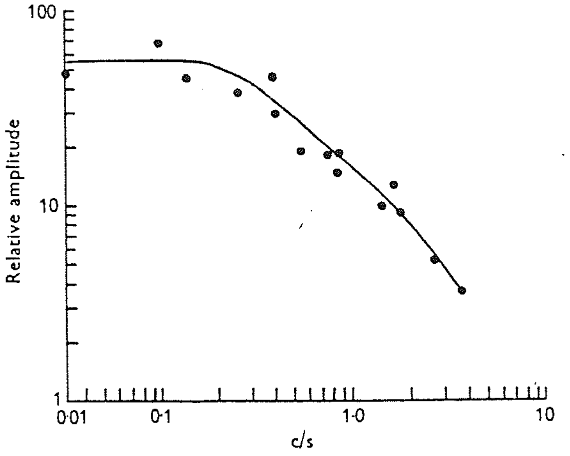


Figure 7.3 Plot of accommodative response amplitude against temporal frequency of a sinusoidally-modulated accommodative stimulus (from Campbell and Westheimer, 1960).

7.3 RESULTS

Examination of the recordings from the initial 10 subjects revealed a wide variability in amplitude of pupil response and in some instances no response occurred at all. Pupil response amplitude was generally low compared to that reported in earlier literature of around 0.5mm pupil diameter change per dioptre accommodative stimulus (Marg and Morgan, 1950). The mean response amplitude (measured from peak to trough of the response at each stimulus cycle) at each temporal frequency was measured directly from the recorded traces and shows a peak at 0.2Hz and a decline at higher and lower frequencies (see figures 7.4 and 7.5). This was incompatible with the concept of pupil response being primarily driven by accommodation as the high accommodation gain at low frequency should be reflected in large amplitude of pupil response. The second part of the experiment attempted to investigate the relationship between pupil and accommodation responses further by recording both pupil and accommodative responses and using 3 accommodative stimulus ranges.

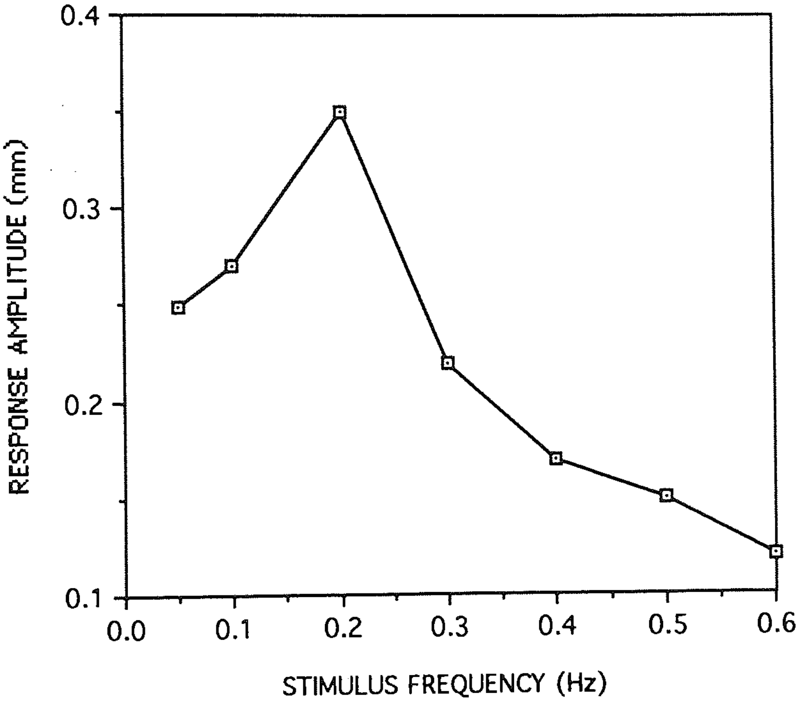


Figure 7.4 Average pupil response amplitude plotted against stimulus temporal frequency for the 10 subjects used in the initial part of the experiment.

Results from the second part of the experiment using 3 subjects showed that if all cues other than blur are minimised, then accommodation response is robust and shows reduction in amplitude with increase in stimulus temporal frequency (see figure 7.6 and figures 7.8, 7.9, 7.10). Under the same conditions, pupil response is of low amplitude or, in 2 of the 3 subjects, could be completely absent (see figures 7.8 and 7.9). The average amplitudes of pupil response obtained are shown in figure 7.7 and did not vary greatly across the 3 accommodative stimulus ranges (see figure 7.7). Substitution of a triangular waveform using 1 subject (NP) produced essentially similar results to those obtained using sinusoidal waveform (see figure 7.10).

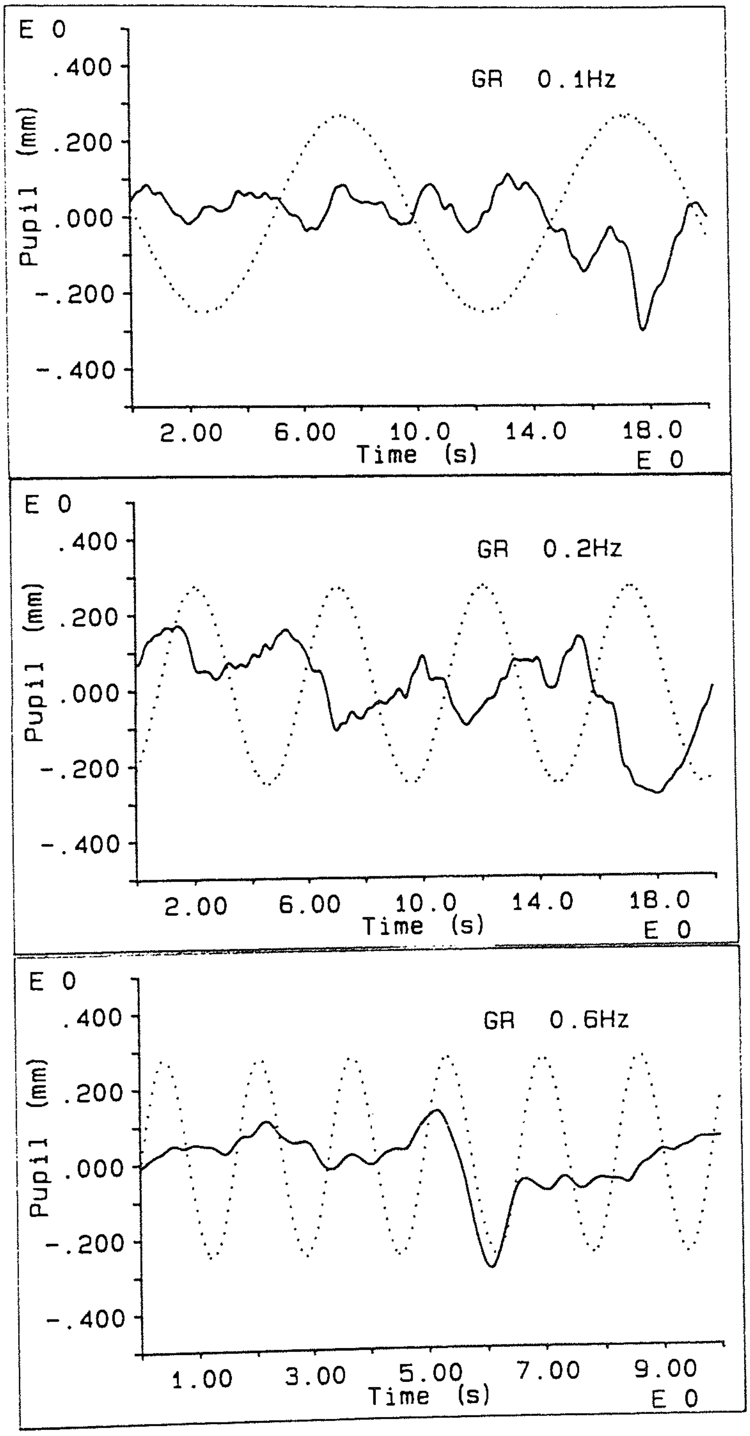


Figure 7.5 Examples of pupil recordings shown as variation about mean diameter for subject GR at stimulus temporal frequencies of 0.1, 0.2 and 0.6Hz. The stimulus waveform is shown dotted, vertical change upward indicating increase in accommodative demand. Note low amplitude of pupil response at 0.1Hz, increased at 0.2Hz and reduced again at 0.6Hz.

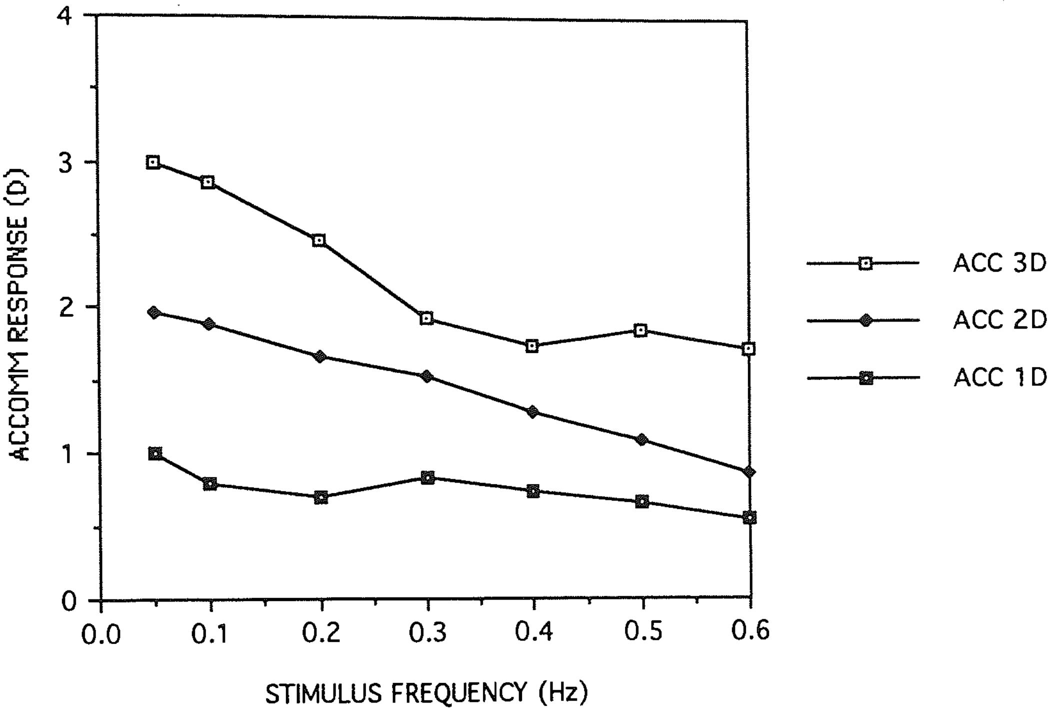


Figure 7.6 Plot of average accommodation response in D against stimulus temporal frequency for the 3 observers over the 3 accommodative stimulus ranges used.

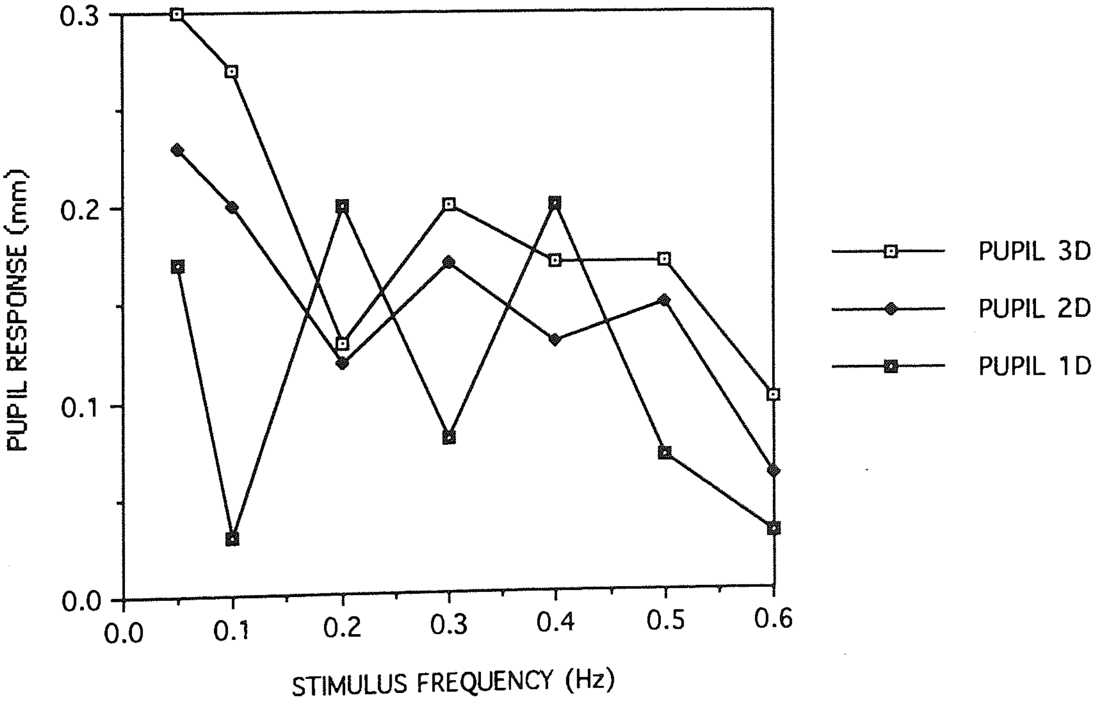


Figure 7.7 Plot of pupil response amplitudes against stimulus temporal frequency for the 3 stimulus amplitude conditions. Results are from the 3 subjects used in the 2nd part of the experiment.

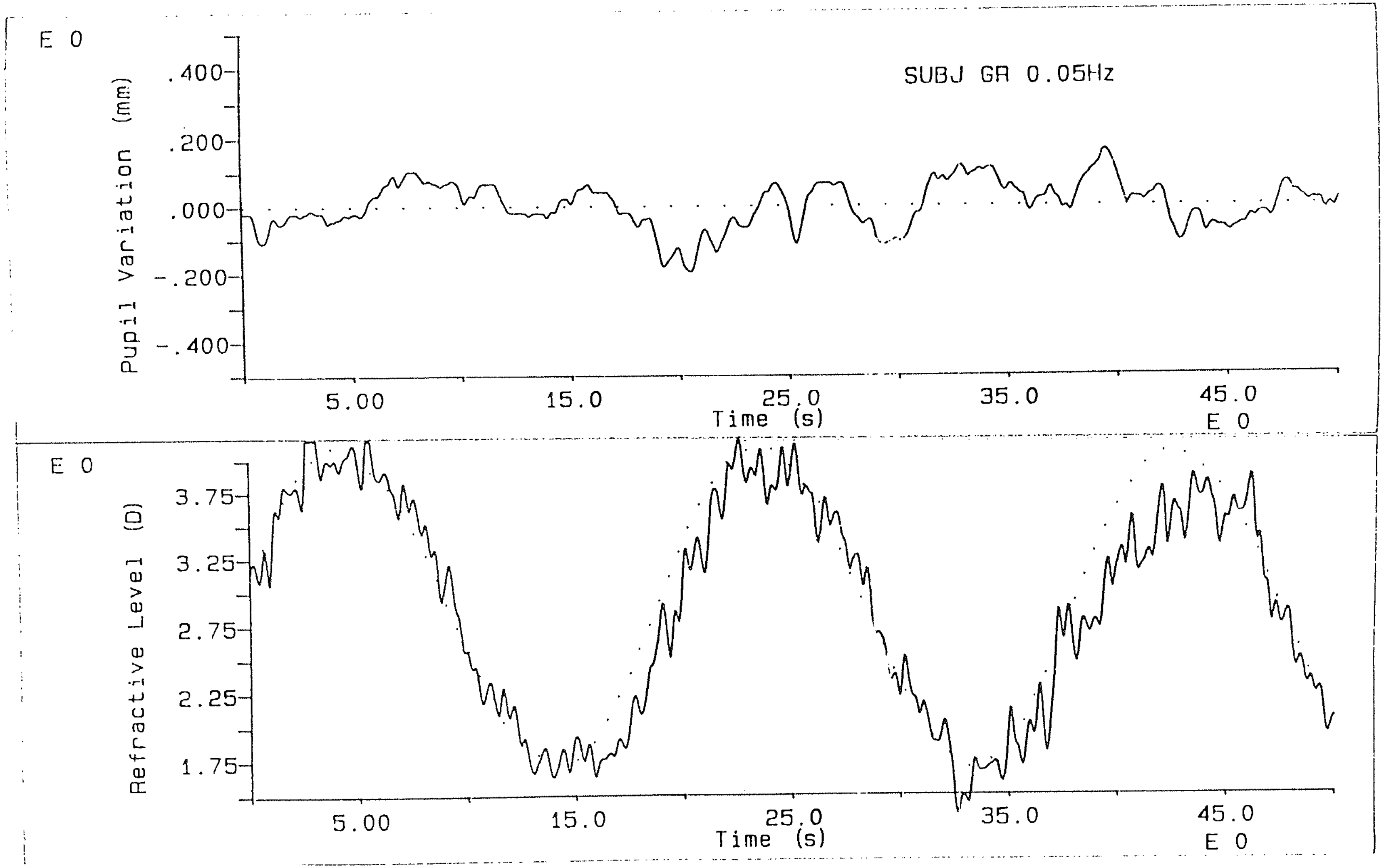


Figure 7.8 Simultaneous, continuous recording of pupil diameter (shown as variation about the mean) and accommodative response over a 50 second recording period. The stimulus is shown dotted (lower plot) and represents a 2.25D accommodative task sinusoidally-modulated at 0.05Hz. Note minimal pupil response despite robust, periodic accommodation response. Traces smoothed to 5Hz. Mean pupil diameter = 6.99mm.

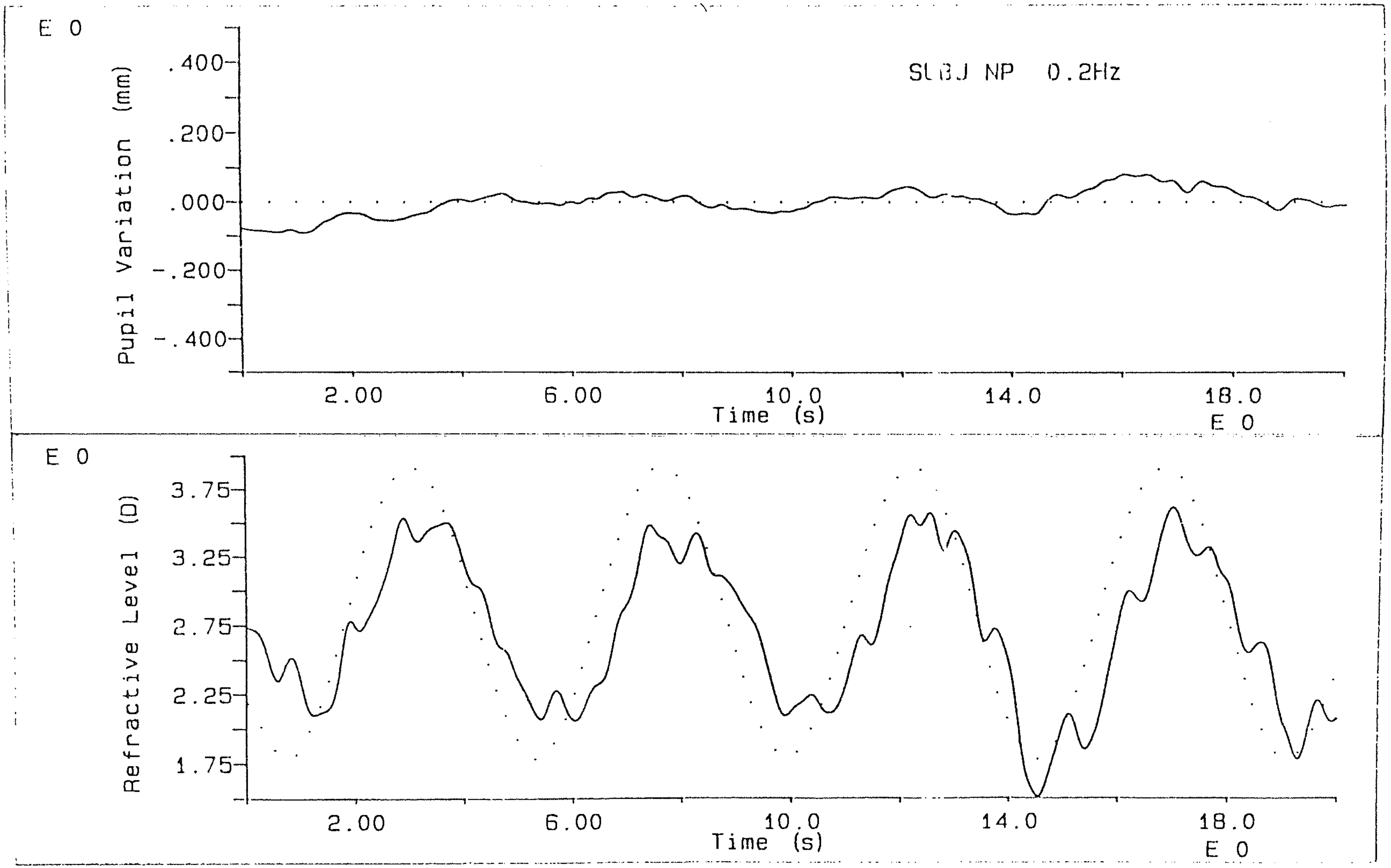


Figure 7.9 Simultaneous, continuous recording of pupil diameter (shown as variation about the mean) and accommodative response over a 20 second recording period. The stimulus is shown dotted (lower plot) and represents a 2.25D accommodative task sinusoidally-modulated at 0.2Hz. Note minimal pupil response despite robust, periodic accommodation response. Traces smoothed to 5Hz. Mean pupil diameter = 5.78mm.

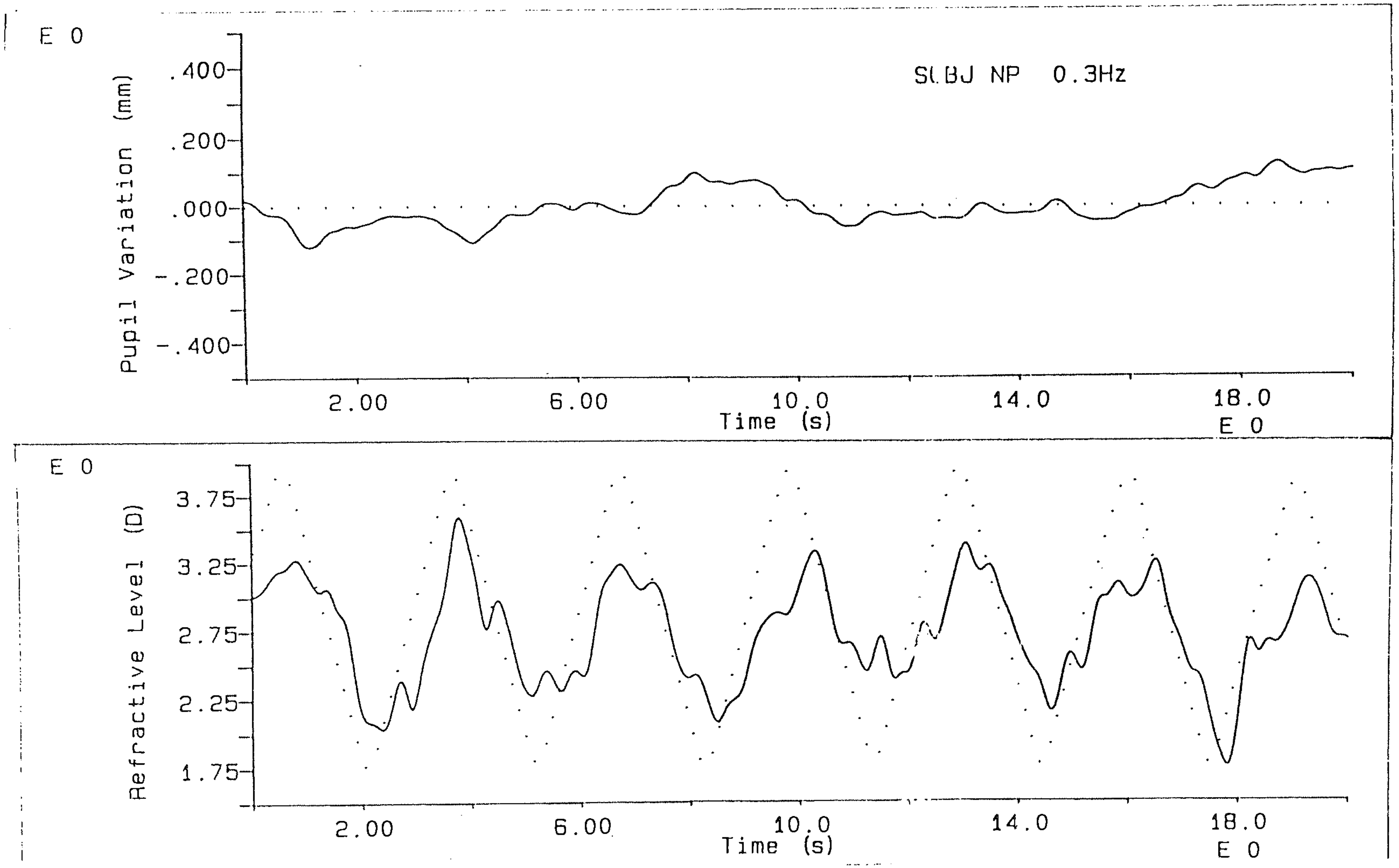


Fig 7.10 Simultaneous, continuous recording of pupil diameter (shown as variation about the mean) and accommodative response over a 20 second recording period. The stimulus is shown dotted (lower plot) and represents a 2.25D accommodative task temporally-modulated using a 0.2Hz triangular waveform. Note minimal pupil response despite robust, periodic accommodation response. Traces smoothed to 5Hz. Mean pupil diameter = 5.39mm.

7.4 DISCUSSION

The results of this experiment support those reported by Stakenburg (1991) and show that if all cues to accommodation other than blur are minimised, then pupil response may be of low amplitude or absent. Further, the results show that this is so despite the presence of robust accommodation response. Tsuchiya, Ukai and Ishikawa (1989) have also recorded accommodative change without concomitant pupil response and this finding was supported by the results of the experiments reported in Chapters 5 and 6 of this thesis. These results are incompatible with the previously held view that the pupil constriction associated with near fixation is driven primarily by accommodation or vergence. Although vergence was not monitored in this study, it is reasonable to assume that vergence responses occurred in the occluded eye and Stakenburg (1991) reported vergence responses to an accommodative stimulus which he used as a means of monitoring accommodation response.

As blur-driven accommodation alone does not feed through to and drive the pupil, it seems that other cues must be present to trigger a pupil response. Stakenburg (1991) showed that target alignment may be a factor and that visible lateral displacement as the target moved led to increase in pupil response. Size change was also eliminated in the current study and that of Stakenburg (1991), and it may be that size change and target drift both act as cues to the proximity of the target and that it is the awareness of target proximity that is important to pupil near response. It has already been shown that size change acting as a depth cue can be a powerful stimulus to open-loop accommodation response (Kruger and Pola, 1983, 1985, 1986, 1987). The remaining experiments reported were designed with these thoughts in mind and in an attempt to clarify the role of pupil response in near vision.

SUPPORTING PUBLICATIONS

Phillips, N. J., Winn, B., Gilmartin, B. and Sculfor, D. L. An investigation of accommodative-driven pupil response to periodic variations in stimulus vergence. *Ophthal. Physiol. Opt.* **11**, 282 (1991).

Phillips, N. J., Winn, B., Gilmartin, B., Sculfor, D. L. and Ukai, K. The effect of periodic variations in target vergence on accommodation-driven pupil response. *Invest. Ophthalmol. Visual Sci.* **32** (suppl.), 1124 (1991).

Phillips, N. J., Winn, B. and Gilmartin, B. Absence of pupil response to blur-driven accommodation. *Vision Res.* **32**, 1775-1779 (1992).

CHAPTER 8

DISCRETE PUPIL RESPONSE TO ILLUSORY MOVEMENT IN DEPTH (LOOMING)

8.1 INTRODUCTION

Previous literature relating to the stimulus to pupil near response has been discussed in Chapters 2 and 7. Investigators attempting to isolate the principal stimulus to the pupil constriction associated with near fixation have generally started with the prior assumption that pupil near response occurs as a result of accommodation or vergence. As Marg and Morgan (1950) pointed out, the possible influence of other factors such as those relating to awareness of the proximity of an object have largely been ignored. Tsuchiya, Ukai and Ishikawa (1989), Stakenburg (1991) and Phillips, Winn and Gilmartin (1992) have reported accommodative change without concomitant pupillary constriction under differing experimental conditions, thus questioning the strength of the previously-accepted association between accommodation and pupil reponse.

The studies of Stakenburg (1991) and Phillips, Winn and Gilmartin (1992) both used accommodative stimuli in which the only cue was blur and subsidiary cues such as size change and lateral or vertical target displacement were minimised. Both studies reported that under these conditions pupil response was of small amplitude and could be absent. Phillips, Winn and Gilmartin (1992) confirmed that accommodation response was maintained under blur-only conditions using a predictable, repetitive stimulus.

The finding that pupil response may be absent in the presence of substantial accommodative change is supported by the experiments discussed in Chapters 5, 6 and 7 of this thesis. It appears therefore that blur-driven accommodation alone (and the attendant vergence response) may not be sufficient to drive pupil near response and that other cues such as lateral or vertical displacement of a moving target (Stakenburg, 1991) or size change (Phillips, Winn and Gilmartin, 1992) may be necessary either alone or as a supplement to accommodation for pupil near response to take place. Hence this study aimed to investigate possible pupil response to an inferred-proximity cue using size change.

As early as 1838, Wheatstone (cited by Regan and Beverley, 1979) recorded that changing the size of an object can produce the illusion that the object is moving in depth. The possibility that accommodation and vergence may respond to change in the perceived distance of a target produced by such an illusion has attracted considerable interest. Ittleson and Ames (1950) used playing cards of varying size viewed at the same physical distance and reported that the perceived distance of the cards varied inversely with card size. They were able to record small changes in both accommodation and vergence (around 0.25D and 2 prism dioptres respectively on quadrupling the size of the card) in a direction corresponding to the change in perceived distance. Ittleson and Ames (1950) also reported that if image size was changed continuously, observers noted blurring of the image as it apparently receded, presumably due to accommodation changes inappropriate to the maintenance of a clear retinal image. Hofstetter (1942) and Alpern (1958) also demonstrated proximal vergence effects although neither they nor Hennessy *et al* (1976) were able to show proximal accommodative effects.

Subsequently, Kruger and Pola (1985, 1987) have confirmed that illusory movement in depth created by dynamic size change alone can act as a stimulus to accommodation response. In order to remove the constraints on closed-loop accommodative response imposed by the need to maintain image clarity, Kruger and Pola kept accommodation open-loop during these experiments by using a servo-driven target linked to the optometer. Any change in accommodation led to change in target position to maintain clarity and thus image clarity was independent of accommodative level. This arrangement led to large accommodation responses of up to 2 or 3D to a looming Maltese cross target. It has also been shown that when size change is added to blur as an accommodative stimulus, the magnitude and accuracy of accommodation response is increased (Kruger and Pola, 1985, 1986, 1987, McLin, Schor and Kruger, 1988).

Marg and Morgan (1950) describe early experiments by Kestenbaum and Eidleberg (1928) showing no effect of proximity on the pupil but were highly critical of the methods used. Marg and Morgan (1950) then attempted to assess the influence of awarenesss of proximity on pupil near response by driving accommodation with negative lenses while subjects viewed targets at varying distances. By comparing the pupil size obtained for equal accommodative levels at different target distances they concluded that out of 7 subjects used, proximity had a possible effect on the pupil size of only one subject. In order to maintain constant target luminance at the various distances used, Marg and Morgan (1950) had the subjects view the targets through field stops and subjects were only fully aware of target distance before measurements began. Although a slight proximity cue during measurements may have been present due to slight blemishes on the surface of the target, the sensation of target proximity may have been weak.

The aim of this experiment was to investigate any influence on the pupil of dynamic size change acting as a proximity-only stimulus. The investigation used a target similar to that used by Kruger and Pola (1985, 1987) and McLin, Schor and Kruger, (1988) but accommodation was kept closed-loop by the use of a high contrast target to prevent changes in accommodation larger than depth-of-focus which would blur the target. Closed-loop accommodation was necessary to maintain a static mean accommodative level and to isolate any pupil response to the stimulus that occurred independent of accommodation response.

8.2 METHODS

The looming target consisted of a high contrast Maltese cross positioned centrally behind a variable-diameter circular aperture, the aperture being driven mechanically from an X-Y plotter using a triangular waveform derived from a frequency generator. Thus,as the aperture opened and closed, the apparent size of the target increased and decreased without any alteration in its shape. With the rest of the apparatus screened off and the laboratory in darkness, the size change in the target provided an illusion of movement in depth. Several trials showed that, subjectively, use of a triangular waveform at frequencies around 0.3Hz produced the most striking illusion.

An electroluminescent panel bulb was used to back-illuminate the target and provide even illumination across the surface of the target. The bulb consists of a thin, flat panel and provides even luminance over its surface and is capable of maximum luminance of 12cdm^{-2}. To counteract change in light output with variation in aperture size which would trigger pupil light reflex, the waveform used to drive the aperture was fed into the electroluminescent lamp 180 degrees out of phase to the size change, so that as the target size increased, the bulb dimmed. To ensure adequate control for light reflex effects, the maltese cross target was replaced with a featureless background to give the same mean luminance as the target. Following some adjustment, testing on 5 young subjects (mean age 25.8, SD 2.7) fixating a small, central fixation cross while the aperture size was varied showed that with this arrangement no significant light reflex occurred (see figure 8.2).

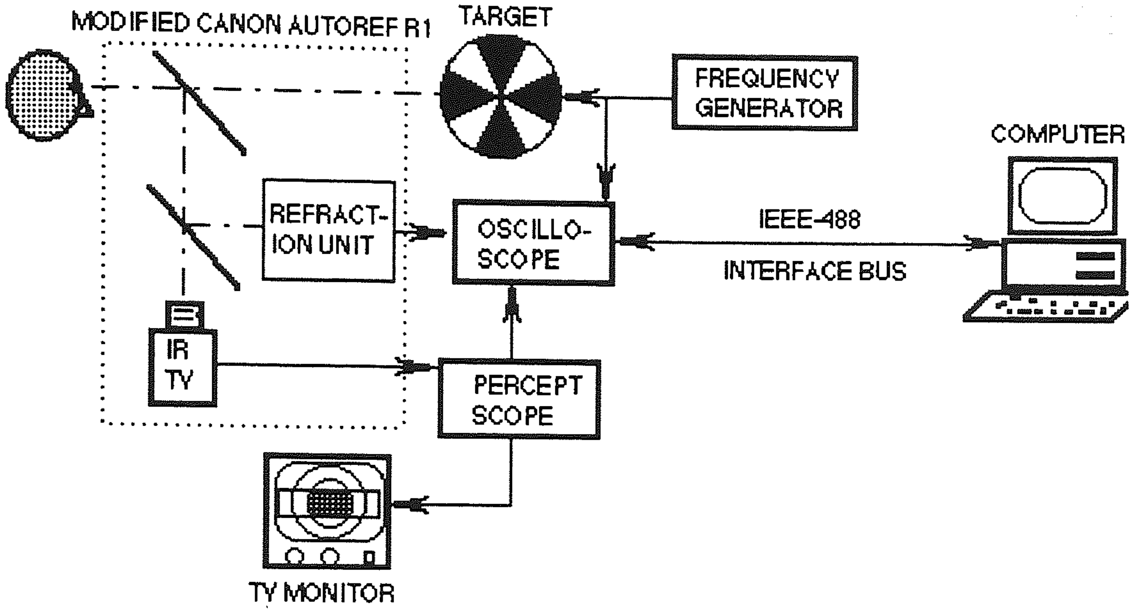


Figure 8.1 Schematic diagram of the apparatus used in the investigation.

As the aperture size varied, the diameter of the target changed by a factor of 2.5X. The target was viewed at a distance of 59cm and acted as a closed-loop stimulus to accommodation. To verify this, accommodation was recorded continuously using a modified Canon Autoref R1 infrared (IR) objective optometer. Pupil reponse was measured continuously and simultaneously using a Hamamatsu C3160 Percept Scope Video Area Analyser connected to the optometer (see Chapter 4 for details of instrumentation).

Outputs from the optometer and the Percept Scope and the stimulus waveform were fed into three channels of a four channel digital storage oscilloscope for storage and later transfer to the computer. Subjects were 5 young, visually normal members of the Aston Vision Sciences Department (3 male, 2 female, mean age 25.4 SD 3.0). Four were emmetropic and one

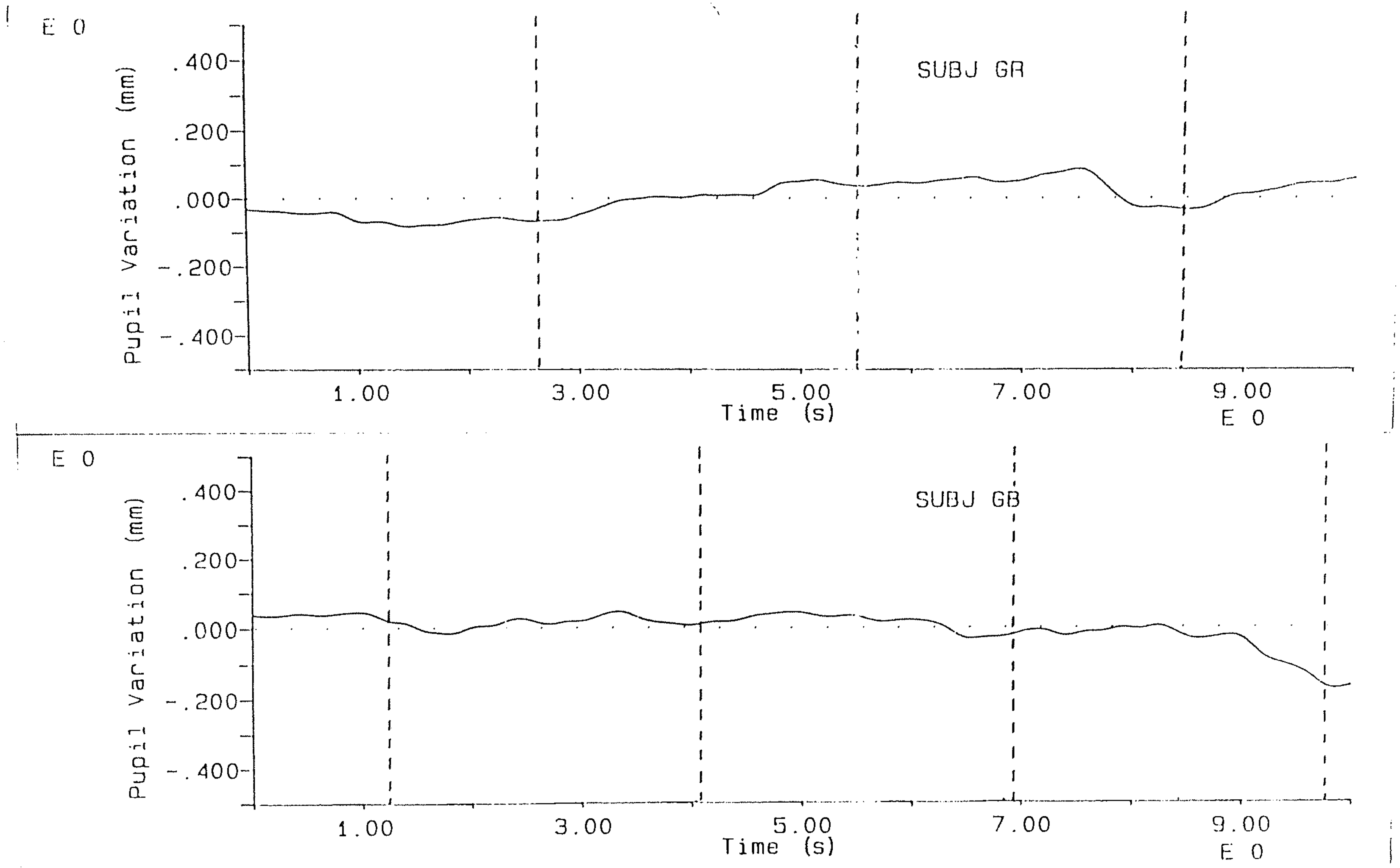


Figure 8.2 Continuous recordings of pupil diameter for subject GR (top plot) and GB (lower plot) viewing a featureless background while aperture size and luminance of the electroluminescent bulb were modulated using a triangular waveform at a temporal frequency of 0.3Hz. Note absence of pupil response. Traces smoothed to 5Hz.

(GB) wore soft contact lenses to correct low myopia. They were kept steady using a chinrest, dental bite and head restraint and were asked to fixate the centre of the target and maintain image clarity. The target aperture was initially driven at a frequency of 0.3Hz while pupil diameter, accommodation response and stimulus waveform were recorded. Subsequently, using the 4 subjects who were able to maintain image clarity, the aperture was also driven at frequencies of 0.1, 0.2, 0.4, and 0.5Hz and further recordings made.

8.3 RESULTS

In 4 out of the 5 subjects, periodic pupil responses could be demonstrated to the looming stimulus at the 0.3Hz stimulus temporal frequency (see figures 8.3 and 8.4). Closed-loop accommodation response displayed microfluctuations but no systematic response to the stimulus (see figures 8.3 and 8.4). The microfluctuations of accommodation had amplitudes of around 0.2D which is in agreement with previous reports (see Charman and Heron, 1988).

In one subject (GR), large amplitude (2-3D) accommodation responses occurred which were sufficient to overcome the constraint of blur. This subject found it impossible to keep the target clear and did not take part in further recordings.

Change in the stimulus temporal frequency resulted in change in the temporal frequency of pupil response (see figures 8.5 and 8.6). A systematic variation in the phase relationship of pupil response to the stimulus was found with change in the stimulus temporal frequency (see Figures 8.5, 8.6 and 8.7). A plot of phase lag against stimulus temporal frequency is shown in figure 8.7. Each point represents the mean of four stimulus cycles for each

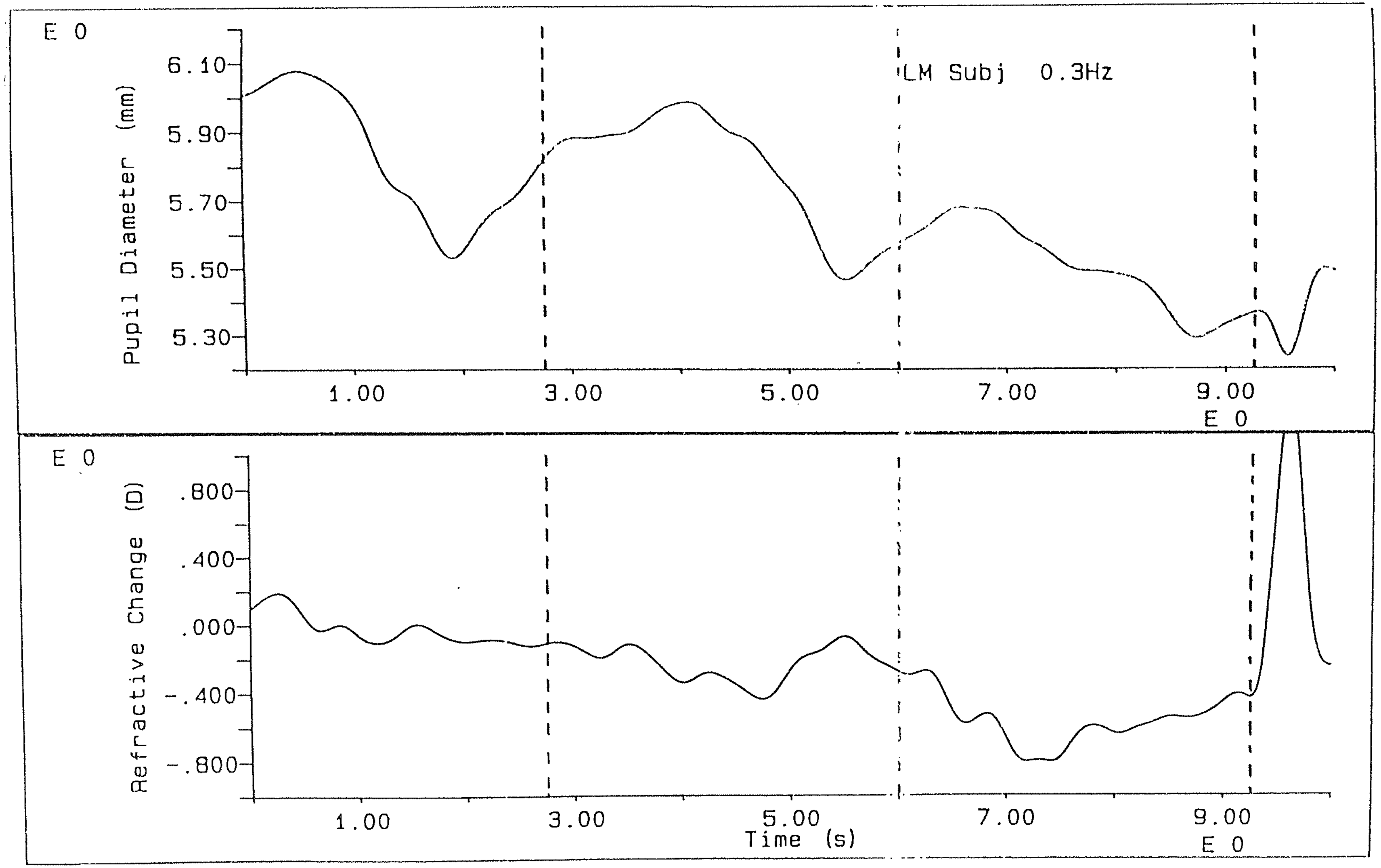


Figure 8.3 Simultaneous and continuous recordings of pupil diameter (top plot) and accommodation (lower plot) responses to the looming stimulus driven at a temporal frequency of 0.3Hz for subject LM. Vertical change upwards indicates increase in pupil diameter and increase in accommodative level. Vertical dotted lines indicate beginning (or end) of stimulus cycle i.e. target at its smallest size or appearing most distant. Traces smoothed to 5Hz.

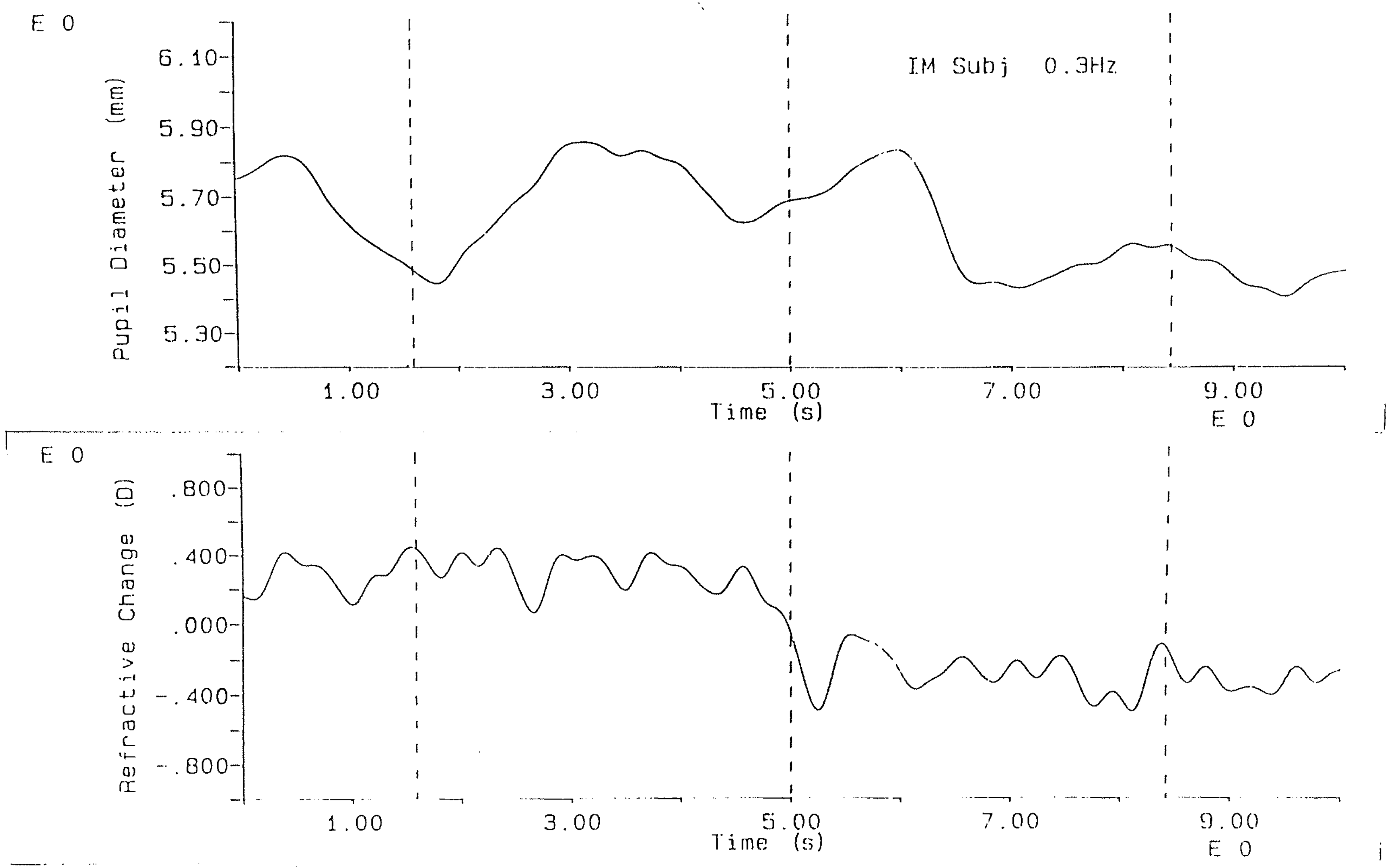


Figure 8.4 Simultaneous and continuous recordings of pupil diameter (top plot) and accommodation (lower plot) responses to the looming stimulus driven at a temporal frequency of 0.3Hz for subject IM. Vertical change upwards indicates increase in pupil diameter and increase in accommodative level. Vertical dotted lines indicate beginning (or end) of stimulus cycle i.e. target at its smallest size or appearing most distant. Traces smoothed to 5Hz.

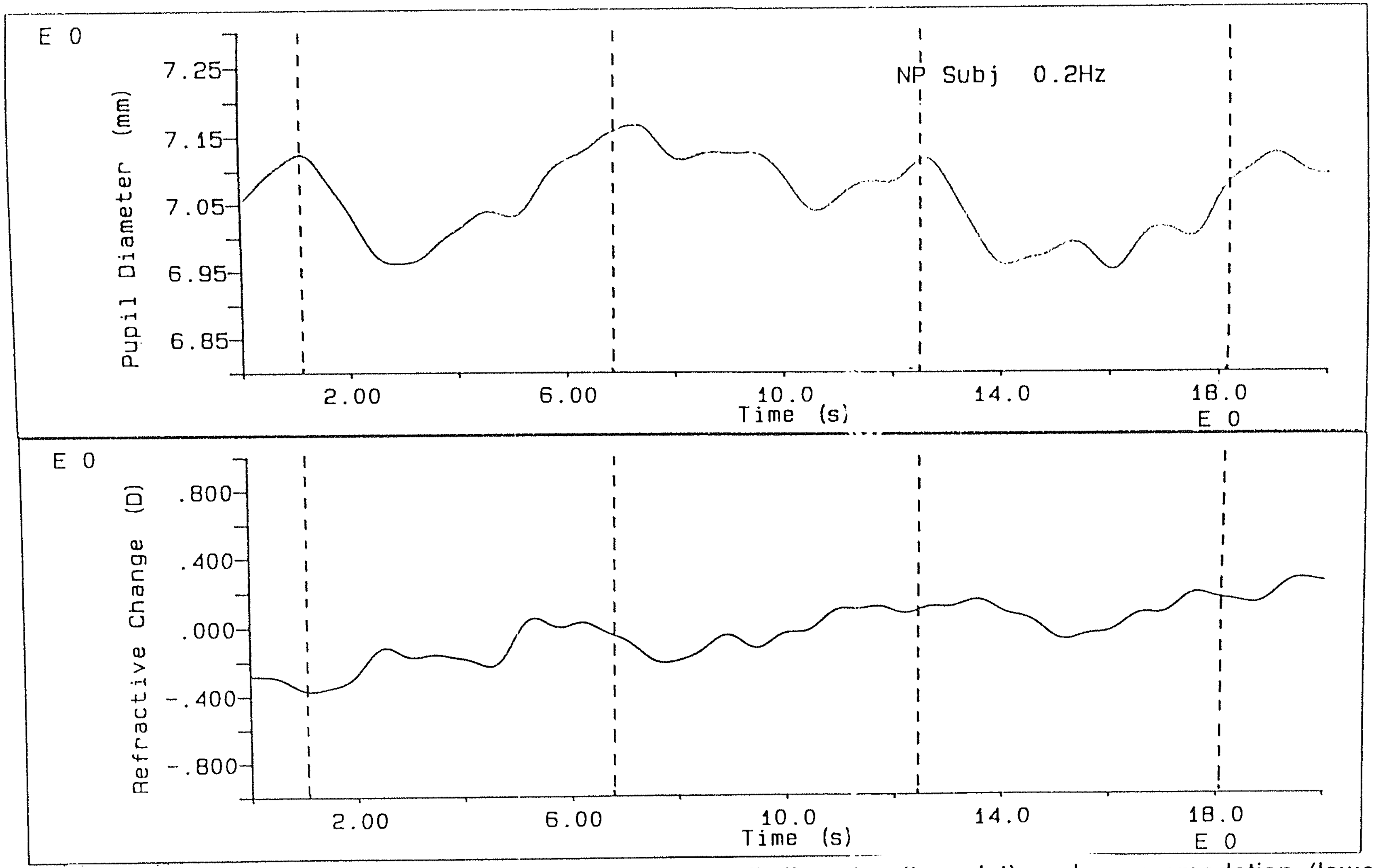


Figure 8.5 Simultaneous and continuous recordings of pupil diameter (top plot) and accommodation (lower plot) responses to the looming stimulus driven at a temporal frequency of 0.2Hz for subject NP. Vertical change upwards indicates increase in pupil diameter and increase in accommodative level. Vertical dotted lines indicate beginning (or end) of stimulus cycle i.e. target at its smallest size or appearing most distant. Note reduced phase lag compared to responses in figure 8.3 at 0.3Hz. Traces smoothed to 5Hz.

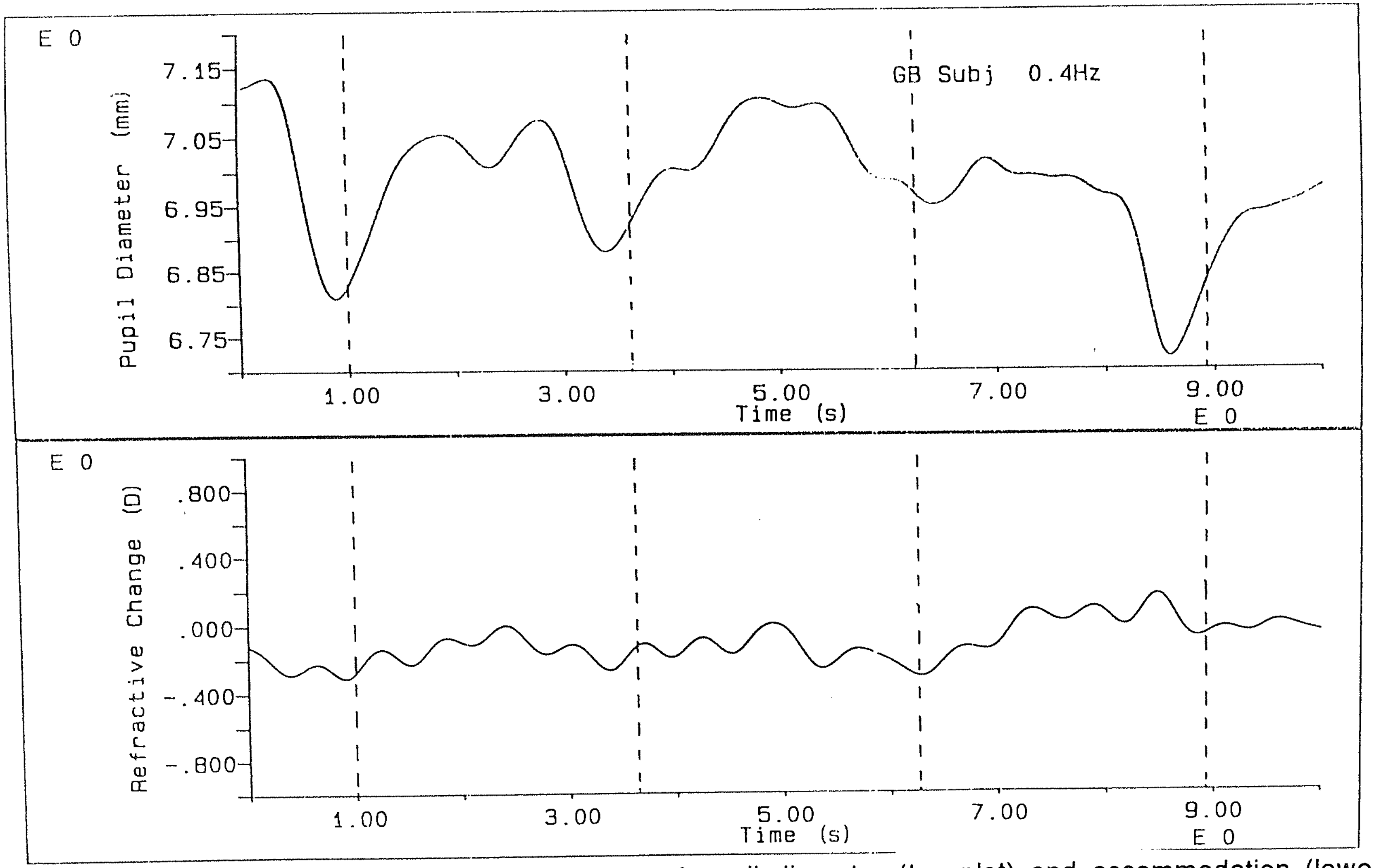


Figure 8.6 Simultaneous and continuous recordings of pupil diameter (top plot) and accommodation (lower plot) responses to the looming stimulus driven at a temporal frequency of 0.4Hz for subject GB. Vertical change upwards indicates increase in pupil diameter and increase in accommodative level. Vertical dotted lines indicate beginning (or end) of stimulus cycle i.e. target at its smallest size or appearing most distant. Note increased phase lag compared to responses in figure 8.3 at 0.3Hz. Traces smoothed to 5Hz.

observer at each frequency except at 0.1Hz where two stimulus cycles are used. There is no clear reason for the apparent reversal of trend in phase between 0.1 and 0.2Hz, although the slow change in target size at this frequency tended to produce a poorer illusion of movement in depth than that which occurred at the higher frequencies. The amplitude of pupil response showed no systematic variation with stimulus temporal frequency.

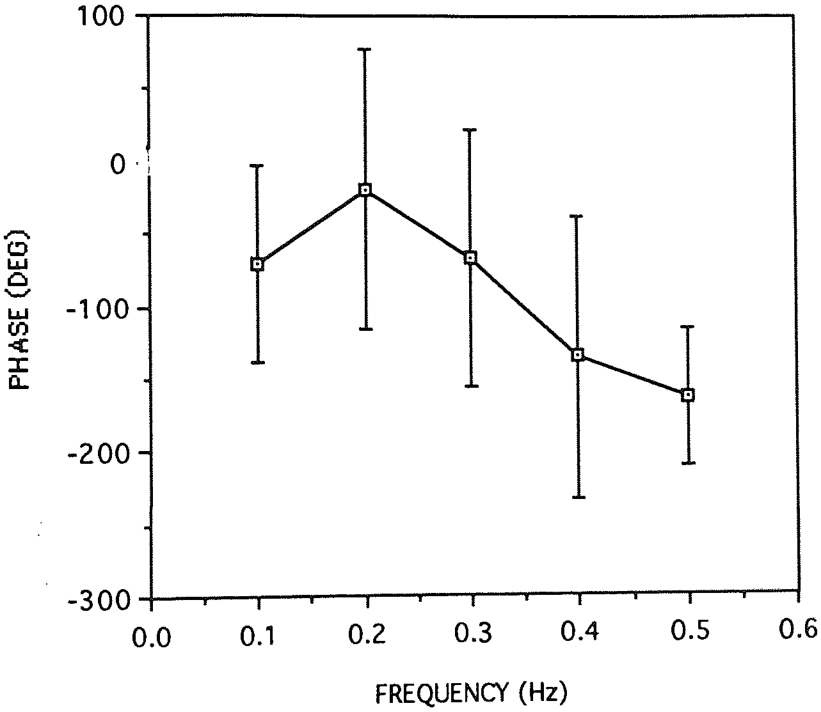


Figure 8.7 Plot showing phase lag of pupil response against stimulus temporal frequency. Results are the mean for 4 stimulus cycles at each frequency for each of the 4 observers.

8.4 DISCUSSION

The present experiment has demonstrated that pupil response can be independent from accommodation response when an inferred-proximity cue is created using illusory movement in depth. This supports the findings of Stakenburg (1991), Phillips, Winn and Gilmartin (1992) and those reported in Chapters 5, 6 and 7 of this thesis, that is, blur-driven accommodation alone may not be sufficient to drive pupil near response and that other factors may be involved. Marg and Morgan (1950) found only a small effect in one out of seven subjects attributable to awareness of target proximity which may be because the sensation of target proximity was weak in their experiment due to the subject only being fully aware of target distance before and not during measurements. Also Marg and Morgan (1950) used static targets and it may be that dynamic change in perceived depth is necessary to elicit pupil response.

In one subject the illusion was strong enough for the size change cue to accommodation to override blur and drive accommodation to the detriment of image clarity. Previous investigators (Kruger and Pola 1985, 1986, 1987, 1989, McLin, Schor and Kruger, 1988) have demonstrated the potency of size change as a cue to open-loop accommodation response. Ittleson and Ames (1950) also reported changes in closed-loop accommodation to dynamic size change of a target which was sufficient to cause blurring. Thus it would appear that size change as a cue can be more potent as a stimulus to accommodation than blur and when the two cues are placed in conflict, size change may override blur to the detriment of image clarity. To demonstrate pupil response to dynamic size change in the absence of accommodative change thus depends on the subjects being able to maintain a steady accommodative level which may be a facility restricted to trained observers. Despite the use of a target providing a closed-loop stimulus to accommodation in this experiment, accommodation is never static and always displays microfluctuations of the order of 0.2D. The pupil responses found in this experiment may have occurred within an accommodation dead zone, and accommodative change may be needed to elicit larger and more reliable responses.

Recent publications (North, Henson and Smith, 1992, Schor et al , 1992a, 1992b) have placed emphasis on the importance of proximal cues in accommodation and vergence responses. Schor *et al* (1992a, 1992b) consider that spatiotopic (body referenced) cues giving rise to awareness of target proximity may act as the initial stimulus to the accommodation and vergence mechanisms and trigger a large, open-loop primary reponse. Following this primary response, retinotopic (eye referenced) cues such as blur and disparity act as stimuli to small, closed-loop response which refine the initial response and are subsequently responsible for the maintenance of a clear, single image of the stationary target. The role of pupil response has not been considered, and further investigation is needed into the contribution of pupil response to image clarity to determine how pupil response may fit into the model proposed by Schor *et al* (1992a, 1992b).

A criticism of this experiment is that local spatial changes in retinal illumination without change in mean illumination can influence the pupil (Ukai, 1985, Barbur and Forsyth, 1986) and may have been a contaminating factor. Although light reflex effects were controlled for, this may not have been an adequate control once the target was in place. Unfortunately, spatial changes in retinal illumination will be a factor in all experiments involving size change as indeed they will be in pupil near response in the normal visual environment. To separate totally light reflex effects from near response effects may therefore be impossible. More sophisticated apparatus possibly using computer-generated images would allow further investigations into the effect of proximity cues on the pupil. Of particular interest would be the effect of large depth changes which are cited by Schor *et al* (1992b) as an initial cue to the accommodation and vergence mechanisms.

SUPPORTING PUBLICATIONS

Phillips, N. J., Gilmartin, B. and Winn, B. Evidence for discrete pupil response synchrony with periodic variation in target size (looming). *Invest. Ophthalmol. Visual. Sci.* **33** (suppl.) 1148 (1992).

Phillips, N. J., Gilmartin, B. and Winn, B. Pupil response to periodic variation in target size (looming). *Ophthal. Physiol. Opt.* **12**, 501 (1992).

CHAPTER 9

PUPIL DIAMETER DURING A NEAR VISION TASK

9.1 INTRODUCTION

The literature relating to the function of the pupil constriction that accompanies accommodation and convergence during near vision was reviewed in Chapter 2. It is usually stated that increased depth-of-focus is achieved through pupil constriction at near (e.g. Toates, 1968, Phillips, Krishnan and Stark, 1975, Charman, 1983, Hung, Semmlow and Ciuffreda, 1984) and it has also been proposed that the increased depth-of-focus allows moderation of accommodative effort by increasing tolerance to optical defocus (Phillips, Krishnan and Stark, 1975, Toates, 1968, Charman, 1983). Schematic models of the near vision response triad often include a feedback loop from pupil to accommodation to account for the effect on accommodation of depth-of-focus (e.g. Phillips, Krishnan and Stark, 1975). Pupil size has also been shown to effect the microfluctuations of accommodation that are present even during fixation of a static target. It is well documented (for review see Charman and Heron 1988) that the microfluctuations are characterised by a low frequency component (LFC, less than 0.6Hz) and a high frequency component (HFC, between 1.0 and 2.3Hz) with amplitude around 0.2D. In a recent study, Gray and Winn (1992) investigated the effect of pupil size on accommodative microfluctuations and found that the magnitude of the LFC increased as pupil size decreased. They consider that the increased magnitude of the LFC is a result of the increased depth-of-focus associated with smaller pupils and that this is evidence that the LFC is used to control steady-state accommodation. No change in the HFC with pupil size was found. Although these findings are in agreement with previous studies, Charman and Heron (1988) consider that there is insufficient evidence to definitely ascribe an accommodative control function to the LFC which could alternatively represent instability in the accommodation control system.

Most studies show that at pupil diameters above 3mm, depth-of-focus (Campbell, 1957, Tucker and Charman, 1975, Charman and Whitefoot, 1977) and contrast sensitivity (Legge *et al*, 1987, Kay and Morrison, 1987) are relatively insensitive to change in pupil size. Ripps *et al* (1962) measured the accommodative response to a range of accommodative stimulus levels viewed through artificial pupils of diameters between 3.0 and 0.5mm. They showed that pupil diameter must drop below 1.5mm before any reduction in accommodative level could be recorded. Similar results are shown by Hennessy *et al* (1976) and Ward and Charman (1987).

Schafer and Weale (1970) investigated the pupil diameter associated with a range of accommodative stimulus levels at two luminance levels and in four age groups. Their data show that at accommodative stimulus levels of 3D, their pre-presbyopic observers had pupil diameters above 3mm at both luminance levels. Roth (1969) demonstrated that for a given accommodative stimulus level, pupil diameter increases as illumination is reduced and suggests, as did Schafer and Weale (1970) that the pupil near reflex and the light reflex are mutually antagonistic. However, it is known (Johnson, 1976) that as luminance decreases, depth-of-focus increases as accommodative level has less effect on retinal image quality. Therefore the light reflex and near reflex cannot be truly considered antagonistic as the balance achieved between the two systems may act to optimise visual function.

Campbell and Gregory (1960) and Woodhouse (1975) investigated the optimum pupil size for maximum visual resolution at a range of luminance and contrast levels. The data in both studies indicated that the actual pupil diameter occurring naturally at any given luminance level closely approximates that which gives highest resolving power. Campbell and Gregory (1960) used near targets and correcting lenses to relax accommodation and found that at a luminance level close to 100cdm^{-2}, a 3mm diameter pupil was optimum. Woodhouse (1975) also used near targets but makes no mention of accommodative level although results were similar to those of Campbell and Greory (1960) and optimum pupil diameter of between 2 and 4mm was found at a similar luminance level for high contrast targets.

Recent findings (Tsuchiya, Ukai and Ishikawa, 1989, Stakenburg, 1991, Phillips, Winn and Gilmartin, 1992) have indicated that the links between accommodation and pupil responses may be weaker than previously believed and thus the role of pupil constriction during near vision requires further investigation. For any clear interaction to occur between pupil size and accommodation during near vision, pupil diameter would need to be maintained well below 3mm. No data has been found which gives the actual pupil diameters occurring during a commonly-encountered and sustained near vision task such as reading and it is not possible to determine what benefit is gained by pupil constriction during near vision without this information. The lack of data on pupil diameter under naturalistic conditions is surprising given the importance of pupil diameter to the success of single vision, cosmetic tinted and, particularly, bifocal contact lenses (Borish, 1988, Phillips, 1990, Benjamin and Borish, 1991, Terry, Guillon and Chissadon, 1992).

This experiment aimed to investigate the pupil diameters of young and elderly subjects who undertook a reading task under controlled illumination over a 5 minute period. The young subjects were used to represent efficient oculomotor function before detriment due to the effects of ageing. Elderly subjects were used to assess any contribution made to near vision by the pupil in the absence of active accommodation.

9.2 METHODS

Ten young (mean age 21.0 SD 0.94, 6 female, 4 male) and ten elderly (mean age 74.5 SD 6.6, 5 male, 5 female) subjects took part in the study. The young subjects were undergraduate students in the Vision Sciences Department at Aston University and were all visually normal and in good health. Those who were ametropic wore their normal distance correction in the form of contact lenses or spectacles. The elderly subjects were taken from the undergraduate training clinics which they attend as paid subjects to allow the undergraduate students to practise refraction techniques. Those used in this experiment had at least 6/9 corrected acuity in each eye, no ocular pathology and were in good health for their age. During the near vision task, the elderly subjects wore single vision reading spectacles if they had them or a pair of +2.75D single vision over-readers taken from a *Varilux* trial set on top of their distance correction.

The subjects were seated comfortably and placed in the chin rest of the Canon Autoref R1 optometer. Printed text (high contrast, 12 point black figures on a white background) was placed in a stand on top of the optometer at a distance of 35cm from the subjects' eyes. A constant luminance of 100 cdm^{-2} was maintained using an anglepoise lamp. This luminance was chosen as being slightly above the average taken from readings in the University library and at several points around the Vision Sciences building in addition to being well above the level necessary to ensure full and accurate accommodation response (Johnson, 1976). Measurements of luminance were taken from the text using a Minolta hand-held photometer.

Pupil diameter was measured from the image of the RE on the TV monitor connected to the optometer. Readings of pupil diameter were taken directly from the screen using electronic calipers and were later divided by 8.2 to correct for image magnification on the screen (see Chapter 4). A correction factor was applied to account for the magnification or minnification caused by any spectacle lenses worn. This technique was adopted rather than using the Hamamatsu C3160 Percept Scope Video Area Analyser which has been used in the previous experiments described in this thesis. Pupil diameter measurements with the

Percept Scope connected to the optometer have been found to be possible only with certain iris colours leading to the rejection of many possible subjects. Hence an alternative technique was chosen to allow measurements to be taken on all the required subjects. To ensure the validity of this technique, a series of window widths was created on the TV monitor and measured both with the Percept Scope and with the electronic calipers. Each measure was repeated four times and the results averaged and plotted. These results are shown in figure 9.1 and demonstrate close correlation between the two techniques. Standard deviation was of the order of 0.08mm.

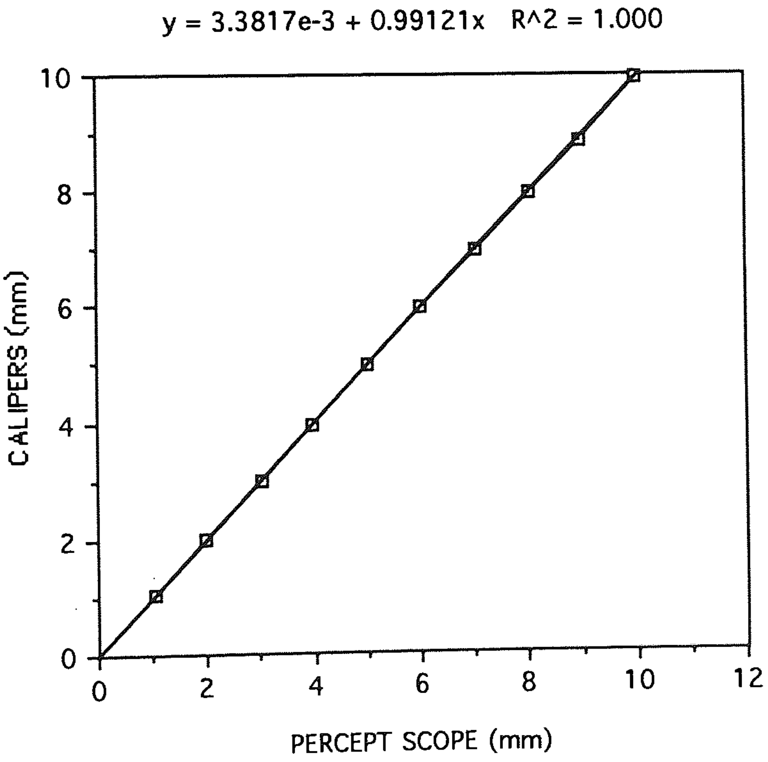


Figure 9.1 Comparison of the measurement results obtained using the electronic calipers to measure pupil diameter directly from the TV monitor screen and those obtained using the Percept Scope to measure pupil diameter from the TV signal derived from the optometer.

Subjects viewed the text binocularly and horizontal pupil diameter measurements were taken from the RE. In view of the consensuality of pupil responses, it can reasonably be assumed that the results represent the pupil diameter of both RE and LE. Each subject read the prepared text for a period of 5 minutes and pupil diameter was measured every 30 seconds as determined using a stop-clock. Subjects indicated when they had finished reading a page of the text and the next page was then introduced. To ensure accommodative response in the young subjects, 5 readings of refractive level were taken using the Canon Autoref R1 in static mode with the subject viewing first a distance target and then the text. The elderly subjects were all above 55 years of age and can therefore be safely considered to have no active accommodation (Charman, 1983, Ramsdale and Charman, 1989).

9.3 RESULTS

All the subjects reported that they had found the text easy to read both in terms of clarity and comprehension. The ten young subjects all showed accommodative response to the text with a mean amplitude of response of 2.42D (SD 0.53D) as compared to the accommodative stimulus of 2.86D. This response lag is in agreement with the previously reported accommodative lag at near (Toates, 1972, Charman, 1983, Ramsdale and Charman, 1989). The pupil results for the 10 young subjects are shown in figure 9.2. and represent the mean pupil diameter and standard deviation at each of the 30 second intervals starting at time 0 when the reading task began. Overall group mean pupil size over the entire task period for the ten subjects was 3.64mm.

The minimum individual mean pupil diameter was 3.16mm and thus all the young subjects displayed mean pupil diameters greater than the 3mm diameter below which a significant increase in depth-of-focus would be obtained. In only 2 subjects was pupil diameter ever below 3mm at any point during the experiment and for those 2 subjects the mean diameter over the five minute period was above 3mm. In one subject, pupil diameter was never below 4mm throughout the experiment (see figure 9.3).

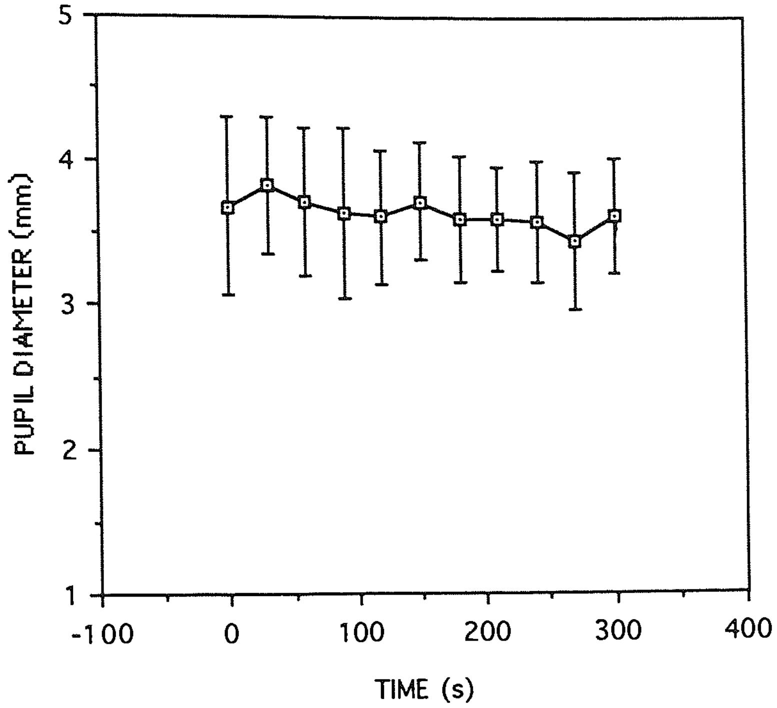


Figure 9.2 Mean pupil diameter plotted against time during the reading task for the group of 10 young subjects. Error bars indicate +/-1SD of the mean.

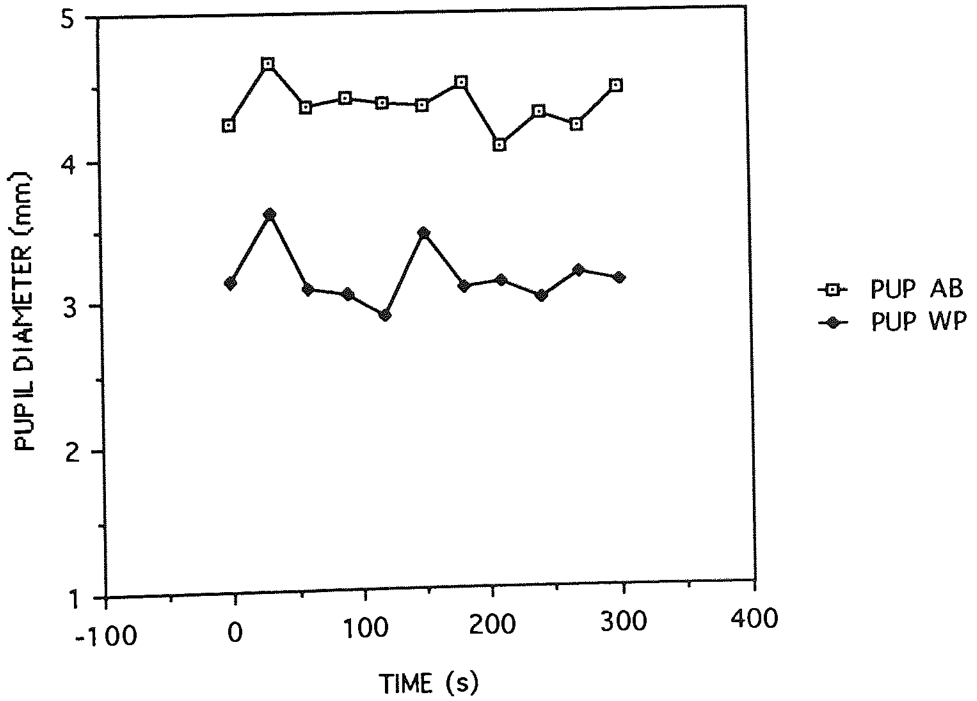


Figure 9.3 Individual results for the young subject with the largest overall mean pupil diameter (4.36mm, AB shown in top plot) and the subject with the smallest overall mean pupil diameter (3.16mm, WP shown in the lower plot).

Pupil results for the 10 elderly subjects are shown in figure 9.4 and represent the mean at each 30 second time interval with the standard deviation. Pupil diameters were mostly below 3mm and ranged from means of 1.51mm and 3.93 (see figure 9.5). Overall group mean pupil size was 2.61mm.

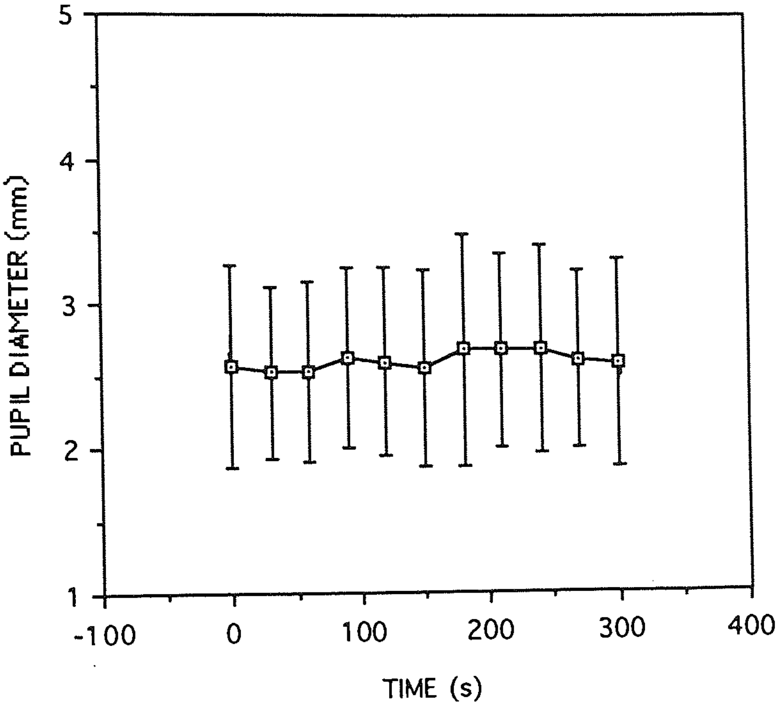


Figure 9.4 Mean pupil diameter plotted against time during the reading task for the group of 10 elderly subjects. Error bars indicate +/-1SD of the mean.

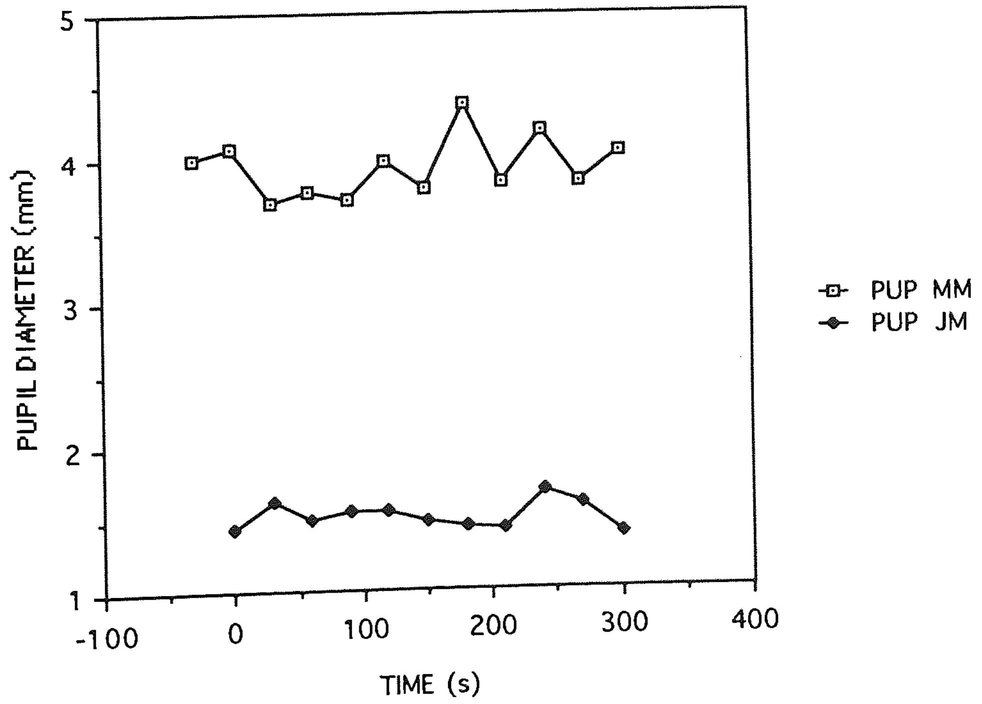


Figure 9.5 Individual results for the elderly subject with the largest overall mean pupil diameter (3.93mm, MM shown in top plot) and the subject with the smallest overall mean pupil diameter (1.51mm, JM shown in the lower plot).

9.4 DISCUSSION

For the ten young subjects used in this study, mean pupil diameter was well above 3mm throughout the five minute reading task. The range of pupil sizes was too large therefore to have any significant effect on depth-of-focus. Although higher luminance of the text may have resulted in smaller pupil diameters, it was considered that the luminance chosen was appropriate and all subjects found the text easy to read. Hence the only clear effect of the pupil constriction associated with near vision tasks is to reduce retinal illumination and any optical benefits may be minor.

In view of these results, interaction between pupil diameter and the accommodation system therefore seems unlikely as in the absence of increased depth-of-focus, no moderation of accommodative level would be possible. The feedback loop carrying depth-of-focus information from the pupil to accommodation often shown in models of the near vision triad would therefore seem to be superfluous.

Campbell and Gregory (1960) and Woodhouse (1975) found that pupil diameters of 3mm and 2-4mm respectively gave maximum resolution of high contrast targets at a luminance level similar to that used in this study. These ranges encompass the pupil diameters found in the young subjects in this investigation. Campbell and Gregory (1960) and Woodhouse (1975) suggested that the role of the pupil light reflex is to set pupil diameter such as to maximise acuity at varying light levels. It may be that the pupil diameter during a near vision task is related more closely to maximising resolution than to increasing depth-of-focus. Reflex constriction may occur during near vision tasks as it seems likely that they almost always require greater resolution than distance tasks.

For the elderly subjects, pupil diameter was generally below 3mm and thus would act to increase depth-of-focus for most of them. Although this may be of some advantage, it may only be a chance benefit from the smaller pupil associated with age and does not apply to all individuals. Any advantage may be outweighed by the reduction in retinal illumination and it is known that elderly people have lower retinal sensitivity and benefit from increased illumination during reading (Rumney, 1992). A recent study investigated the effects of pupil dilation carried out on patients to facilitate ophthalmoloscopic examination (Montgomery and MacEwan, 1989). The authors reported that none of the presbyopic subjects had any difficulty reading with their reading glasses on once their pupils were dilated and therefore seemed to suffer no detriment when the increased depth-of-focus caused by small pupils was removed.

The age trend in pupil diameter was highly significant (student t-test, p<.001) and supports previous studies suggesting that pupil size decreases with age (see Chapter 2 for review). A further study (Winn, Whitaker and Phillips and Elliott, in preparation) gives further evidence of significant age-related decline in pupil diameter at a range of luminance levels. However, considerable overlap occurs and a wider range of pupil diameters was found in the elderly compared to the young subjects. This may be because the reduced pupil diameters found in elderly persons represent a detrimental effect of ageing which affect different individuals to different degrees.

In conclusion, this study indicates that little or no benefit is gained from the pupil constriction occurring during near vision tasks. Further investigation is needed to clarify the role of the pupil in the near vision triad. There is a paucity of data available on pupil size under naturalistic task conditions and further data would be of great benefit to the designers of vision aids such as bifocal contact lenses as well as aiding attempts to model oculomotor function and to assess the optical contribution to the decline of visual function with age.

CHAPTER 10

AN INVESTIGATION OF PUPIL AND ACCOMMODATION RESPONSES TO A TEMPORALLY-MODULATED ACCOMMODATIVE STIMULUS

10.1 INTRODUCTION

The accommodation response to temporally-modulated accommodative stimuli has been extensively investigated under both open-loop and closed-loop conditions (e.g. Campbell and Westheimer, 1960, Randle and Murphy, 1974, Phillips, Krishnan and Stark, 1975, Kruger and Pola, 1985, 1986, 1987, 1989, McLin, Schor and Kruger, 1988, Sun *et al*, 1989). A variety of stimulus configurations designed to include one or more cues to accommodation have been used to investigate the frequency characteristics of accommodation response and the relative importance to accommodation response of, for example, blur, size change and chromatic aberration. In contrast, only one study has been found which reports the effect on pupil near response of a stimulus temporally-modulated at a range of frequencies (Phillips, Krishnan,and Stark, 1975). Phillips, Krishnan and Stark (1975) studied the frequency response characteristics of eight oculomotor systems including blur-driven accommodation and accommodation-driven pupil response. To stimulate accommodation, a target was viewed through a Badal stimulus optometer and accommodation and pupil responses recorded using a single subject as the target was sinusoidally-modulated at a range of temporal frequencies. No details of the target or accommodative stimulus range used are given by Phillips, Krishnan and Stark (1975) although the use of a Badal stimulus optometer would have eliminated size change as the target moved. Their results showed that what they termed accommodation-pupil response showed a small phase lag to accommodation response at all but the lowest frequencies. This would be consistent with the view that pupil near response is driven by accommodation.

In Chapter 2 the literature relating to pupil near response was reviewed and it was shown that it is widely believed that pupil near response is driven by either the accommodation or vergence systems. It is difficult to separate the effects of the two systems due to their close synergistic links (Myers and Stark, 1990). Recent investigations, however, have demonstrated that under certain conditions, substantial changes in accommodation can take place without concomitant pupil response and thus have questioned the previously accepted tight coupling between accommodation and pupil response (Tsuchiya, Ukai and Ishikawa, 1989, Stakenburg, 1991, Phillips, Winn and Gilmartin, 1992). Stakenburg (1991) and Phillips, Winn and Gilmartin (1992) have shown that if all cues other than blur are excluded from an accommodative stimulus, then pupil near response may be absent even though accommodation response is maintained.

It has been shown that size change is an important cue to accommodation reponse (Kruger and Pola, 1985, 1986, 1987, 1989, McLin, Schor and Kruger, 1988) and may act as a cue to pupil response (Phillips, Gilmartin and Winn, 1992). Hence the present study used an accommodative target containing all cues in order to provide optimum, naturalistic conditions for accommodation and pupil responses. A Maltese cross target was modulated along the visual axis of the subjects' RE using a triangular waveform at a range of frequencies over an accommodative stimulus range of 2.25D. Accommodation, pupil responses and the stimulus waveform were recorded simultaneously and continuously and the phase and gain of the responses relative to the stimulus assessed. The hypothesis was that if pupil response is primarily accommodation-driven, phase and gain of pupil response relative to the stimulus should mirror phase and gain of accommodation response across a range of frequencies. Results show, in fact, that this is not the case.

10.2 METHODS

Five young subjects were used in this study (3 male, 2 female, mean age 25.0 yrs, SD 3.5), all were emmetropic having at least 6/6 uncorrected acuity in each eye, normal binocular vision and were in good health. The target used was a slide transparency of a Maltese cross mounted onto an X-Y plotter connected to a frequency generator. A triangular waveform from the frequency generator was used to drive the target over an accommodative stimulus range of 2.25D (from -5D to -2.75D) at frequencies of 0.1, 0.2, 0.3, 0.4, and 0.5Hz. Subjects viewed the target and were asked to keep it as clear as possible as it moved. Illumination was provided by directing the light from an anglepoise lamp onto a white wall behind the target system and allowing the reflected light to back-illuminate the target providing luminance of 40 cdm^{-2}. A check was made prior to each experimental trial to ensure absence of pupil light reflex by moving the target while the subjects maintained fixation on the wall beyond. No optical system was used and therefore cues of blur and size change were both present as part of the predictable, repetitive stimulus.

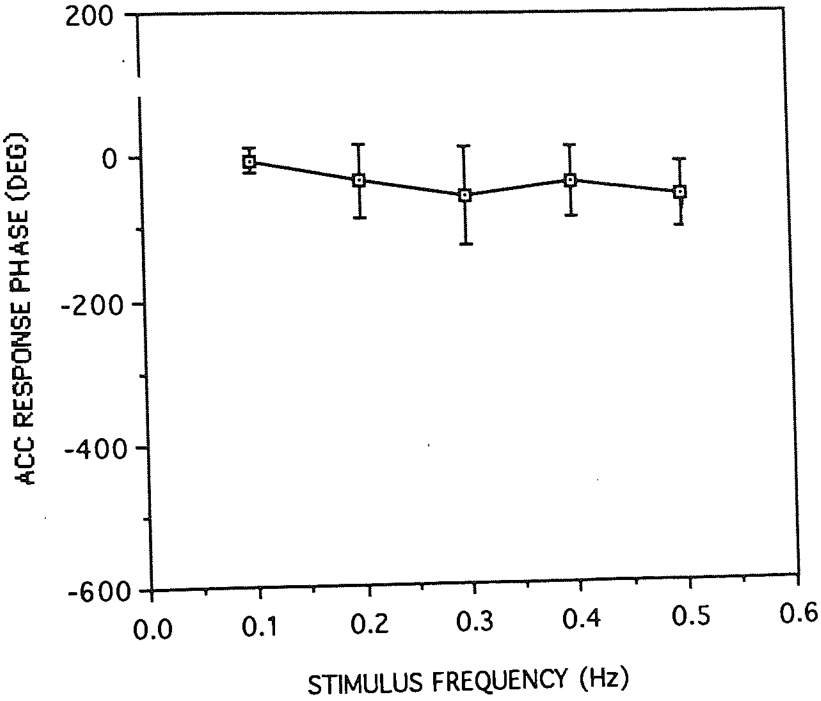
Accommodation and pupil responses were recorded continuously and simultaneously using the modified Canon Autoref R1 and the Hamamatsu C3160 Percept Scope as described in Chapter 4. Accommodation and pupil responses and stimulus waveform were fed into three channels of a digital storage oscilloscope for storage and later transfer to the IBM-clone desktop computer. Prior to experimental trials, an accommodation calibration run was recorded for each subject as described in Chapter 4. Pupil zero level was recorded at the same time. All recordings were made from the subjects' RE with the LE occluded.

The stimulus temporal frequencies were presented in random order and the time base used on the oscilloscope was varied to ensure that at least four complete stimulus cycles were recorded at each frequency for each subject. Subjects were kept steady using chin rest and dental bite and were given frequent breaks to maintain pupil diameter above the 3.9mm needed for continuous accommodation recording (see Chapter 4). The recordings made were later analysed and the gain and phase values of accommodation and pupil reponses relative to the stimulus derived. Amplitude and phase values were measured from the original recordings following smoothing to 5Hz and with the assistance of an overlaid grid. Phase lag or lead was taken from the point of maximum accommodation response and maximum pupil constriction compared to the point of maximum accommodative stimulus. This process was made somewhat easier by the use of a triangular stimulus waveform which allows peaks of stimulus and response to be determined more easily than is the case with a sine wave. To allow comparison between accommodation and pupil, a gain of 1 was allocated to the highest mean amplitude of response which occurred at 0.1Hz for both accommodation and pupil.

10.3 RESULTS

Accommodation findings were in agreement with previous studies in which predictable, repetitive, closed-loop accommodative stimuli were used (e.g. Kruger and Pola, 1986, 1987, Sun *et al* 1989). Figure 10.1 shows response gain and phase plotted against stimulus temporal frequency. Each point represents the mean of twenty reponses (four stimulus cycles for each of the five observers). Accommodation response is phase-locked to the stimulus by the closed-loop constraint of blur and thus shows only a small mean phase lag at all the stimulus frequencies used. Although some reduction of gain occurs with increasing stimulus frequency, the use of well-trained subjects gives relatively high gain even at 0.5Hz.

Pupil response showed a systematic increase in phase lag and decrease in gain (see figure 10.2) relative to the stimulus as temporal frequency increased. A comparison of the phase plots for accommodation and pupil response shows that whilst at 0.1Hz they appear closely correlated (see figures 10.3 and 10.4), pupil



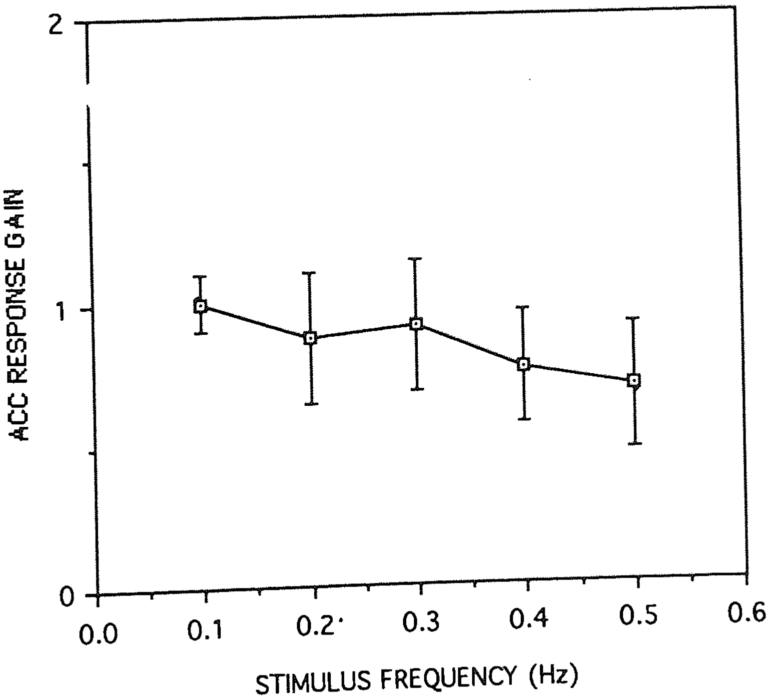
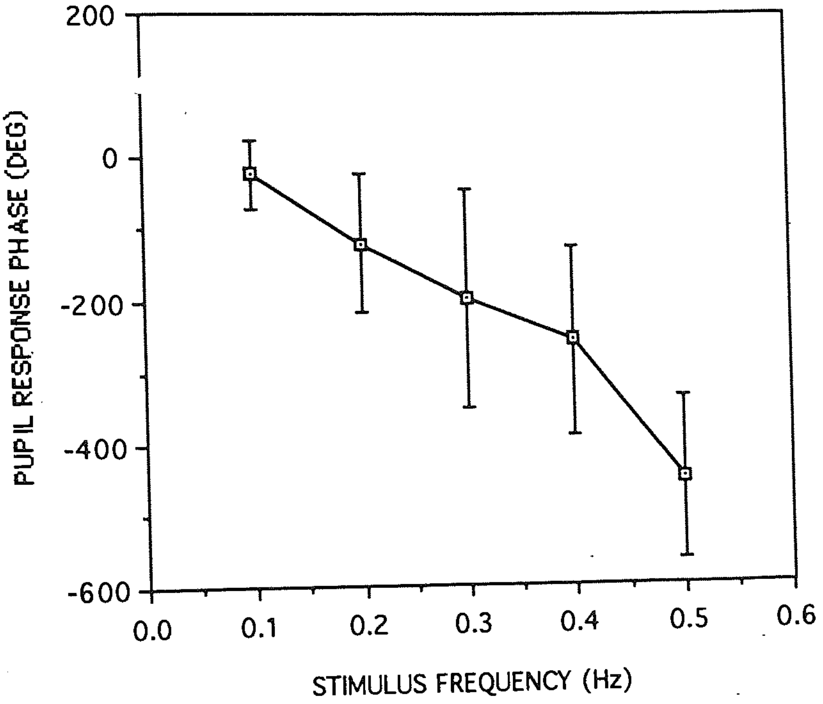


Figure 10.1 Plots showing relationship between mean phase (top) and mean gain (bottom) of accommodation response and stimulus temporal frequency. A gain of 1 was allocated to the highest mean amplitude of reponse which occurred at 0.1Hz. Error bars indicate +/- 1SD of the mean.



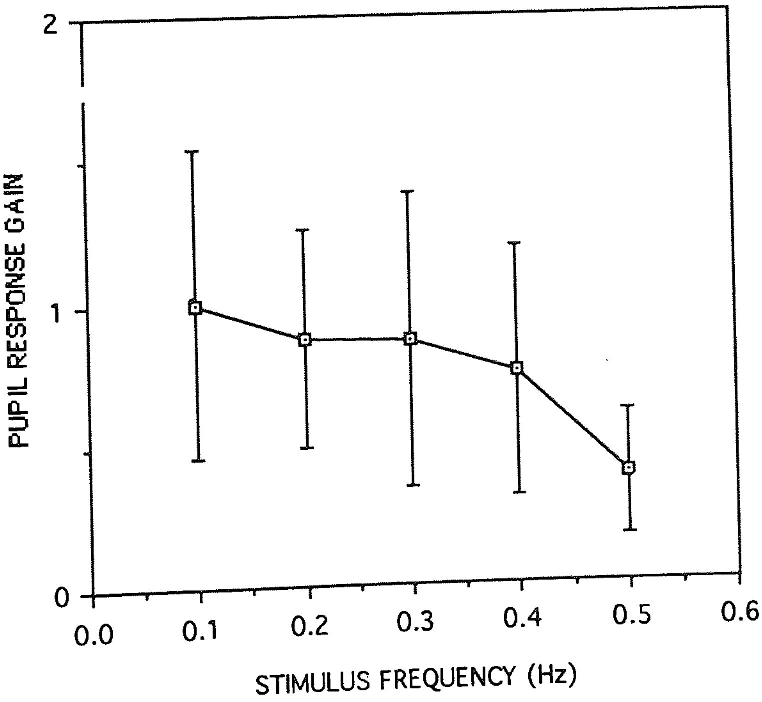


Figure 10.2 Plots showing relationship between mean phase (top) and mean gain (bottom) of pupil response and stimulus temporal frequency. A gain of 1 was allocated to the highest mean amplitude of reponse which occurred at 0.1Hz. Error bars indicate +/- 1SD of the mean.

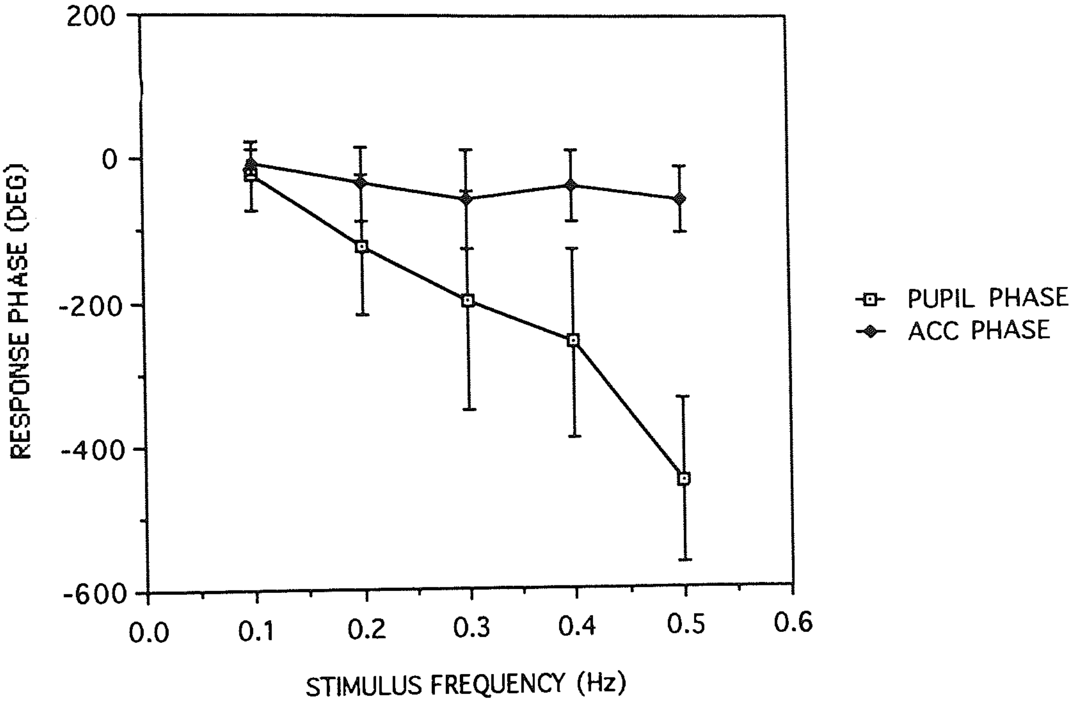


Figure 10.3 Plot showing phase of accommodation and pupil responses relative to stimulus temporal frequency.

response increasingly lags behind both the stimulus and accommodation response as the stimulus temporal frequency increases (see figures 10.3, 10.5 and 10.6).

Figures 10.4, 10.5 and 10.6 show individual results for one subject illustrating pupil and accommodation responses at 0.1Hz, 0.2Hz and 0.3Hz. The variabilty of both gain and phase was much greater for pupil reponse than accommodation response and observation of the individual recordings showed instances of pupil response showing a phase lead compared to accommodation (see figure 10.7).

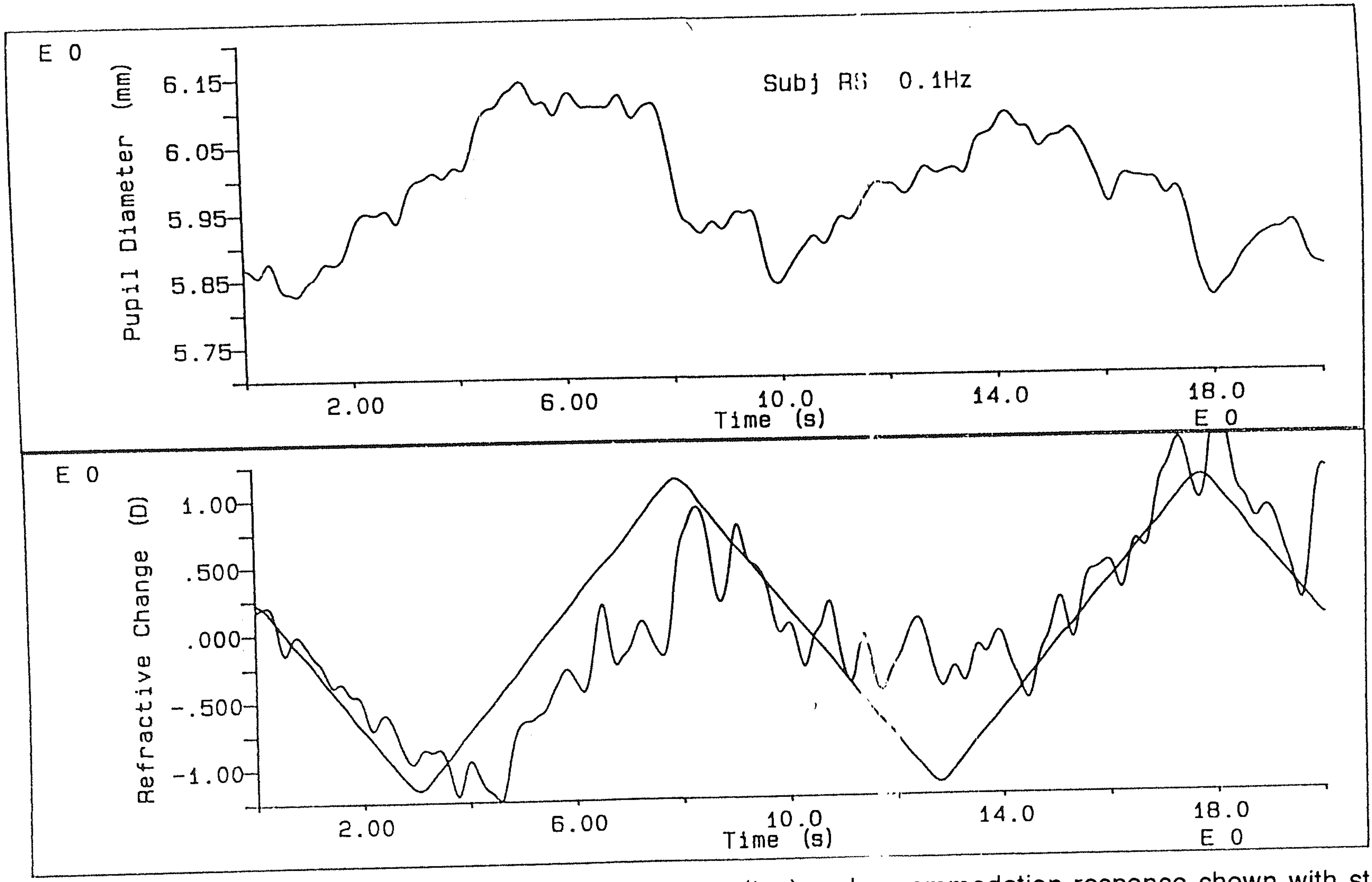


Figure 10.4 Simultaneous, continuous recording of pupil response (top) and accommodation response shown with stimulus waveform (bottom). Accommodation is shown as variation about mean level. Traces smoothed to 5Hz. Shown are results at 0.1Hz over a period of 20 seconds for subject RS.

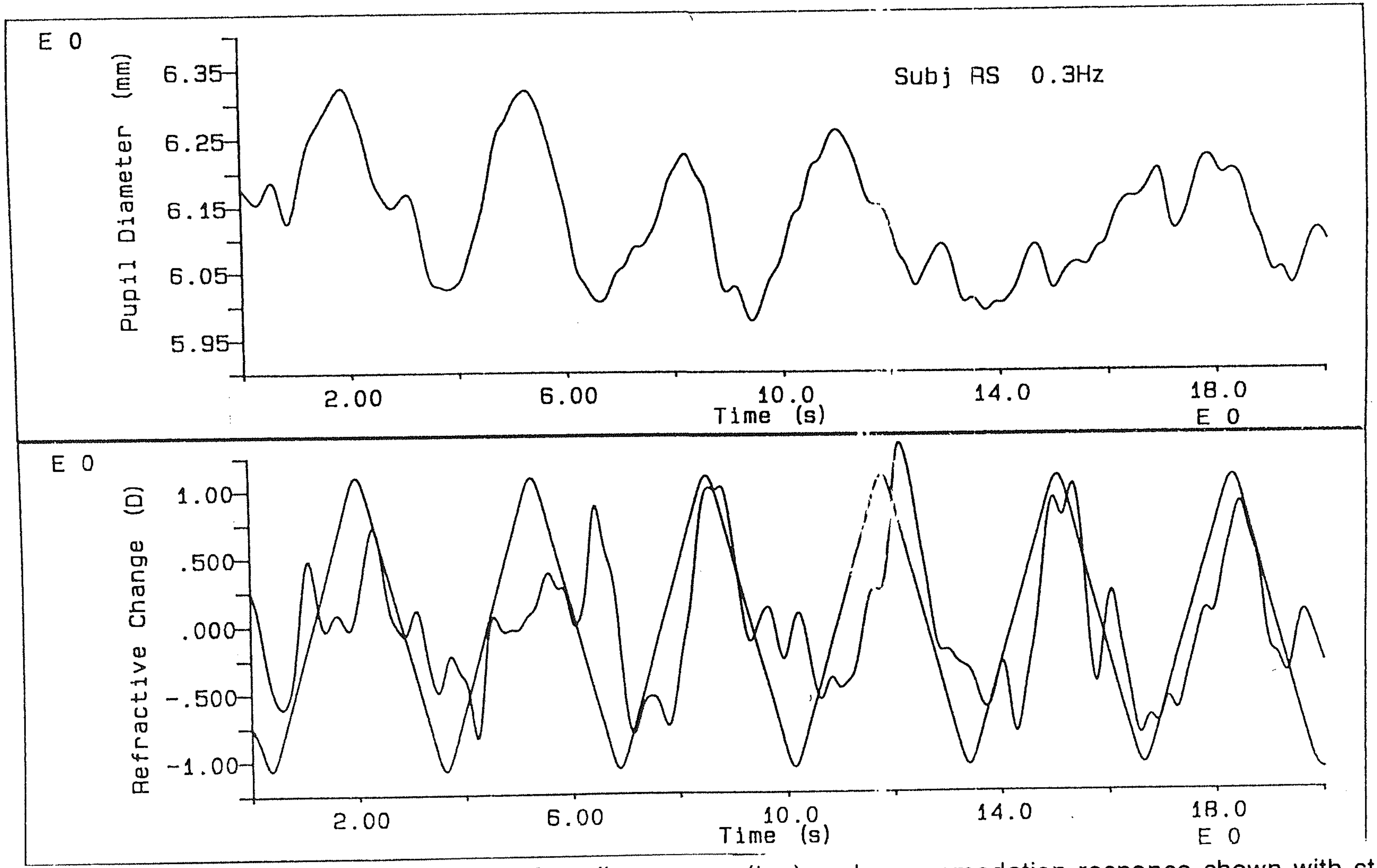


Figure 10.5 Simultaneous, continuous recording of pupil response (top) and accommodation response shown with stimulus waveform (bottom). Accommodation is shown as variation about mean level. Traces smoothed to 5Hz. Shown are results at 0.3Hz over a period of 20 seconds for subject RS.

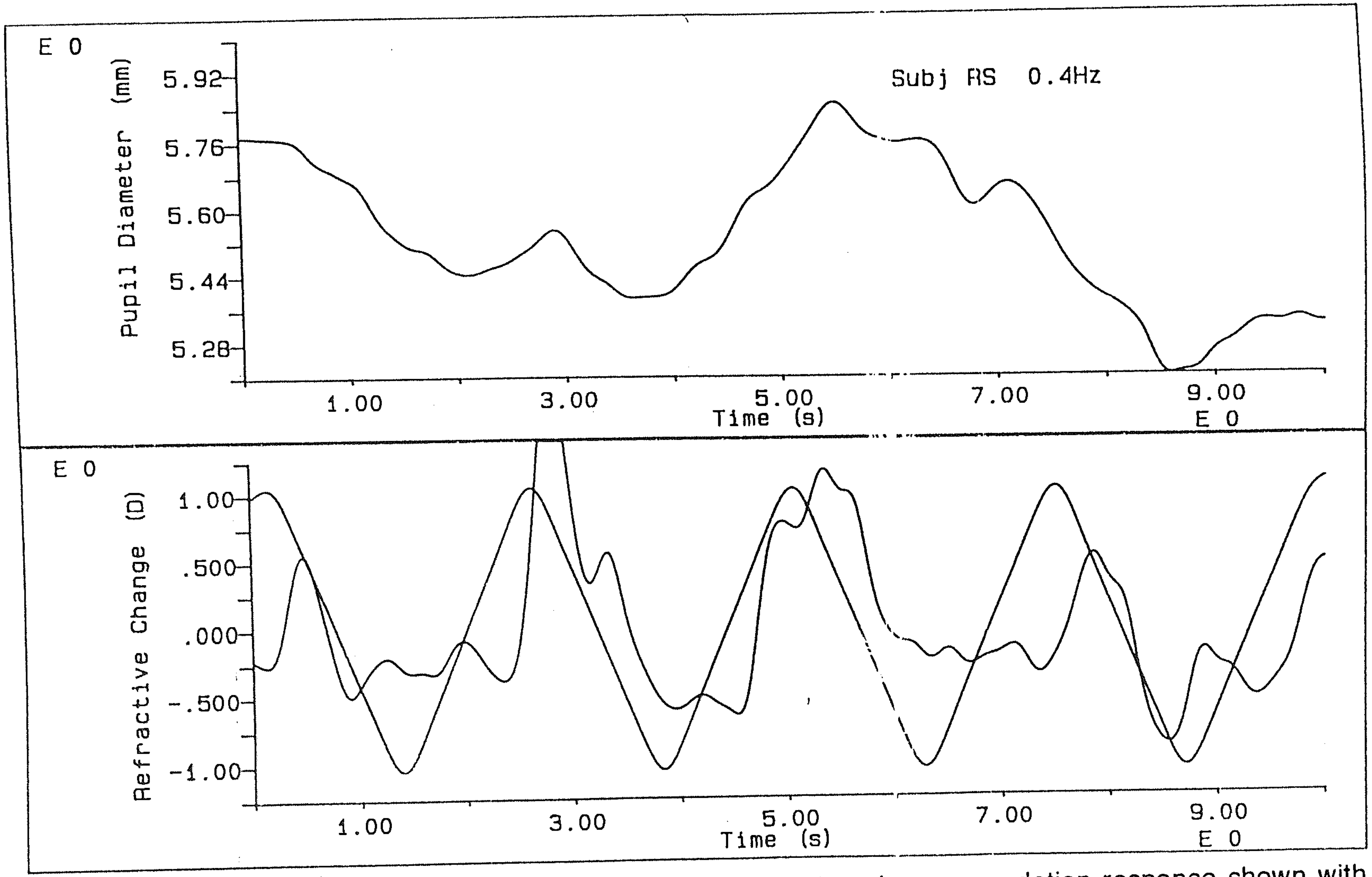


Figure 10.6 Simultaneous, continuous recording of pupil response (top) and accommodation response shown with stimulus waveform (bottom). Accommodation is shown as variation about mean level. Traces smoothed to 5Hz. Shown are results at 0.4Hz over a period of 10 seconds for subject RS.

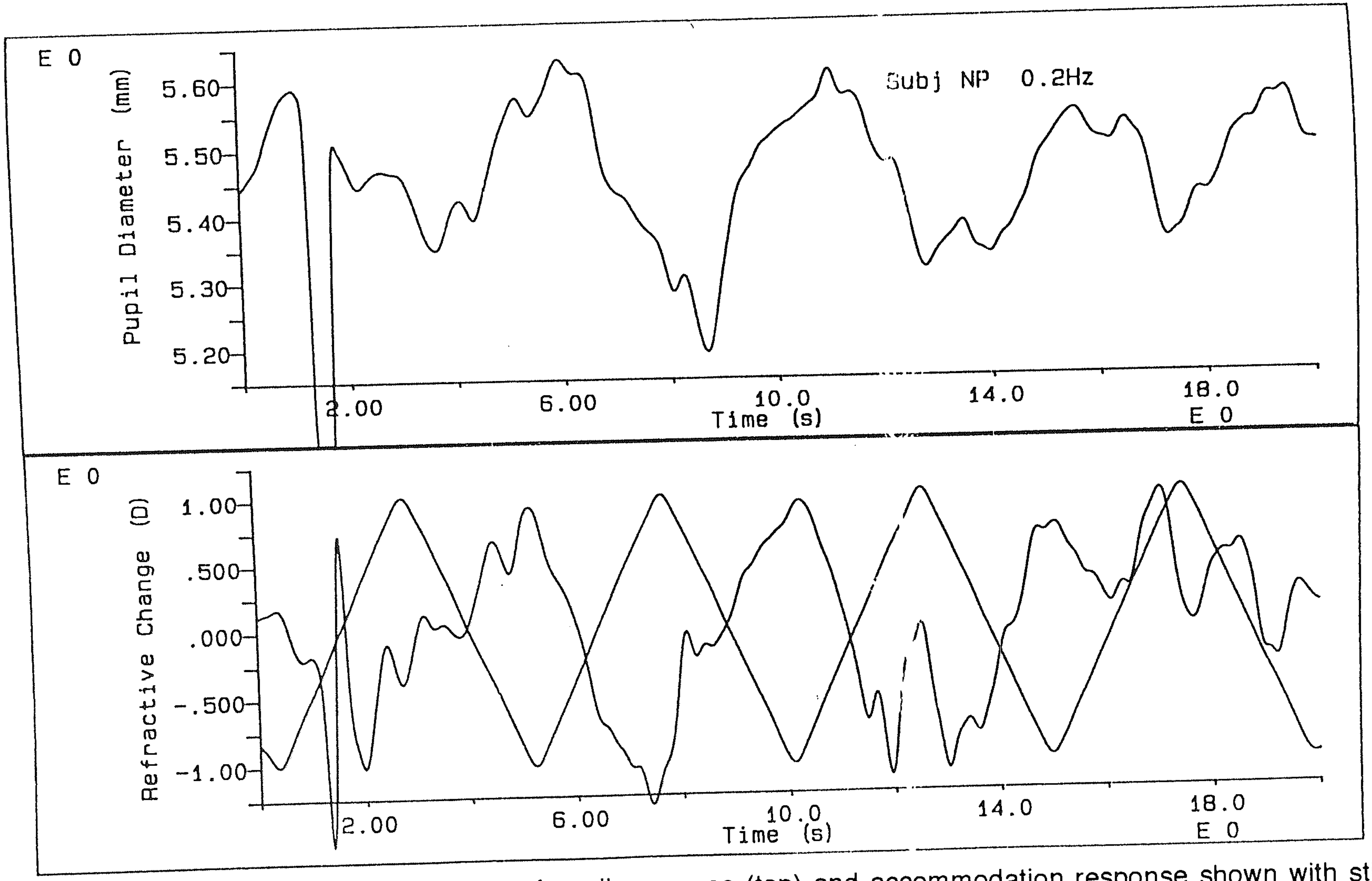


Figure 10.7 Simultaneous, continuous recording of pupil response (top) and accommodation response shown with stimulus waveform (bottom). Accommodation is shown as variation about mean level. Traces smoothed to 5Hz. Shown are results at 0.2Hz over a period of 20 seconds for subject NP.

10.4 DISCUSSION

The accommodation responses found in this investigation are consistent in terms of gain and phase with those of other studies which used closed-loop sinusoidally-modulated accommodative stimuli over similar ranges and young well-trained subjects (e.g. Kruger and Pola, 1986, 1987, Sun *et al*, 1989). Use of a triangular waveform does not therefore appear to substantially affect accommodation response. Under closed-loop conditions, accommodation response is constrained by blur in order to maintain image clarity and so, at least under conditions similar to those used in this study, is phase-locked to the stimulus.

Pupil response was not phase-locked to the stimulus used in this study and showed increasing phase-lag with increasing stimulus temporal frequency. This suggests that there is no feedback constraint on pupil response and that the pupil responses obtained had little or no effect on retinal image quality. A similar conclusion was reached from the results of the study reported in Chapter 10 which showed that during a near reading task the pupil diameter of the young subjects used was too large to make any significant contribution to retinal image quality in the form of increased depth-of-focus. Hung, Semmlow and Ciuffreda (1984) have previously suggested that pupil near response forms essentially an open-loop component of the near vision triad.

The increasing dissociation of pupil and accommodation responses with increasing stimulus temporal frequency demonstrated in the present study has not been previously reported and contrasts with the results of Phillips, Krishnan and Stark (1975). One reason for this may be the absence of size change in the stimulus used by Phillips, Krishnan and Stark (1975) which would have increased accommodation phase lag (Kruger and Pola, 1986, 1987). There is no reason to believe that the increased pupil phase lag is due to mechanical limitations of the iris itself. It has been shown that the pupil light reflex shows higher gain and less phase lag with increase in stimulus temporal frequency than either closed-loop accommodation response or pupil near response (Phillips, Krishnan and Stark, 1975). *

The dissociation between pupil and accommodation responses also suggests that pupil near response is not accommodation-driven but may be a separate response in its own right. This is in contrast to the conclusions of many previous studies (Fry, 1945, Knoll, 1949, Marg and Morgan, 1949, 1950a, Jones, 1989, Myers and Stark, 1990) in which it has been stated or assumed that pupil response is accommodation-driven. The above studies have all used single-step stimuli containing many cues and assumed that because both accommodation and pupil response occurred simultaneously, the two are inextricably linked. However, it may be unwise to make such an assumption as has been demonstrated by Tsuchiya, Ukai and Ishikawa (1989), Stakenburg (1991), Phillips, Winn and Gilmartin (1992) and the experiments reported in Chapters 5, 6 and 7 of this thesis. It is likely that any study using single steps of accommodative stimulus would find results similar to those obtained at 0.1Hz in this study i.e. pupil and accommodation response apparently closely correlated. Further consideration needs to be given to integrating pupil near response into models of the near vision triad and resolving the contradictions in the literature.

* Also Varju (1964) assessed pupillary reactions to sinusoidal light variations and found that at a temporal frequency of 0.5Hz, pupil response showed a phase lag of only approximately 90 degrees.

CHAPTER 11

REVIEW OF EXPERIMENTAL RESULTS AND CONCLUDING OBSERVATIONS

11.1 REVIEW OF EXPERIMENTAL RESULTS

A Hamamatsu C3160 Percept Scope Video Area Analyser has been coupled with a previously-modified Canon Autoref R1 IR automated optometer and employed to make recordings of pupil response alone and pupil and accommodation responses simultaneously. Both static and continuous recordings have been made in order to examine a number of aspects of the pupil near response and its relationship with accommodation. A summary of the findings of the research programme is given below.

1. Coupling of the Percept Scope to the optometer required the design and installation of a separate IR illumination system which could serve both instruments. A calibration factor was determined to allow oscilloscope recordings of the voltage output from the Percept Scope to be converted to absolute values of pupil diameter in mm (see Chapter 4). Providing pupil diameter was maintained above 3.9mm, simultaneous, continuous recordings of pupil and accommodation responses could be made. Direct readout of pupil diameter on the TV monitor screen connected to the optometer allowed pupil diameter to be monitored easily.

2. Pupil and accommodation regression patterns following cessation of a sustained near vision task were recorded in conditions of darkness and bright-empty-field. Recordings were made first quasi-statically and subsequently using continuous recording techniques under a number of trial conditions (Chapters 5 and 6). Results showed that when placed under post-task empty-field conditions, the pupil failed to redilate following the constriction induced by a sustained task despite significant change in accommodative level. Under post-task conditions of

darkness, the pupil redilated rapidly and to a similar diameter regardless of the dioptric level of the task. It was proposed that blur-driven accommodation alone may be insufficient to drive pupil near response but that the absence of pupil response could only be demonstrated under experimental conditions in which no change in luminance took place. Further, it was considered that the rate of change of accommodation may have some influence on pupil response and this was investigated in a subsequent experiment.

3. An investigation of pupil and accommodation responses to an accommodative stimulus viewed through a Badal stimulus optometer and sinusoidally-modulated at a range of temporal frequencies was carried out (Chapter 7). Results showed that if all cues leading to the awareness of target movement including lateral and vertical displacement were eliminated leaving a blur-only stimulus, then the target appeared stationary and pupil response could be absent. This result supported the findings of Stakenburg (1991) and further showed that under such conditions using a predictable, repetitive stimulus, accommodation response is maintained. The results were taken as further evidence that blur-driven accommodation alone may be insufficient to drive pupil near response whatever the rate of accommodative change and that the presence of cues contributing to the awareness of the proximity of an approaching or receding target may be necessary to elicit pupil near response.

4. Pupil response was demonstrated to an inferred-proximity cue created using a target which did not actually move but showed periodic variation in size (Chapter 8). This 'looming' target creates an illusion of movement in depth which has been previously shown to be capable of driving open-loop accommodation response. Although the target was designed to act as a static, closed-loop stimulus to accommodation to constrain accommodation response, one subject was unable to maintain a stable accommodative level and found that the target rapidly became blurred. This experiment confirmed the potency of size change as a cue

to oculomotor response and increased the probability that cues leading to awareness of proximity are important to pupil near response.

5. Surprisingly little data exists on the pupil diameters adopted by human subjects under naturalistic viewing conditions. Without this information, it is not possible to assess the role of the pupil constriction that accompanies near vision and what contribution it may make to image quality. Although it is usually stated that pupil near response increases depth-of-focus, study of the relevant literature revealed that pupil diameter would need to be below 3mm for any significant benefit to be gained. Measurement of pupil size during a reading task at 35cm and under a luminance of 100 cdm^{-2} revealed a mean pupil diameter of 3.6mm for young subjects, a level too large therefore to have a significant influence on depth-of-focus (Chapter 9). Under the same conditions a group of elderly subjects showed pupil diameters of 2.6mm and may therefore have gained increased depth-of-focus by pupil constriction at near. It was concluded that in the young subjects, the function of pupil near response remains to be fully explained and that in the elderly subjects, increased depth-of-focus at near may be of benefit but is probably a by-product of the effects on the pupil of ageing.

6. Pupil and accommodation responses to a temporally-modulated accommodative stimulus were further investigated using a naturalistic stimulus containing all cues including size change (Chapter 10). A triangular waveform was used to drive the stimulus at a range of temporal frequencies and results showed that with increase in stimulus temporal frequency, closed-loop accommodation response exhibited little phase lag. This is in agreement with previous studies and the small phase lag can be attributed to feedback from blur and to voluntary effort due to the predictable nature of the stimulus change. Pupil response showed increasing phase lag compared both to the stimulus and to accommodation response as stimulus temporal frequency increased. It was concluded that pupil constriction has little, if any, effect on depth-of-focus as the

increased phase lag compared to accommodation demonstrates absence of the blur-derived feedback loop utilized by accommodation and absence of voluntary control.

11.2 TOWARDS A MODEL TO ACCOUNT FOR THE RELATIONSHIP BETWEEN PUPIL NEAR RESPONSE AND ACCOMMODATION

Most previous studies have assumed or indicated a link from accommodation and/or vergence through to the pupil and that it is this link or links that drive pupil near response. Despite many attempts to isolate the drive to pupil response, there is much disagreement in the literature and at first sight there is no clear reason as to why the experimental results should differ so much. For example, Marg and Morgan (1949, 1950a, 1950b) found pupil constriction associated with accommodation and accommodative convergence but not with fusional convergence. Renard and Massonet-Naux (1951) proposed that pupil constriction is concomitant to convergence rather than accommodation and Backer and Ogle (1964) found clear evidence for pupil response coincident with fusional vergence. Jones (1989) found pupil constriction associated with accommodation but not fusional convergence and Myers and Stark (1990) proposed an asymmetric drive to pupil from both accommodation and vergence. This wide disagreement suggests that the fundamental assumption that pupil near response occurs only as a consequence of accommodation or vergence needs careful examination.

The results of the experiments described in Chapters 5, 6, and 7 each demonstrate in different ways that, under conditions in which cues to target proximity are absent, accommodation response can be induced with no concomitant effect on the pupil . Pupil near response may therefore require the presence of cues relating to the proximity of a target whereas accommodation can respond to blur alone. Under the right conditions, one such proximity cue acting on the pupil may be derived from the accommodative or vergence level.

Vergence was not recorded in any of the present experiments but owing to the strong, synkinetic links between accommodation and vergence, monocular stimulation of accommodation would result in vergence of the fellow occluded eye. Although the dissociation of accommodation and pupil responses demonstrated in the experiments is in support of the recent work of Tsuchiya, Ukai and Ishikawa (1989) and Stakenburg (1991), these results are in contrast to the earlier literature. Despite the variable results in the literature, in those experiments investigating pupil response to incremental increases in accommodation or vergence, a clear relationship between the level of stimulus and amplitude of pupil response was always found, leading to the conclusion that there must be a relationship between the systems.

Recent studies (North, Henson and Smith, 1992, Schor *et al* , 1992) have emphasised the influence of proximal cues on accommodation and vergence response and reflected the increased appreciation of the importance of these cues to the oculomotor systems. North, Henson and Smith (1992) investigated vergence response under conditions in which cues to the proximity of a target were placed in conflict with either blur or disparity and showed that it is the proximity cue that has the largest influence on response. Schor *et al* (1992) have proposed a comprehensive model of accommodation and vergence response (see figure 11.1) that includes both body-referenced cues relating to awareness of target proximity (spatiotopic cues) and eye-referenced cues such as blur and disparity (retinotopic cues).

The Schor *et al* (1992) model represents a collation of the findings of many studies by a wide variey of authors and can be shown to accurately predict accommodation and vergence responses to a number of stimulus conditions. Schor *et al* (1992) consider that the spatiotopic and retinotopic cues act as parallel inputs and that accommodation and vergence respond to both sets of cues in a normal visual environment but can also respond to each input in isolation. Spatiotopic cues such as size, texture and parallax are generally used to interpret substantial changes in target position and produce large, coarse, probably open-loop responses allowing the systems to quickly adopt approximately correct positions. Retinotopic cues such as blur and disparity are then utilised to make small, closed-loop corrections and fine-tune the response to reach its final, optimum level. During steady fixation, retinotopic cues are used to maintain image clarity.

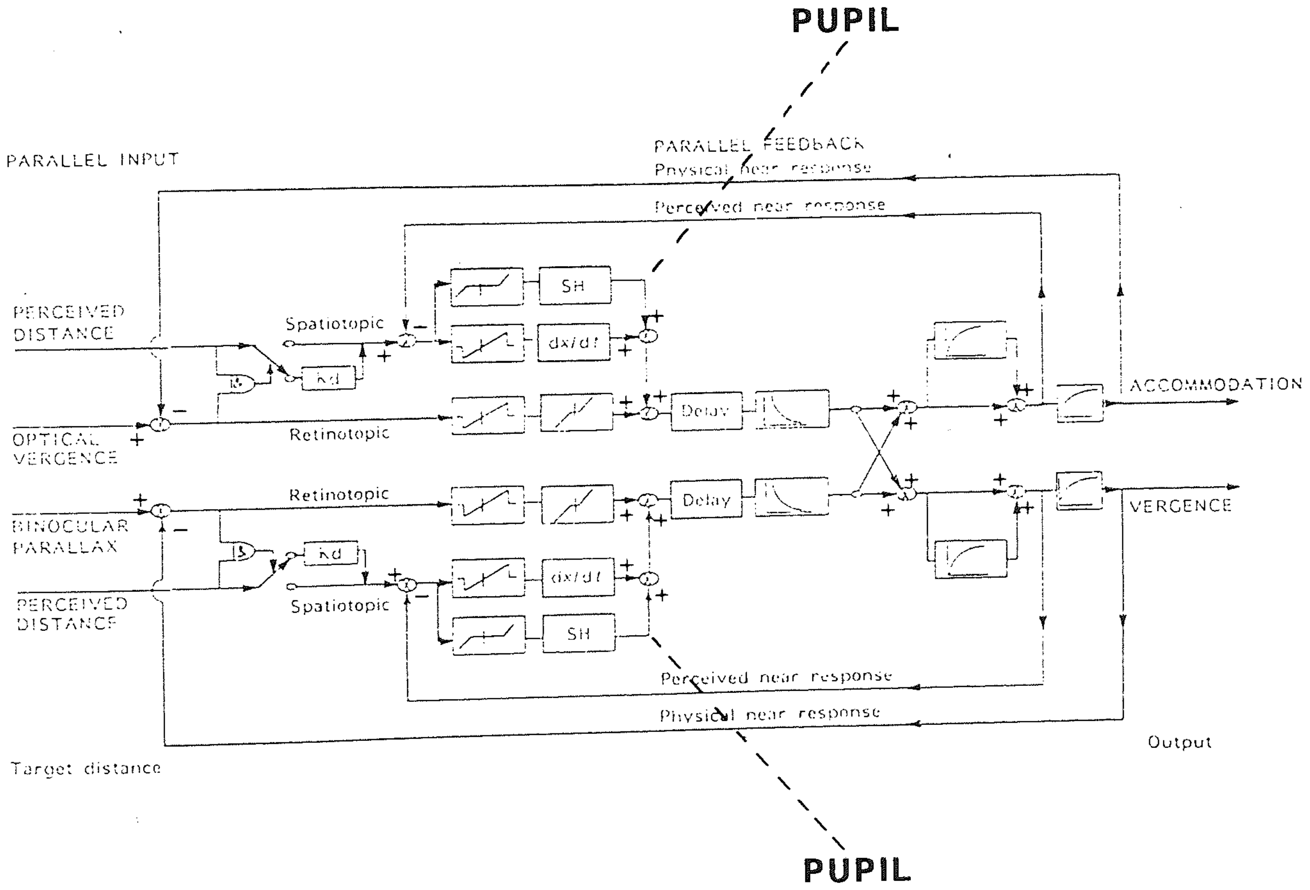


Figure 11.1 Negative feedback control model of accommodation and vergence incorporating the processing of cues relating to target proximity. From Schor *et al* (1992b). The dotted lines indicate the proposed pathways to the pupil.

Studies have shown that accommodation can respond (although with only 50% initial accuracy when a target is first moved) to a retinotopic cue alone in the form of blur (Stark and Takahashi, 1965) with no awareness of target proximity and that vergence can respond to pure disparity (Houtman, Roze and Scheper, 1977).

Equally, it has been demonstrated that accommodation can respond to an inferred-proximity cue (spatiotopic cue only) using a looming target (Kruger and Pola, 1983, 1985, 1987) as can vergence (McLin, Schor and Kruger, 1988). Thus, accommodation and vergence can respond to either spatiotopic or retinotopic cues in isolation although during vision in a normal environment, both set of cues are used in a complementary way.

Schor *et al* (1992) have not included pupil response in their model. Following examination of the literature, the experimental results reported in Chapters 5 to 10 and those of Tsuchiya, Ukai and Ishikawa (1989) and Stakenburg (1991), it is proposed that the drive to pupil response does indeed derive from the accommodation and vergence systems but from the *spatiotopic* cue sensing elements only (see figure 11.1).

The exact point of exit of the drive to the pupil needs much more investigation and application of further modelling considerations. The position shown is intended only to convey the general proposal that drive to the pupil derives from some point in the parallel spatiotopic cue detecting mechanisms of accommodation and vergence rather than the retinotopic cue detecting system.

The implication of this proposal is that if accommodation or vergence are stimulated by purely retinotopic cues in the form of blur or disparity, they will each respond but pupil response will not occur. Accommodation and vergence are capable of response despite the absence of awareness of target proximity. If accommodation or vergence receive both retinotopic and spatiotopic cues, then clearly again both will respond and the activation of the spatiotopic cue detecting mechanisms will result in pupil response. Spatiotopic cues alone will cause reponse in accommodation, vergence and pupil.

With the above in mind, it is worth looking back at the inconsistencies in the literature. It seems likely that those studies in which pupil reponse was found to accompany accommodation or vergence made use of stimuli which included both retinotopic and spatiotopic cues. Those studies finding no response to accommodative or to vergence stimuli were using only retinotopic cues and had succeeded in creating experimental conditions that were capable of excluding spatiotopic cues. Of particular interest is the finding of Stakenburg (1991) that pupil response could be absent to a blur-only accommodative stimulus but that as soon as an extra cue was introduced, in this case misalignment of the targets, pupil response was apparent. Clearly, the blur-only condition contained only the retinotopic cue of blur and thus no pupil response occurred due to the absence of any spatiotopic cues. If a spatiotopic cue in the form of slight target displacement was introduced, then pupil response occurred and the response amplitude increased with further increase in the amount of target displacement present.

The results reported in Chapters 5 to 10 of this thesis can be subjected to similar examination. In Chapters 5 and 6, accommodation response decayed post-task in a bright empty field due to the diminuition in retinotopic cues on task cessation. Pupil constriction was retained as no spatiotopic cues exist in a bright-empty field and subjects presumably retained the same awareness of proximity that had existed when the target was present.

The results in Chapter 7 support those of Stakenburg (1991) and showed that whereas accommodation continued to respond to a target viewed through a Badal stimulus optometer, pupil response was small due to the elimination of the spatiotopic cue of size change and could be completely absent when blur alone was isolated. The predictable, repetitive nature of the accommodative stimulus ensured accurate accommodation response and prevented accommodative errors due to the lack of directional information in a blur-only stimulus. Under such conditions the target appeared stationary and a feature of this experiment and that carried out by Stakenburg (1991) is that only a very small amount of lateral or vertical target displacement is necessary to create awareness of target movement and lead to concomitant pupil response.

In Chapter 8, pupil response to an inferred-proximity cue from a looming target was demonstrated. The spatiotopic cue of inferred-proximity will drive both accommodation and pupil response. Accommodation also responds to the retinotopic cue of blur and thus accommodation response was constrained by the need to maintain image clarity. In one subject, the spatiotopic size change cue overrode the retinotopic cue of blur and caused inappropriate accommodation responses leading to blurring of the target.

Chapter 9 examined the pupil diameter adopted by young and elderly subjects during a near vision task. Pupil diameter in the young subjects was too large to have a significant effect on depth-of-focus and it is therefore difficult to find any feedback loop to control the pupil. It seems likely that the pupil response that was found was driven by the spatiotopic elements of accommodation and vergence and would not therefore need to receive any feedback from retinotopic cues relating to image clarity. In the elderly subjects, pupil constriction at near would still occur despite the absence of the retinotopic cue of blur when corrective spectacles are worn for near tasks. Pupil response would be maintained by the retinotopic cue of disparity and the spatiotopic proximity cues.

In Chapter 10, dissociation of accommodation and pupil responses was again demonstrated and shown to increase with increase in the temporal frequency of a temporally-modulated accommodative stimulus. No Badal optometer was used and thus both retinotopic and spatiotopic cues were present throughout. Accommodation response was tightly coupled to the stimulus by its response to both sets of cues. Pupil response occurred to the spatiotopic cues only and thus received no image quality feedback constraint resulting in differing response characteristics to those displayed by accommodation.

In conclusion, it can be seen that placing the drive to pupil near response from the spatiotopic input only of accommodation and vergence can clarify the disagreement in the literature as to whether pupil drive derives from accommodation or vergence and the paradoxical existence of often linear relationships between pupil response and accommodation or vergence can be explained. The findings of Stakenburg (1991) can also be explained, in particular the apparent sensitivity of pupil response to small degrees of target misalignment. Further, the results described in Chapter 5 to 10 also fit into the model. Pupil response does, therefore, fit into and form part of the near vision triad, but it seems to be a more primitive response and may contribute little to retinal image quality or depth-of-focus. Laughlin (1992) comments that the pupil diameter that is optimum in order to maximise the use of the information contained in the retinal image is dependent on several factors, one of which is the spatial frequency content of the object being viewed. Resolution of high spatial frequencies is optimised by a small pupil at the loss of detection sensitivity. It may be that pupil near response serves the function of maximising resolution of fine detail during near vision tasks. Distance viewing is generally more concerned with the detection of objects and a larger pupil will maximise sensitivity albeit with some loss of resolution. This would mean that pupil near response serves a similar function to the light response in optimising visual function under a variety of conditions. Adoption of the optimum pupil diameter is presumably a conditioned response and would not need to depend on a feedback loop relating to image clarity or depth-of-focus like those utilised by accommodation and vergence.

11.3 PROPOSALS FOR FURTHER WORK

11.3i INSTRUMENTATION

Simultaneous, continuous recording of pupil and accommodation responses has been undertaken in several experiments. Although the recording techniques used have provided much information about the responses of the two systems, several problems have been encountered which further development of the apparatus could help alleviate. In order for continuous recordings of accommodation to be made, pupil diameter must be maintained above 3.9mm. This limits the luminance levels and the dioptric demand of near vision tasks that can be imposed and makes investigation of near-presbyopic and older subjects difficult. Subjects must also be able to maintain steady fixation and spectacles cannot be worn when making continuous recordings of accommodation response although soft contact lenses can be used. During experiments, as subjects get bored or tired, mean pupil diameter gradually decreases and subjects must be given frequent breaks.

Continuous recording of pupil diameter with the apparatus currently in use has been found to depend on suitable iris colour. Although it is difficult to be precise, subjects with darker irides have generally proved to be more suitable than those with light irides in whom it can prove impossible to set a satisfactory threshold level for discrimination between the iris border and the pupil. Substitution of a better quality camera could improve this. The camera within the optometer is designed only to provide an image of the eye to aid alignment of the optometer and therefore does not need to be of a high quality. Recordings are again difficult through spectacle lenses and possible usually with soft contact lenses but not with gas permeable contact lenses.

To make simultaneous, continuous recordings of accommodation and pupil depends, therefore, on finding young subjects with large pupils, dark irides, and stable fixation who are emmetropic or capable of correction with soft contact lenses (i.e. astigmatism less than 0.75D). This combination of requirements has led to the rejection both before and during experimental trials of many potential subjects who fail to fulfill one or more of the requirements. Further development of the apparatus should be aimed at widening the variety of subjects and tasks that can be used. This may be achieved by developing the optometer to record over a smaller area of the pupil and improving the illumination system and camera used in order to enhance threshold discrimination by the Percept Scope.

11.3ii FURTHER INVESTIGATION OF PUPIL AND ACCOMMODATION RESPONSES TO TEMPORALLY-MODULATED STIMULI

Evidence has been presented that pupil near response is controlled by only one stage of the control mechanisms that serve accommodation and vergence. Pupil response characteristics to temporally-modulated stimuli are different to those of accommodation. Further investigation of simultaneously-recorded pupil and accommodation responses to a variety of temporally-modulated stimuli could help to clarify more exactly how pupil near response is mediated and how it should be represented in the model of Schor *et al* (1992). There is currently little data available on the latency of pupil near response. A study of pupil and accommodation response latencies to target movement could also prove useful in further modelling. Simultaneous recordings would help to eliminate variabilty between subjects and target setups.

11.3iii HIPPUS

The question of rhythmic elements within the constant fluctuations in pupil size known as hippus has not been adequately resolved. Although considered by many to be random noise, regular periodic changes can often be seen in recordings of pupil response. Although these may vary a great deal, further investigation should include simultaneous recording of accommodation and pupil to investigate any possible correlation between the fluctuations apparent in the two systems. Recent study has shown correlation between pulse frequency and the high frequency component of accommodation and it has been previously suggested that pulse and respiration frequency may be reflected in hippus.

11.3iv PUPIL SIZE AND RESPONSE UNDER NATURALISTIC CONDITIONS

Little data exists on pupil size and behaviour under naturalistic conditions involving controlled luminance and task level across a range of ages. A study currently in preparation (Winn, Whitaker, Phillips and Elliott) has demonstrated that pupil size does decrease with age but that the rate of decrease lessens at higher luminance levels and therefore previous studies measuring pupil size only in darkness may lead to overestimation of the effect. Further data should be gathered and include the effect on pupil of near vision tasks. This will further help to clarify the role of the pupil in human vision and be an aid in design of vision aids such as bifocal contact lenses.

11.3v EFFECT OF PUPIL SIZE ON VISION IN THE ELDERLY

Several studies have aimed to assess the relative contribution of neural factors and pupil size to the loss of visual function found in the elderly (Wright and Drasdo, 1985, Elliott,1987, Tyler, 1989). The consensus seems to be that neural factors predominate. It would be interesting to dilate the pupils of elderly subjects and assess distance and near visual acuity beforeand after dilation. Studies of pupil size with age always reveal a large scatter of values and undoubtedly at any one luminance level there are always some elderly persons with larger pupils than much younger persons. The reason for this is not known but it has been proposed that pupil size could be used as a marker of biological ageing i.e. a measure of the amount of detriment suffered by an individual due to age. Further studies could assess possible correlation between individual pupil size and individual fitness.

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APPENDICES

APPENDIX 1

SETUP PARAMETERS TO INSTRUCT THE HAMAMATSU C3160 PERCEPT SCOPE VIDEO AREA ANALYSER TO MEASURE HORIZONTAL PUPIL DIAMETER

The following parameters must all be set as shown for correct functioning of the Percept Scope. If the Percept Scope is not working correctly, these parameters can be accessed using the keypad on the front of the instrument and pressing 'SETUP' rather than 'START' on switching on the instrument.

PARAMETER:	SET TO:
1. DISCRIMINATION	
1 Method	Binary
2 Polarity	Neg
3 Noise correlation	1
4 Level detect area	Window
5 Auto mode	Constant
6 Offset level	128
7 Threshold level	46
8 Differential edge	B->W
9 Slice area	Window
2. MEASUREMENT	
1Method	Object wid
2 Averaging	Off
3 Realtime averaging	Off
4 Direction	Hor
5 Min, max mode	Off
6 Mean in window	Off

3. DATA ANALYSIS

1 Measuring error	0 out
2 Data filtering	Off
3 Threshold	0
4 Judgement base	0
5 Upper	0
6 Lower	0

4. SCALING

1 Switch	On
2 Scaling factor	797
3 Digits	00.00
4 Unit	m
5 Target	Object
6 Execute	Total width

Field of view 25.00m

5. WINDOW

1 CH-1	
L	219
U	150
R	422
L	206

6. AUXILIARY

1 Buzzer	Off
2 Display position	Lower
3 Display area	80%

7. CAMERA CONTROL

1 Synchro	Auto
2 Interlace	2:1
3 Camera select	ITV 2
4 Display video sel.	Normal
5 Camera sel. intval	0

8. INTERFACE

1 GPIB
2 I/O port logical
3 Parallel out
4 RS232C
5 A/D conv
6 Analog out

9. CROSS HAIR

(not applicable)

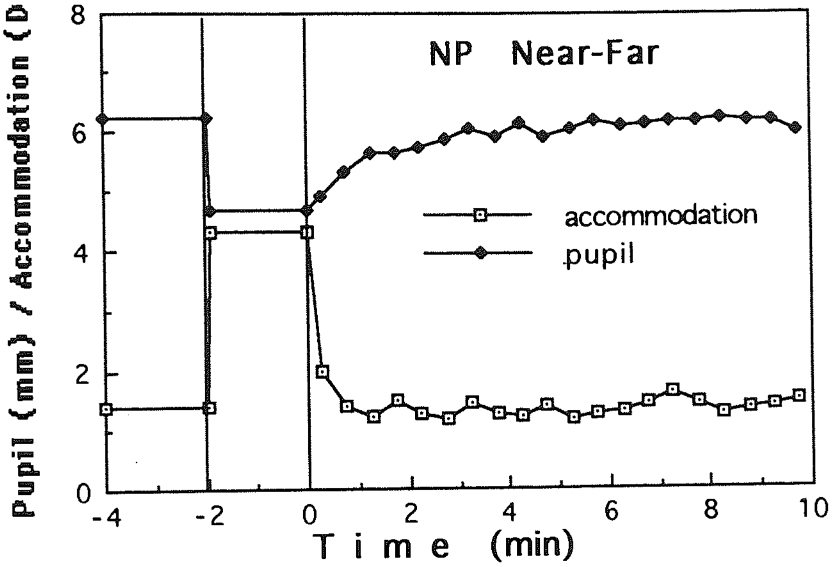
0. FUNCTION

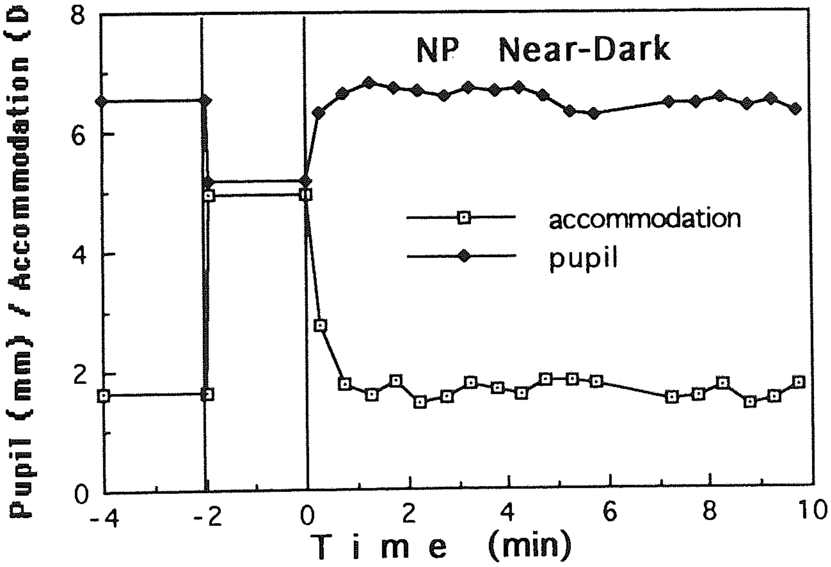
1 Backup data table	Initialize
2 Available channel	CH1
3 CH1 function	Width

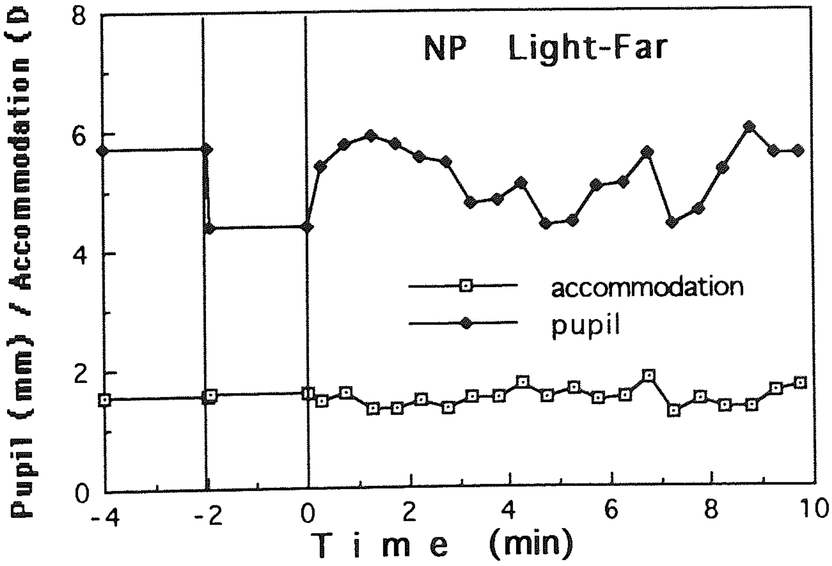
APPENDIX 2

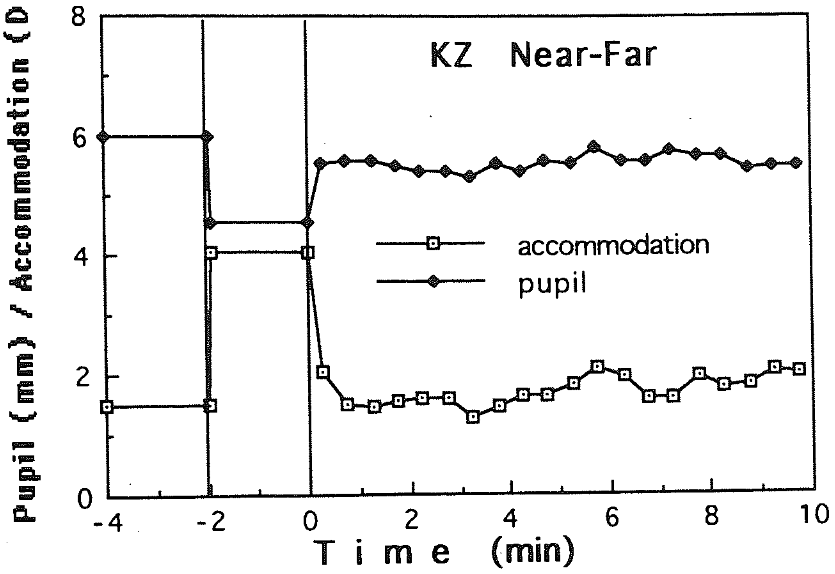
APPENDIX RELATING TO CHAPTER 5

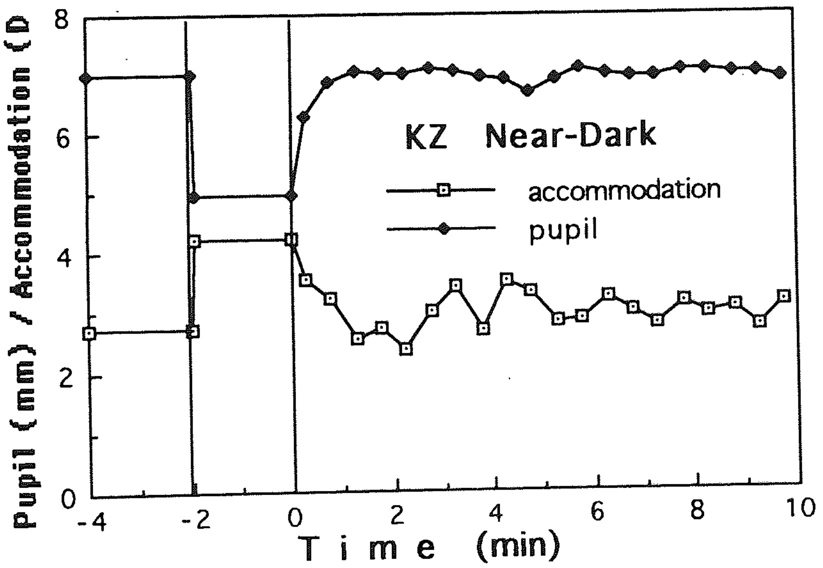
Experimental recordings made using subjects NP AND KZ

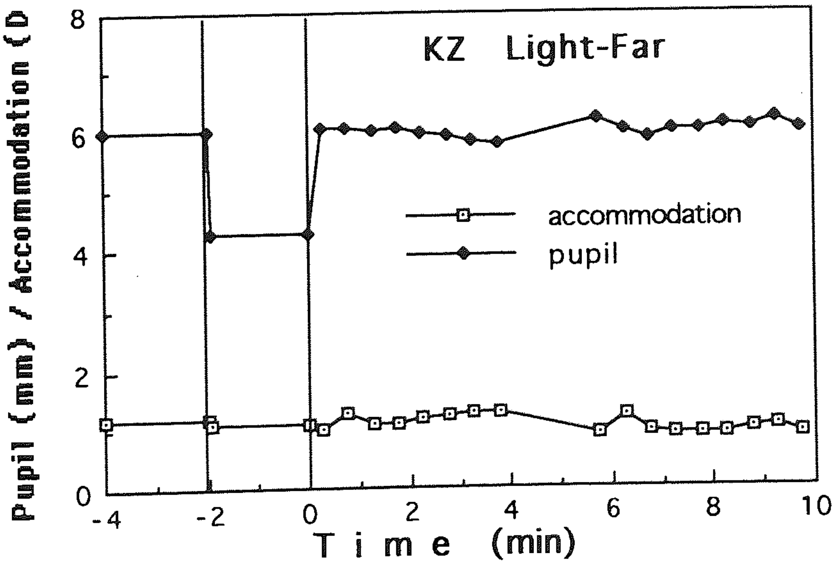







KZ Near-Far
accommodation
pupil
Pupil (mm) / Accommodation (D
0
2
4
6
8
-4
-2
0
2
4
6
8
10
Time (min)

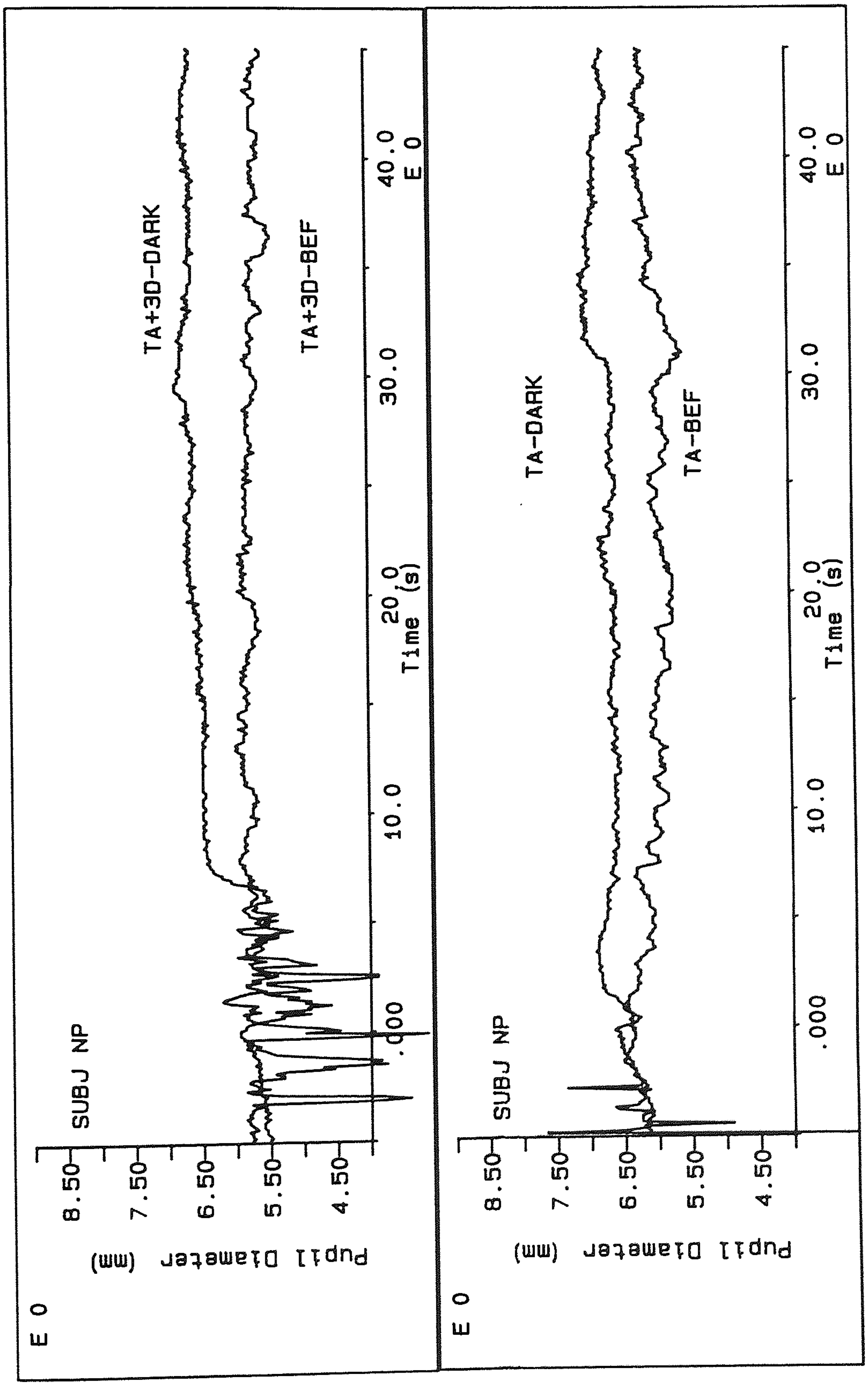

KZ Near-Dark
accommodation
pupil
Pupil (mm) / Accommodation (D
0
2
4
6
8
-4
-2
0
2
4
6
8
10
Time (min)

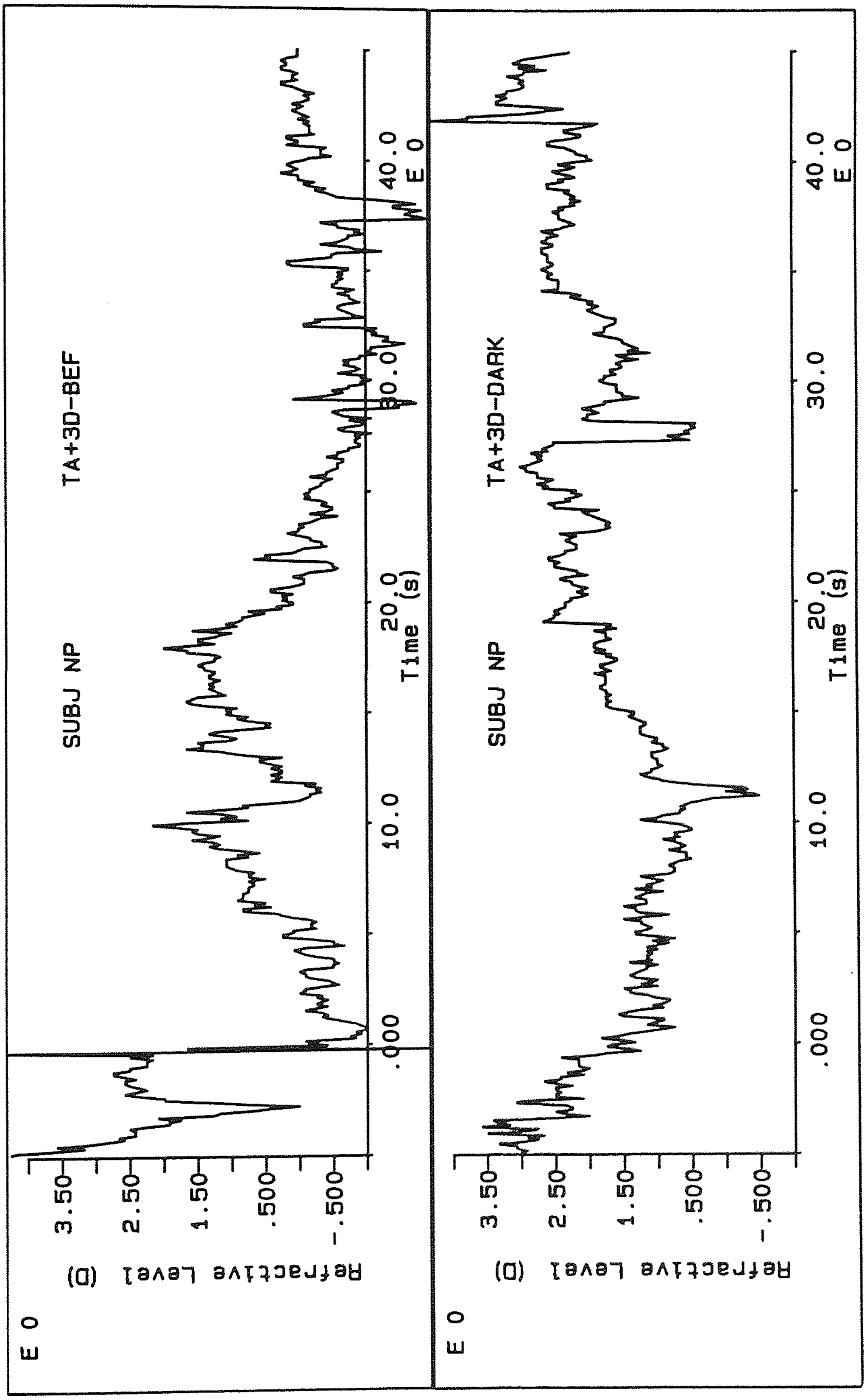

KZ Light-Far
accommodation
pupil
Pupil (mm) / Accommodation (D
0
2
4
6
8
-4
-2
0
2
4
6
8
10
Time (min)

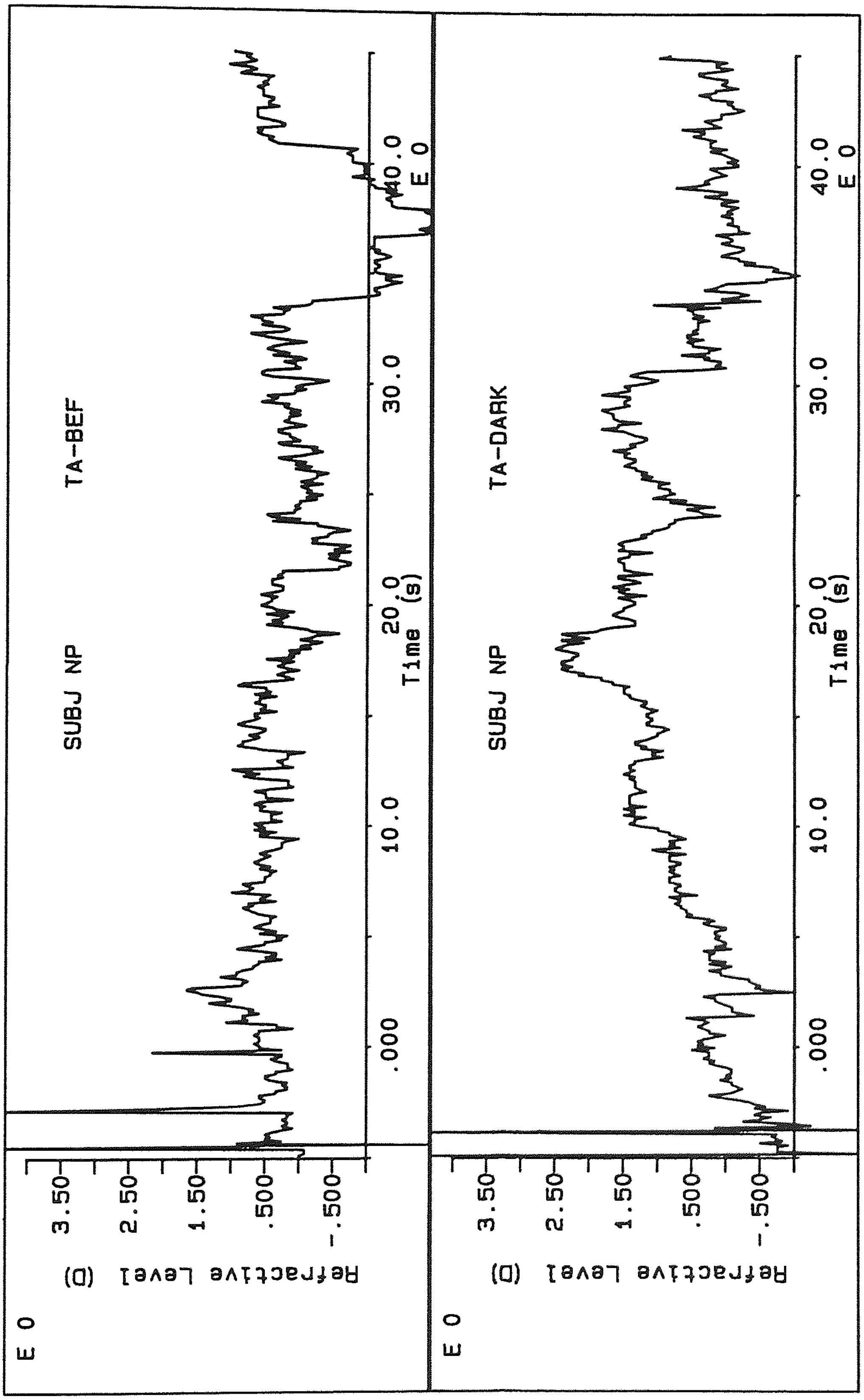
APPENDIX 3

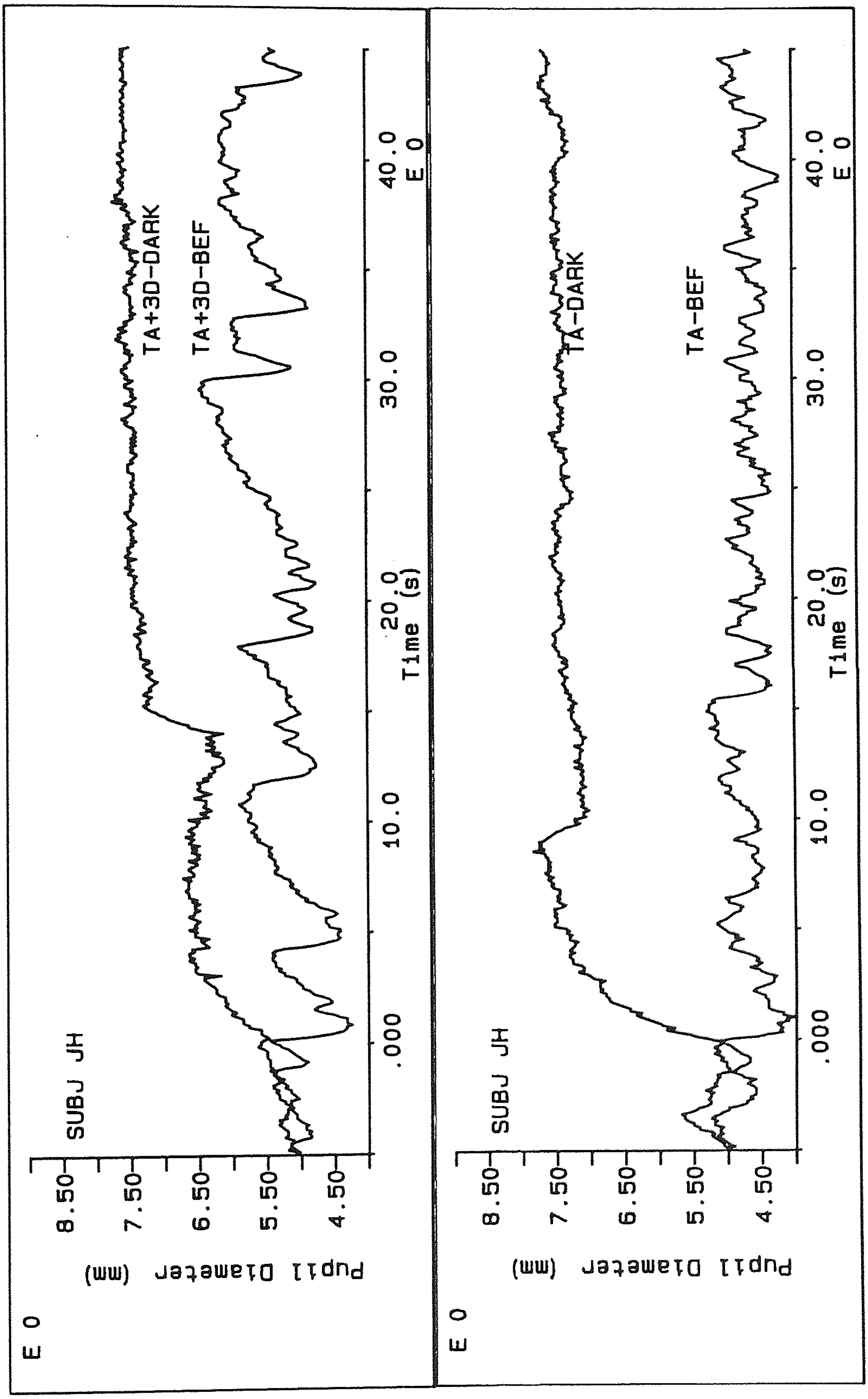
APPENDIX RELATING TO CHAPTER 6

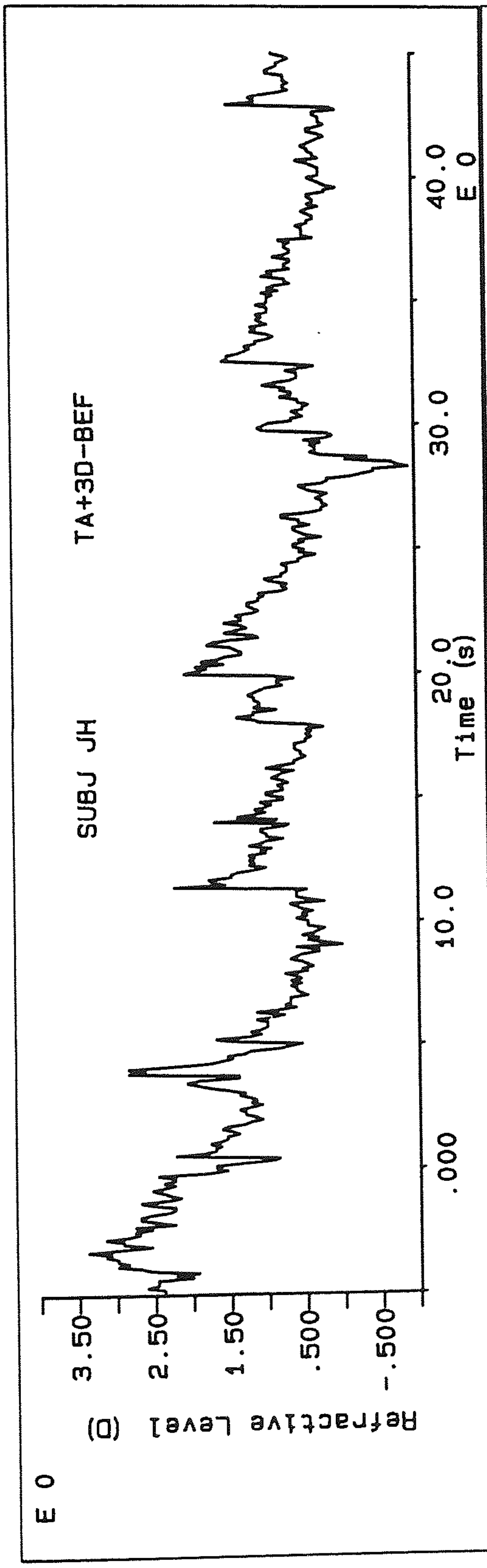
Pupil and accommodation recordings made using subjects NP, JH and FE.




SUBJ NP
TA+3D-BEF
Refractive Level (D)
3.50
2.50
1.50
.500
-.500
.000
10.0
20.0
30.0
40.0
Time (s)
E 0
SUBJ NP
TA+3D-DARK
Refractive Level (D)
3.50
2.50
1.50
.500
-.500
.000
10.0
20.0
30.0
40.0
Time (s)
E 0


E 0
Refractive Level (D)
3.50
2.50
1.50
.500
-.500
SUBJ NP
TA-BEF
.000
10.0
20.0
30.0
40.0
Time (s)
E 0
E 0
Refractive Level (D)
3.50
2.50
1.50
.500
-.500
SUBJ NP
TA-DARK
.000
10.0
20.0
30.0
40.0
Time (s)
E 0


E 0
Pupil Diameter (mm)
8.50
7.50
6.50
5.50
4.50
SUBJ JH
TA+3D-DARK
TA+3D-BEF
.000
10.0
20.0
30.0
40.0
Time (s)
E 0
E 0
Pupil Diameter (mm)
8.50
7.50
6.50
5.50
4.50
SUBJ JH
TA-DARK
TA-BEF
.000
10.0
20.0
30.0
40.0
Time (s)
E 0



SUBJ JH
TA+3D-BEF
Refractive Level (D)
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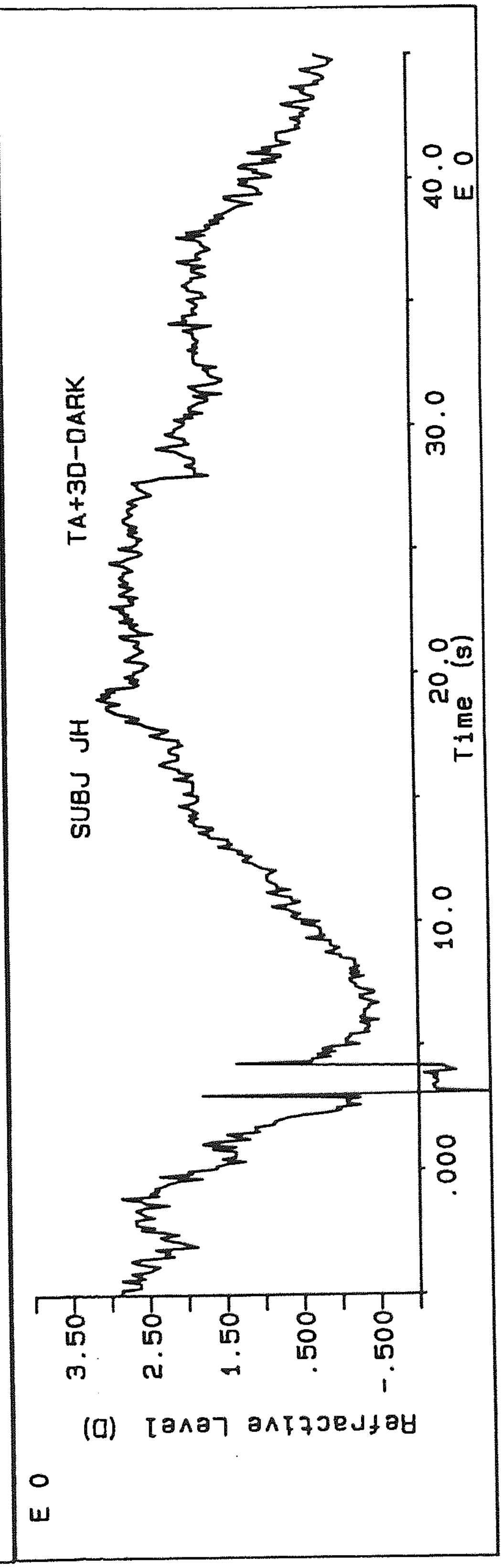
2.50
1.50
.500
-.500
.000
10.0
20.0
30.0
40.0
Time (s)
E 0
E 0



SUBJ JH
TA+3D-DARK
Refractive Level (D)
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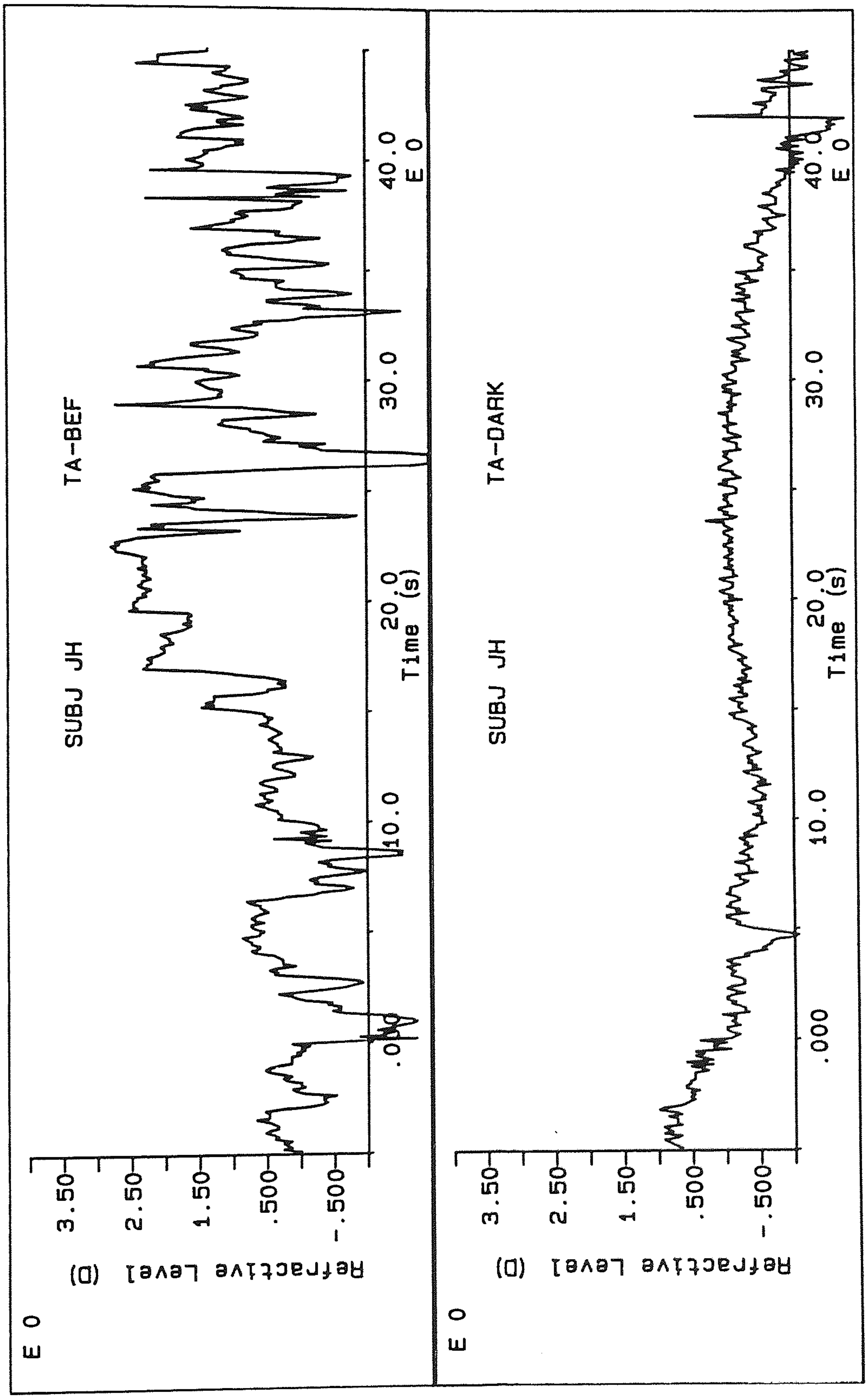
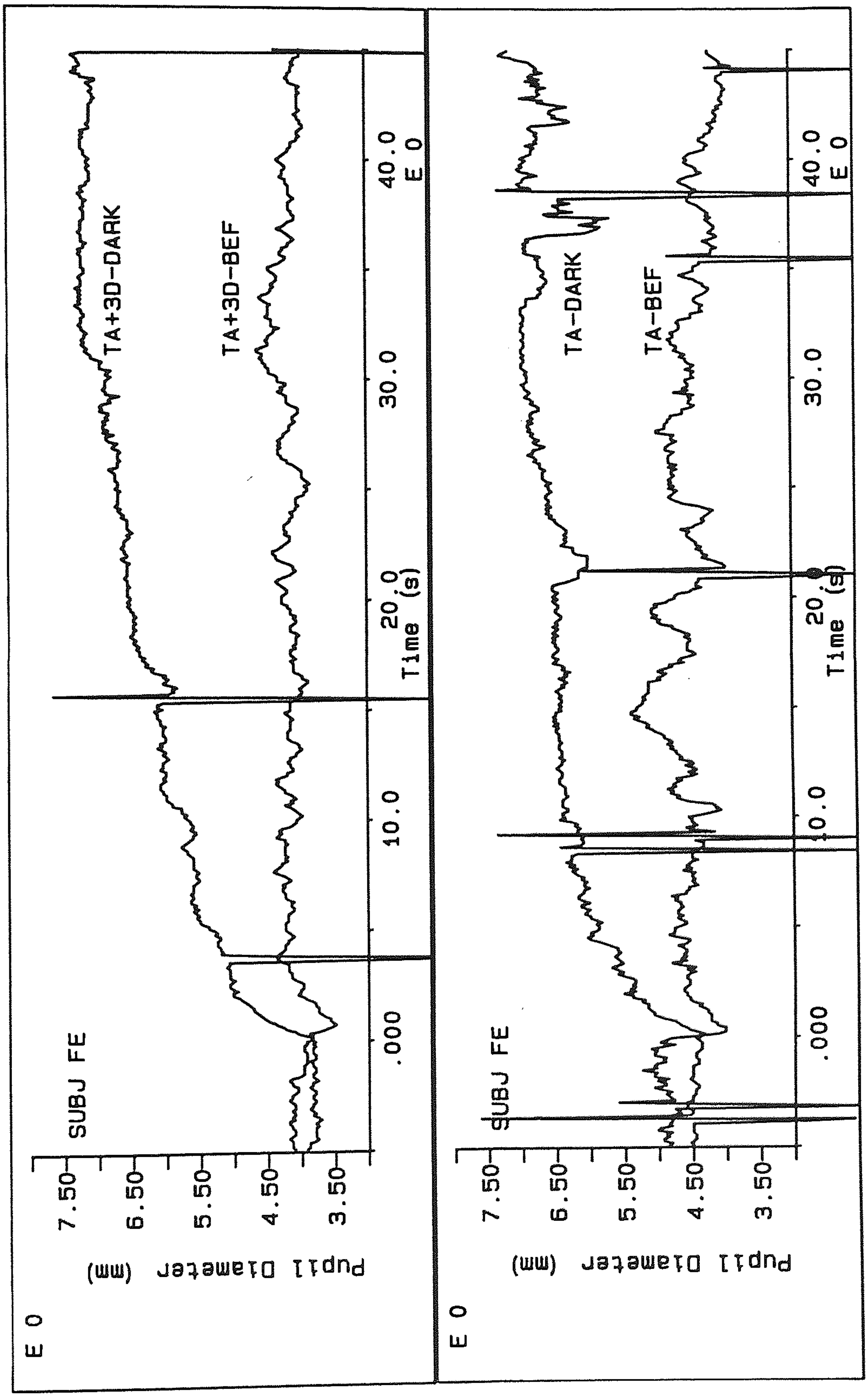
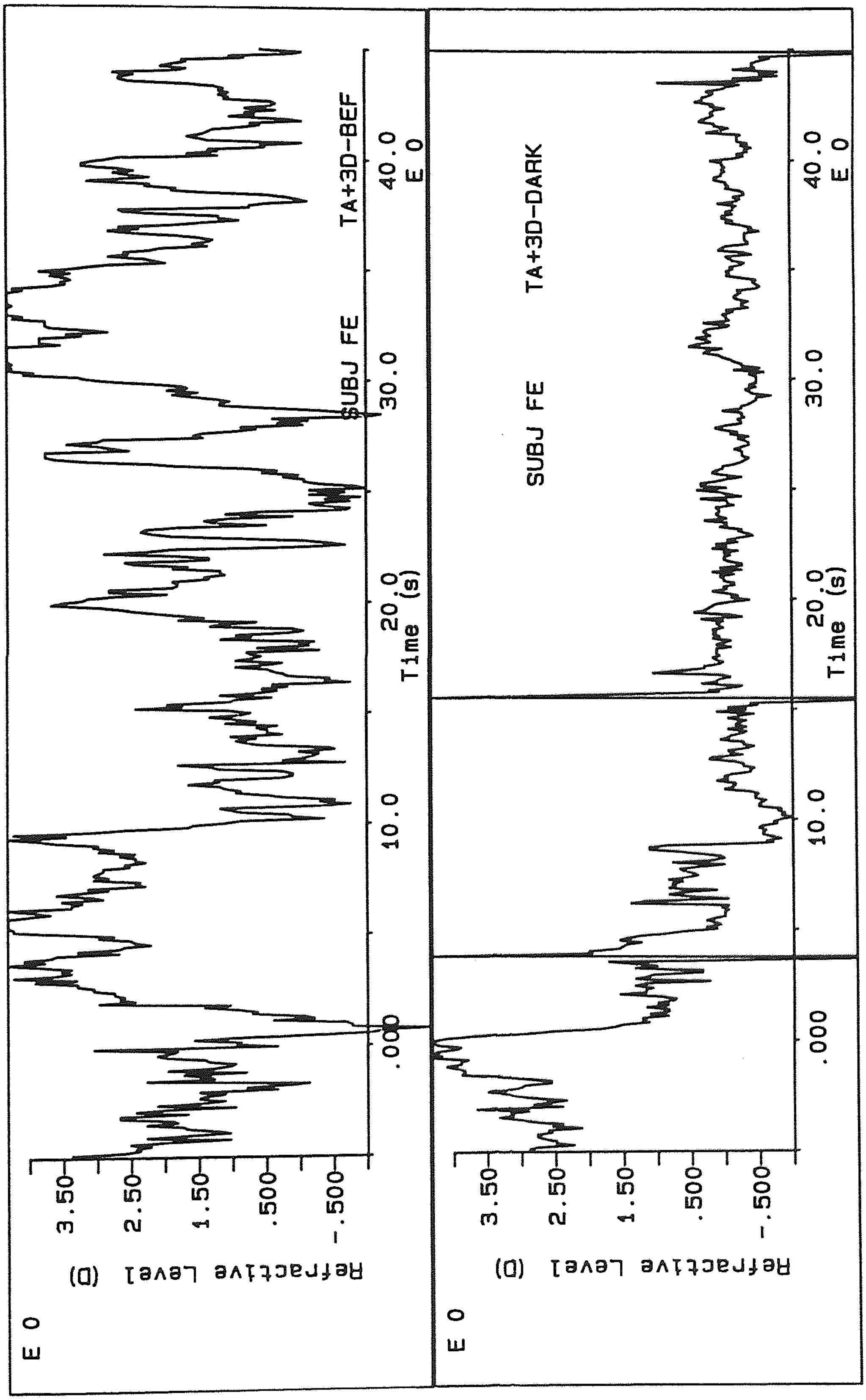
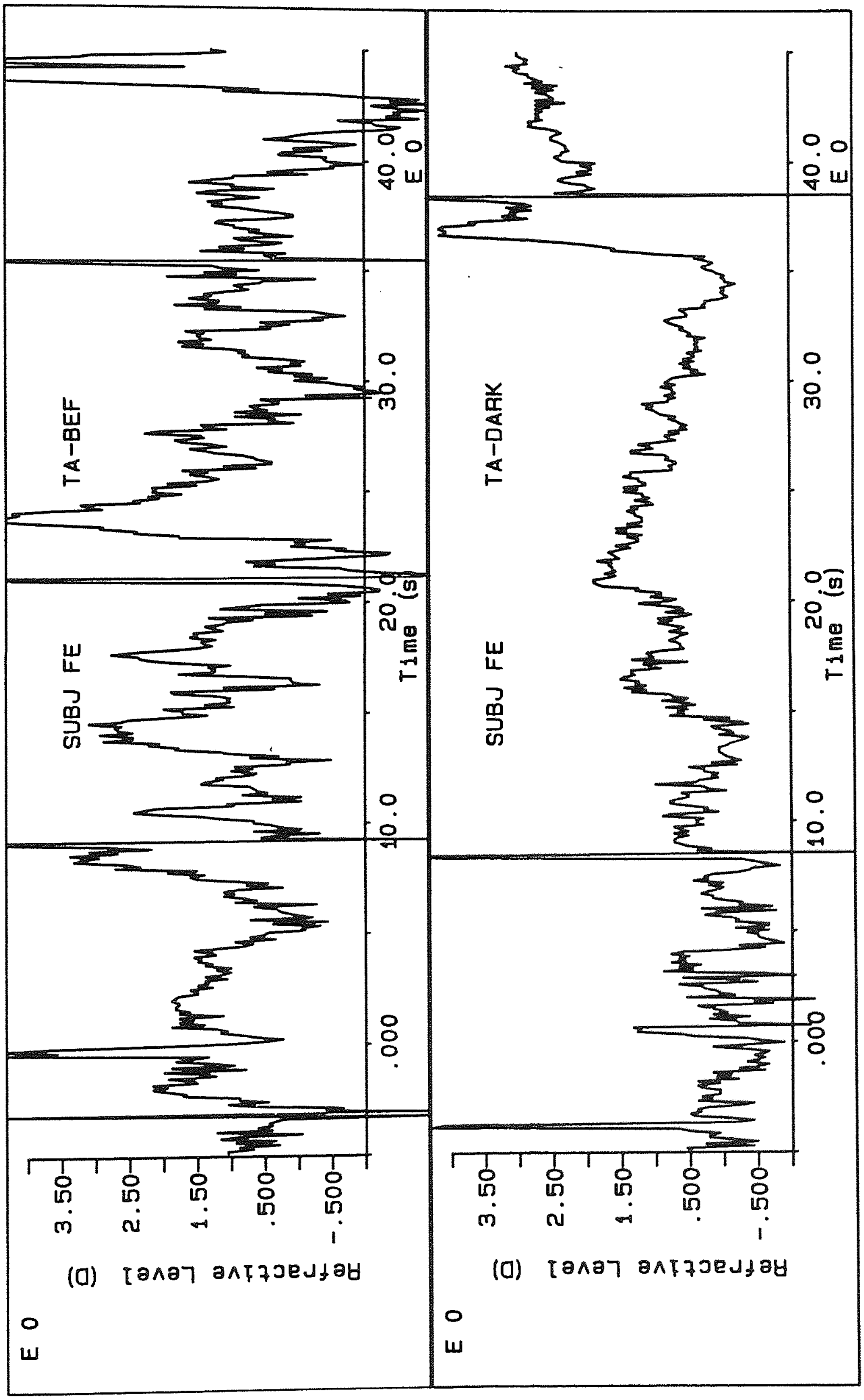
2.50
1.50
.500
-.500
.000
10.0
20.0
30.0
40.0
Time (s)
E 0
E 0


E 0
Refractive Level (D)
3.50
2.50
1.50
.500
-.500
.000
10.0
20.0
30.0
40.0
Time (s)
E 0
SUBJ JH
TA-BEF
E 0
Refractive Level (D)
3.50
2.50
1.50
.500
-.500
.000
10.0
20.0
30.0
40.0
Time (s)
E 0
SUBJ JH
TA-DARK


SUBJ FE
TA+3D-DARK
TA+3D-BEF
Pupil Diameter (mm)
7.50
6.50
5.50
4.50
3.50
.000
10.0
20.0
30.0
40.0
Time (s)
E 0
SUBJ FE
TA-DARK
TA-BEF
Pupil Diameter (mm)
7.50
6.50
5.50
4.50
3.50
.000
10.0
20.0
30.0
40.0
Time (s)
E 0


E 0
Refractive Level (D)
3.50
2.50
1.50
.500
-.500
.000
10.0
20.0
Time (s)
30.0
40.0
E 0
SUBJ FE
TA+3D-BEF
E 0
Refractive Level (D)
3.50
2.50
1.50
.500
-.500
.000
10.0
20.0
Time (s)
30.0
40.0
E 0
SUBJ FE
TA+3D-DARK


E 0
Refractive Level (D)
3.50
2.50
1.50
.500
-.500
.000
10.0
20.0
30.0
40.0
Time (s)
SUBJ FE
TA-BEF
E 0
E 0
Refractive Level (D)
3.50
2.50
1.50
.500
-.500
.000
10.0
20.0
30.0
40.0
Time (s)
SUBJ FE
TA-DARK
E 0

APPENDIX 4

APPENDIX RELATING TO CHAPTER 7

Pupil responsivity expressed as mean response amplitude in mm at each of the stimulus temporal frequencies used for each of the 10 subjects from the initial part of the experiment.

SUBJECT	f=0.05	f=0.1	f=0.2	f=0.3	f=0.4	f=0.5	f=0.6
NP	0	0.3	0.43	0.25	0.25	0.1	0.1
MA	1	1	0.5	0	0	0	0.3
SB	0	0.1	0.1	0.22	0	0	0
JH	0.15	0.28	0.1	0.1	0.1	0.1	0
JL	0.25	0	1	0.9	0.5	0.33	0.1
BE	0.6	0.5	0.2	0.23	0.2	0.2	0.16
GR	0	0.05	0.25	0.17	0	0.02	0.1
JP	0.05	0.25	0.27	0.13	0.28	0.2	0.44
RD	0.45	0.13	0.33	0.13	0.3	0.5	0
RA	0	0.1	0.3	0.03	0.06	0	0
MEAN (SD)	0.25 (0.34)	0.27 (0.30)	0.35 (0.26)	0.22 (0.25)	0.17 (0.17)	0.15 (0.17)	0.12 (0.15)

Pupil responsivity expressed as mean response amplitude in mm at each of the stimulus temporal frequencies used for each of the 3 subjects from the second part of the experiment. Figures relate to the 3 accommodation stimulus ranges used.

SUBJECT	f=0.05	f=0.1	f=0.2	f=0.3	f=0.4	f=0.5	f=0.6
NP (1D)	0	0.1	0.2	0.05	0.1	0	0
GR (1D)	0	0	0	0	0.1	0	0
BE (1D)	0.5	0	0.4	0.2	0.4	0.2	0.1
MEAN (1D)	0.17	0.03	0.2	0.08	0.2	0.07	0.03
NP (2D)	0.2	0.1	0	0.1	0.13	0	0
GR (2D)	0	0.1	0.2	0.13	0.05	0.16	0.03
BE (2D)	0.47	0.4	0.15	0.27	0.2	0.3	0.15
MEAN (2D)	0.23	0.2	0.12	0.17	0.13	0.15	0.06
NP (3D)	0.4	0.4	0.1	0.2	0.1	0.1	0.1
GR (3D)	0.2	0.2	0	0	0	0.2	0
BE (3D)	0.3	0.2	0.3	0.4	0.4	0.2	0.2
MEAN (3D)	0.3	0.27	0.13	0.2	0.17	0.17	0.1

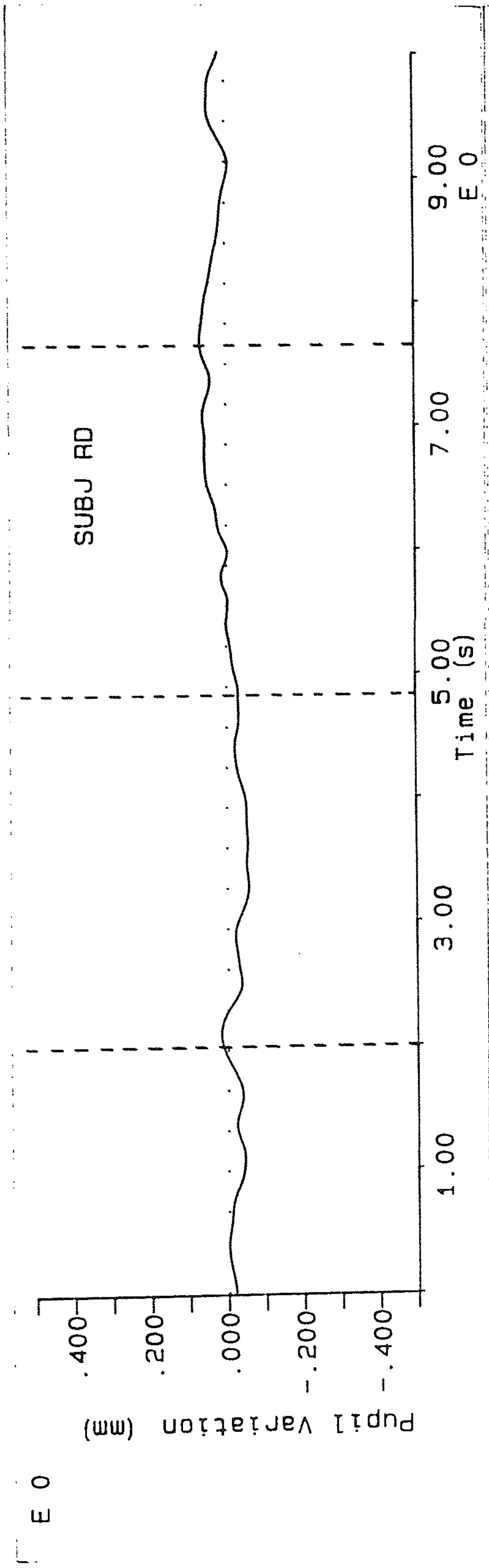
Accommodation responsivity expressed as mean response amplitude in D at each of the stimulus temporal frequencies used for each of the 3 subjects from the second part of the experiment. Figures relate to the 3 accommodation stimulus ranges used.

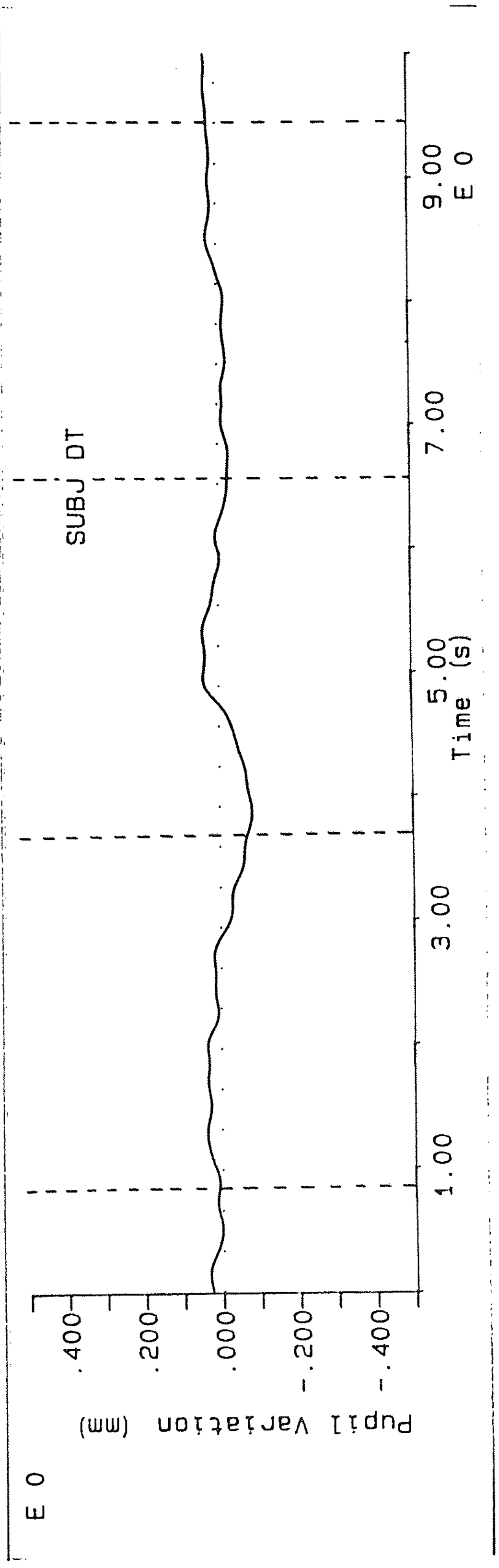
SUBJECT	f=0.05	f=0.1	f=0.2	f=0.3	f=0.4	f=0.5	f=0.6
NP (1D)	1	1	0.86	0.86	1	0.89	0.67
GR (1D)	1	0.56	0.64	1	0.45	0.41	0.41
BE (1D)	1	0.8	0.63	0.65	0.73	0.71	0.58
MEAN (1D)	1	0.79	0.71	0.84	0.73	0.67	0.55
NP (2D)	2	1.8	1.6	1.4	1.3	1.3	1
GR (2D)	1.9	1.9	1.8	1.7	1.38	0.8	1
BE (2D)	2	2	1.6	1.5	1.2	1.2	0.6
MEAN (2D)	1.97	1.9	1.67	1.53	1.29	1.1	0.87
NP (3D)	3	3	3	2.28	2	1.73	1.36
GR (3D)	3	3	1.8	1.2	0.81	1.52	1.45
BE (3D)	3	2.58	2.57	2.31	2.4	2.34	2.39
MEAN (3D)	3	2.86	2.46	1.93	1.74	1.86	1.73

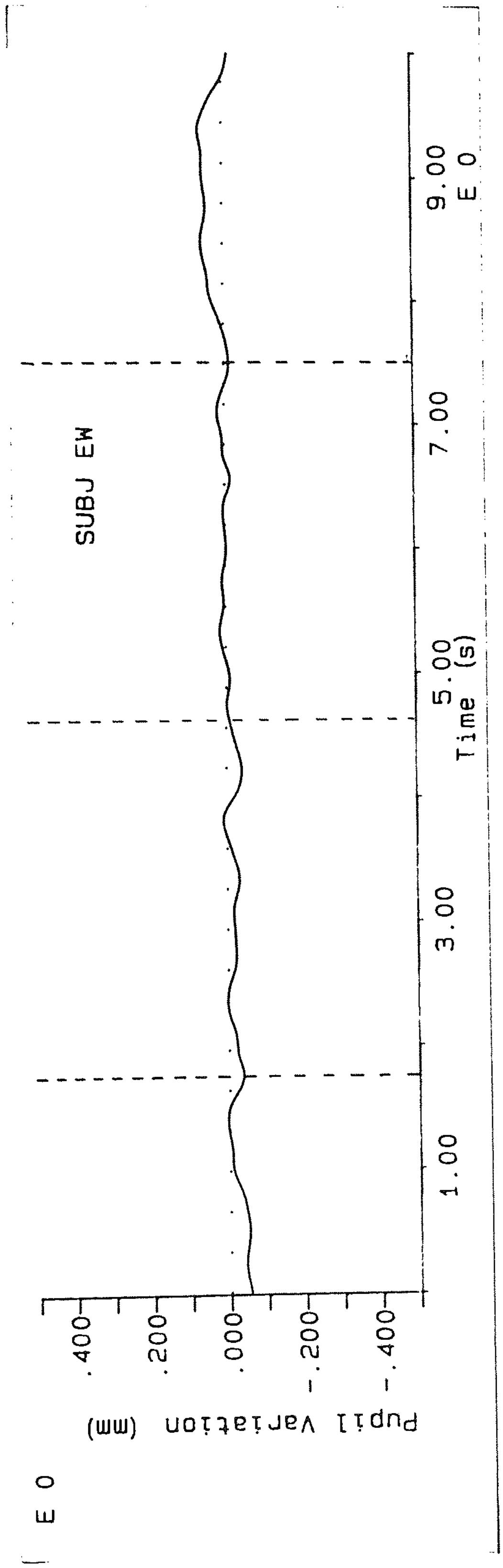
APPENDIX 5

APPENDIX RELATING TO CHAPTER 8

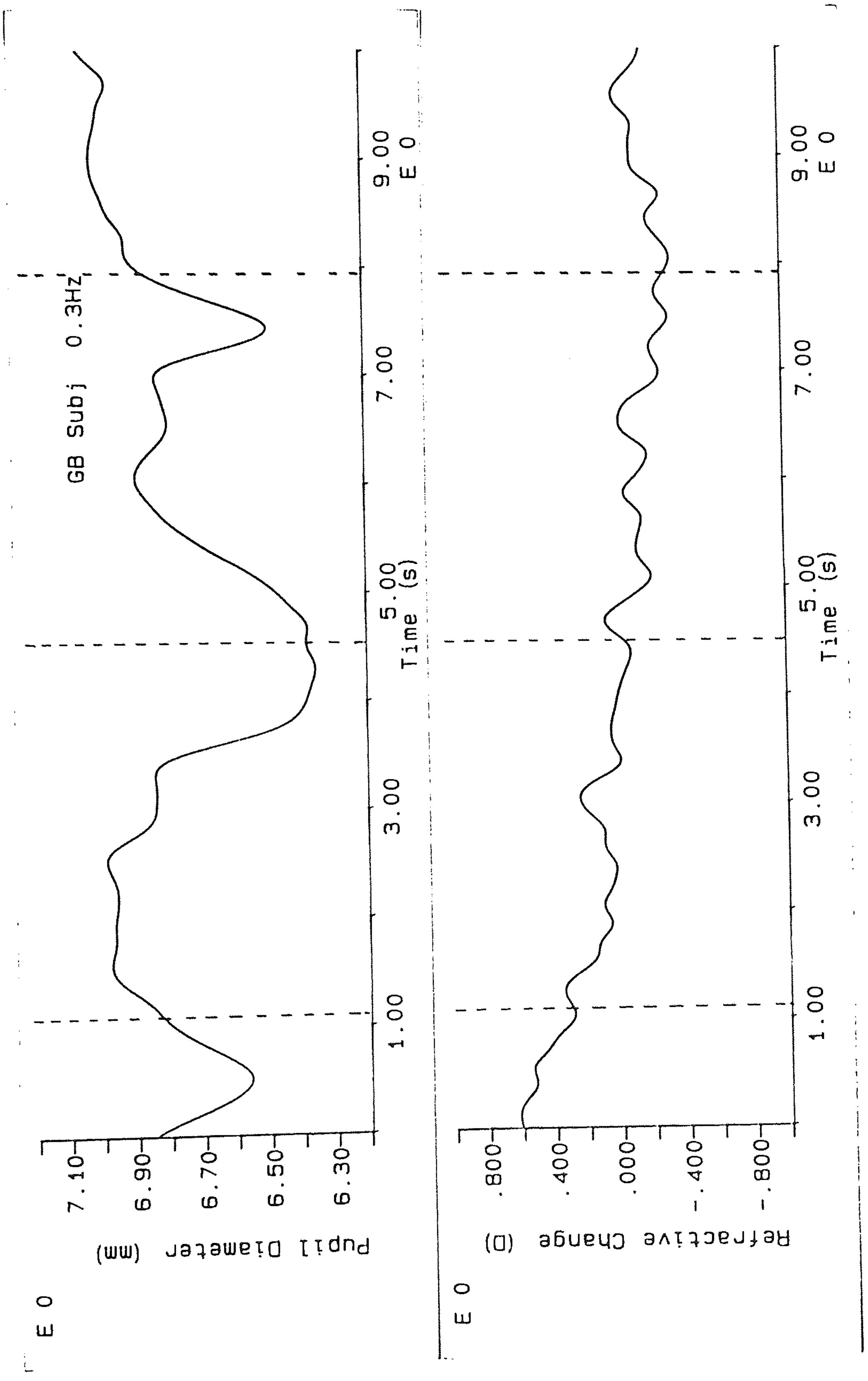
Recordings of pupil diameter taken using subjects RD, DT and EW under light reflex control condition to illustrate lack of pupil response.

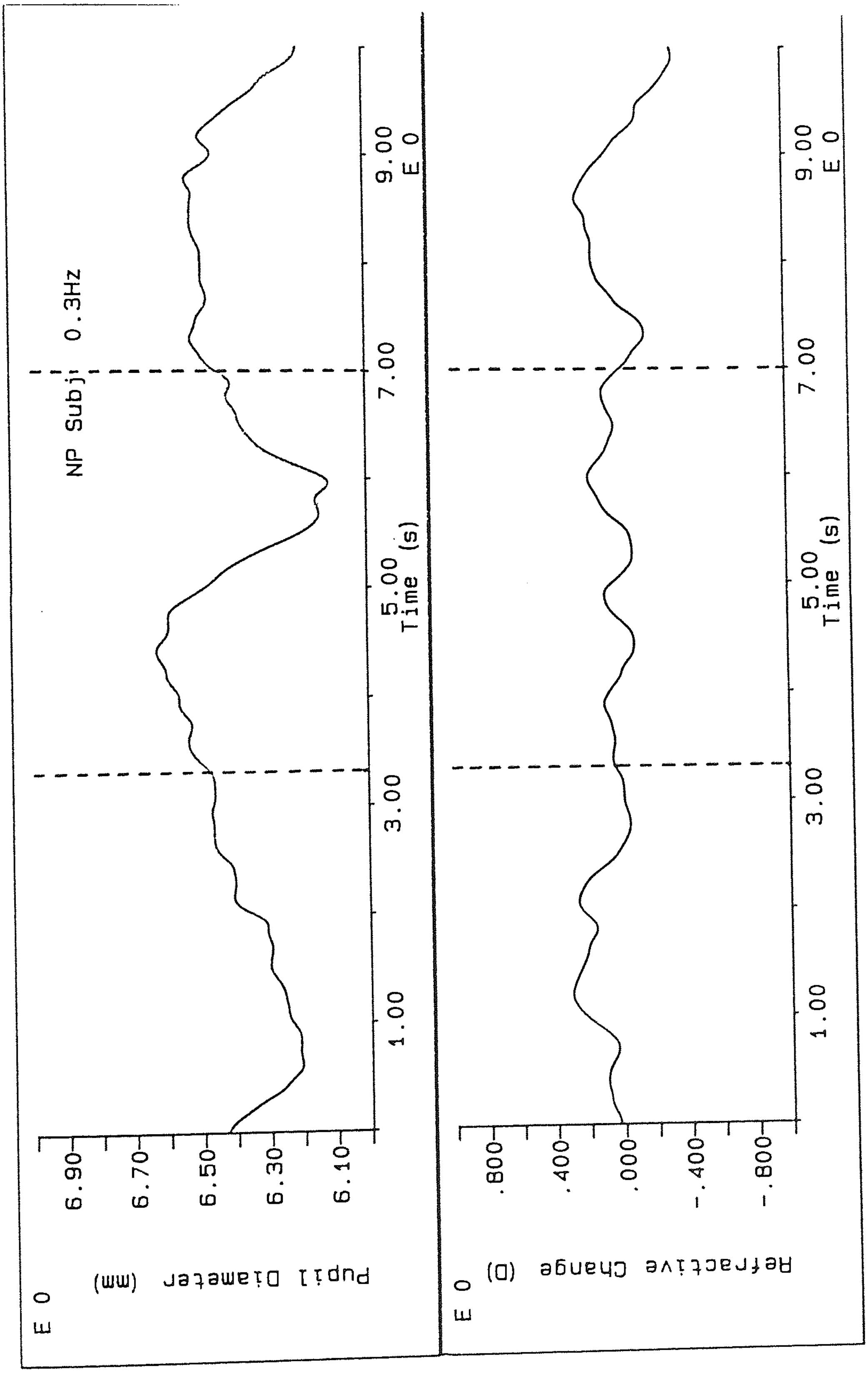





SUBJ EW
Pupil Variation (mm)
.400
.200
.000
-.200
-.400
1.00
3.00
5.00
7.00
9.00
Time (s)
E 0
E 0

Recordings of pupil diameter and accommodation response using sujects GB and NP viewing the looming target at a stimulus temporal frequency of 0.3Hz.




NP Subj: 0.3Hz
Pupil Diameter (mm)
6.90
6.70
6.50
6.30
6.10
E 0
1.00
3.00
5.00
7.00
9.00
Time (s)
E 0
Refractive Change (D)
.800
.400
.000
-.400
-.800
E 0
1.00
3.00
5.00
7.00
9.00
Time (s)
E 0

Phase lag of the pupil response to the looming stimulus at each of the temporal frequencies used for each of the 4 observers. Figures are derived from 4 stimulus cycles at each temporal frequency except at 0.1Hz where 2 stimulus cycles are used.

SUBJECT	f=0.1	f=0.2	f=0.3	f=0.4	f=0.5
IM	-180	0	16	-180	-267
IM	-180	28	-113	-180	-97
IM		115	-180	0	-207
IM		72	-86	-180	-180
NP	-40	-115	0	17	-117
NP	-60	0	-154	-17	-117
NP		0	111	-127	-136
NP		86	-83	-238	-136
LM	-103	0	-180	-166	-120
LM	-46	-196	-87	36	-180
LM		-180	-103	-288	-120
LM		-180	-86	-252	-240
GB	0	0	-138	-168	-151
GB	-110	0	-94	-180	-142
GB		65	83	-117	-140
GB		0	33	-130	-198
MEAN	-89.86	-19.06	-66.3	-135.63	-163
SD	68.82	97.11	89.15	97.56	47.46

APPENDIX 6

APPENDIX RELATING TO CHAPTER 9

Pupil diameter measurements taken at 30s intervals using the 10 young subjects.

SUBJ/TIME	0	30	60	90	120	150	180	210	240	270	300
KM	3.13	3.38	3.32	3.11	3.17	3.14	3.1	3.1	3.05	3.02	3.25
HM	3.04	3.41	3.06	2.84	3.29	3.34	3.27	3.32	3.34	3.23	3.26
CL	3.14	3.27	3.36	3.32	3.25	3.35	3.24	3.27	3.32	3.61	3.37
SK	3.22	3.47	3.55	3.5	3.57	3.63	3.68	3.7	3.47	3.03	3.47
CS	3.69	3.91	3.86	3.66	3.78	3.66	3.75	3.88	3.85	3.82	3.7
SC	4.62	4.22	3.74	4.62	3.63	3.87	3.76	3.71	3.84	2.74	3.75
PK	4.22	3.96	4.22	3.86	4.09	4.17	3.76	3.72	3.59	3.67	3.77
KJ	4.31	4.36	4.51	4.03	4.02	4.18	3.89	4.02	4.03	3.95	3.9
WP	3.14	3.61	3.09	3.05	2.9	3.47	3.08	3.12	3	3.18	3.12
AB	4.25	4.65	4.35	4.42	4.37	4.36	4.51	4.08	4.3	4.21	4.46
MEAN	3.68	3.82	3.71	3.64	3.61	3.72	3.6	3.59	3.58	3.45	3.61
SD	0.61	0.47	0.52	0.59	0.46	0.41	0.44	0.36	0.42	0.47	0.4

Pupil diameter measurements taken at 30s intervals using the 10 elderly subjects.

SUBJ/TIME	0	30	60	90	120	150	180	210	240	270	300
SM	2.13	1.98	2.11	2.14	1.95	1.83	1.95	2.1	1.91	2	2.11
JH	2.02	2.12	1.85	2.08	2.37	2.17	2.06	2.28	2.32	2.36	1.98
DD	2.29	2.26	2.3	2.5	2.34	2.17	2.43	2.34	2.44	2.33	2.43
DM	2.38	2.28	2.71	2.61	2.48	2.5	2.67	2.88	2.47	2.74	2.51
JM	1.44	1.63	1.5	1.55	1.55	1.47	1.44	1.42	1.68	1.58	1.38
MM	4.07	3.7	3.77	3.72	3.97	3.79	4.38	3.83	4.18	3.83	4.03
BS	2.71	2.52	2.9	2.76	2.63	2.64	2.96	2.97	3.16	2.83	2.77
NL	2.93	2.81	2.71	2.65	2.82	2.81	2.89	2.88	2.68	2.85	2.85
KF	2.74	2.99	2.7	3.05	2.91	3.03	2.86	2.82	2.67	2.63	2.7
PD	2.95	2.98	2.85	3.26	3.02	3.11	3.16	3.26	3.28	3	3.18
MEAN	2.57	2.53	2.54	2.63	2.6	2.55	2.68	2.68	2.68	2.62	2.6
SD	0.7	0.6	0.63	0.62	0.65	0.68	0.8	0.67	0.72	0.61	0.72

APPENDIX 7

APPENDIX RELATING TO CHAPTER 10

Pupil response in mm to the 2.25D accommodative stimulus at each of 4 stimulus cycles for each of the stimulus temporal frequencies used.

SUBJ/f	0.1	0.2	0.3	0.4	0.5
GR	0.2	0.25	0.5	0.35	0.2
GR	0.35	0.25	0.7	0.35	0.1
GR	0.15	0.25	0.6	0.3	0.1
GR	0.25	0.4	0.6	0.25	0.25
IM	0.4	0.45	0.7	0.7	0.4
IM	0.5	0.3	0.6	0.7	0.2
IM	0.7	0.5	0.1	0.4	0.1
IM	0.4	0.75	0.1	0.15	0.4
NP	0.4	0.3	0.15	0.15	0.12
NP	0.35	0.4	0.1	0.08	0.15
NP	0.4	0.4	0.2	0.09	0.1
NP	0.25	0.3	0.25	0.17	0.15
LM	0.7	0.75	0.6	0.2	0.1
LM	0.7	0.35	0.4	0.7	0.1
LM	1	0.4	0.2	0.4	0.2
LM	0.8	0.5	0.32	0.4	0.2
RS	0.25	0.25	0.3	0.32	0.15
RS	0.2	0.3	0.3	0.25	0.08
RS	0.35	0.1	0.2	0.25	0.08
RS	0.25	0.25	0.25	0.25	0.1
MEAN	0.43	0.37	0.36	0.32	0.16
SD	0.23	0.16	0.21	0.19	0.09

Pupil response phase relative to the accommodative stimulus used. Figures show response phase in degrees at each of 4 stimulus cycles at each of the temporal frequencies used. Negative figures indicate phase lag, positive figures indicate phase lead.

SUBJ/f	0.1	0.2	0.3	0.4	0.5
GR	42	-122	-112	-275	-360
GR	-77	-114	-281	-207	-380
GR	0	-180	-405	-329	-473
GR	-139	0	-652	-260	-473
IM	-96	-180	-360	-520	-360
IM	0	-306	-360	-520	-360
IM	-26	-252	-180	-306	-720
IM	0	-40	-180	-153	-720
NP	-7	-38	-180	-300	-305
NP	-10	-54	-90	-321	-399
NP	24	-77	0	-360	-360
NP	54	-15	-180	-370	-562
LM	-46	-61	-56	-77	-408
LM	0	-92	-90	-123	-408
LM	11	0	-90	-92	-420
LM	-23	-38	-90	-115	-360
RS	-70	-200	-197	-310	-391
RS	-10	-320	-151	-253	-545
RS	-28	-152	-84	-106	-483
RS	-68	-152	-228	-131	-534
MEAN	-23.45	-119.65	-198.3	-256.4	-451.05
SD	47.42	96.75	152	131.42	115.5

Accommodation response in D to the 2.25D accommodative stimulus at each of 4 stimulus cycles for each of the stimulus temporal frequencies used.

SUBJ/f	0.1	0.2	0.3	0.4	0.5
GR	2	1	1.25	1.25	1
GR	2	1.25	1.25	1.25	1
GR	2	1.25	1	1.25	1
GR	2	2	1.5	0.6	1
IM	2	1.2	2	2	1.2
IM	2	1.2	1.5	2	0.8
IM	2	2	2	1.2	1.2
IM	2	1.6	1.5	1.2	1.2
NP	1.8	1	2	1.2	0.8
NP	1.8	1	2	1.2	1.5
NP	1.6	2	1.2	1.2	0.8
NP	1.6	2	1.4	1	1.4
LM	2	2.2	2.6	2	1.2
LM	2	2.2	2.2	2	2.2
LM	2.2	2.2	2.4	1.4	2.2
LM	2.2	2.2	2.4	1.8	1.6
RS	2	1.6	1.5	1.4	1.6
RS	2	2	1.6	1.7	1.8
RS	1.8	1.8	1.7	1.7	1.5
RS	1.4	1.6	1.8	1.6	1.6
MEAN	1.92	1.67	1.74	1.45	1.33
SD	0.2	0.45	0.45	0.39	0.42

Accommodation response phase relative to the accommodative stimulus used. Figures show response phase in degrees at each of 4 stimulus cycles at each of the temporal frequencies used. Negative figures indicate phase lag, positive figures indicate phase lead.

SUBJ/f	0.1	0.2	0.3	0.4	0.5
GR	-12	0	0	-180	-28
GR	-15	-53	-56	-77	-28
GR	-12	0	0	0	-28
GR	0	0	0	0	-30
IM	0	-38	-43	0	-48
IM	0	0	0	-88	0
IM	0	0	54	-53	-38
IM	0	-31	-109	-107	-48
NP	-7	0	-180	0	-66
NP	-10	-15	-180	38	-78
NP	0	-180	-150	0	-180
NP	58	-180	-150	0	-180
LM	0	-30	-34	-31	-30
LM	0	-23	0	-15	-50
LM	0	-22.5	-34	-23	-50
LM	-23	-15	-45	-23	-50
RS	-8	-40	-35	-80	-41
RS	-10	-40	-120	-41	-51
RS	-28	-24	0	-41	-62
RS	-32	0	-48	0	-31
MEAN	-4.95	-34.58	-56.5	-36.05	-55.85
SD	17.83	52.45	68.06	50.15	45.68

APPENDIX 8

SUPPORTING PUBLICATIONS

Refereed published abstracts of conference proceedings

8.1 Gilmartin, B., Ukai, K., Phillips, N. J. and Winn, B. Accommodative adaptation to near-vision: is there a pupil corollary? Transactions of the 2nd International Conference of The British College of Optometrists, London (1990).

8.2 Gilmartin, B., Ukai, K., Phillips, N. J. and Winn, B. Accommodative adaptation to near-vision: is there a pupil corollary? *Ophthal. Physiol. Opt.* **10**, 109 (1990).

8.3 Phillips, N. J., Winn, B., Gilmartin, B. and Ukai, K. Simultaneous recording of accommodation and pupil responses: some preliminary investigations. Paper, Society of Experimental Optometry, July 1990, Birmingham. *Ophthal. Physiol. Opt.* **10**, 412 (1990).

8.4 Ukai, K., Phillips, N. J., Winn, B. and Gilmartin, B. Pupillary adaptation following near vision is masked by darkness. 8th International Neuro-Ophthalmology Symposium Abstracts, **MOO8** (1990).

8.5 Phillips, N. J., Winn, B., Gilmartin, B. and Sculfor, D. L. An investigation of accommodative-driven pupil response to periodic variations in stimulus vergence. Paper, Applied Vision Association Conference, April 1991, UMIST Manchester. *Ophthal. Physiol. Opt.* **11**, 282 (1991).

8.6 Phillips, N. J., Winn, B., Gilmartin, B., Sculfor, D. L. and Ukai, K. The effect of periodic variations in target vergence on accommodation-driven pupil response. Paper, Association for Research into Vision and Ophthalmology meeting, May 1991, Sarasota, Florida, USA. *Invest. Ophthalmol. Visual Sci.* **32** (suppl.), 1124 (1991).

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Refereed papers published in journals

8.9 Phillips, N. J. The ageing pupil? *Optician*, **5252**, 12-14 (1990).

8.10 Phillips, N. J., Winn, B. and Gilmartin, B. Absence of pupil response to blur-driven accommodation. *Vision Res.* **32**, 1775-1779 (1992).

Under review

8.11 Phillips, N., Gilmartin, B. and Winn, B. Pupil response to periodic variation in target vergence lacks the retinotopic feedback control demonstrated by accommodation. Submitted to the Association for Research into Vision and Ophthalmology meeting, May 1993, Sarasota, Florida, USA.

In preparation

8.12 Winn, B., Whitaker, D., Elliot, D. B. and Phillips, N. J. Factors affecting light adapted pupil size in normal human subjects. (In preparation).

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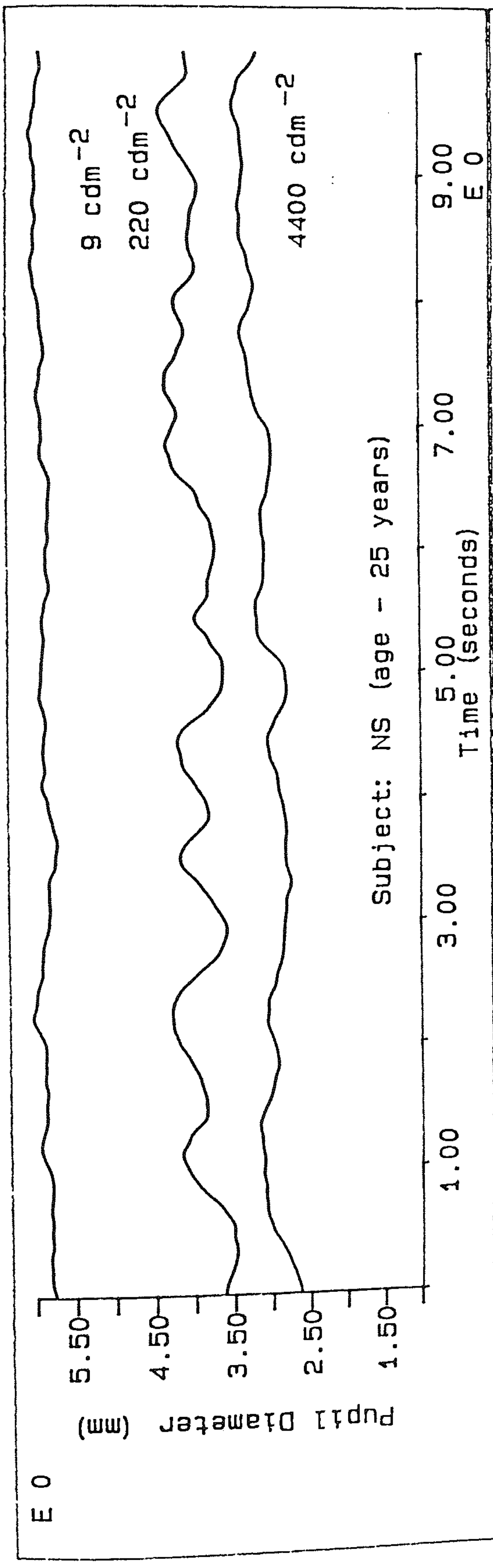
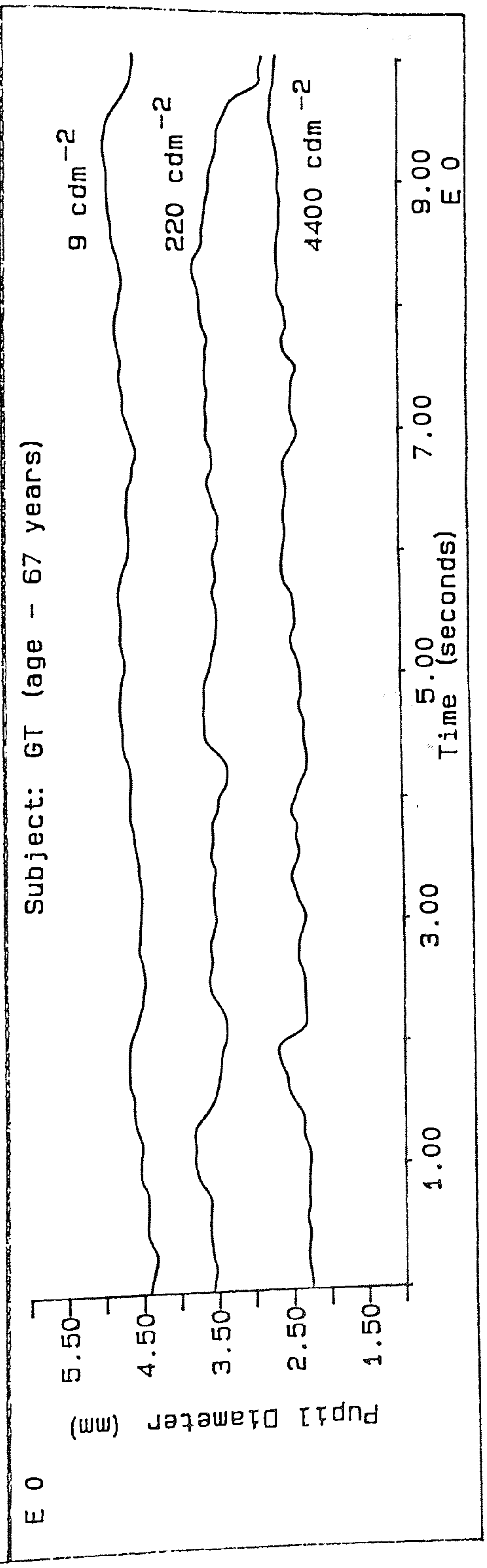

Subject: NS (age - 25 years)
Pupil Diameter (mm)
5.50
4.50
3.50
2.50
1.50
Time (seconds)
1.00
3.00
5.00
7.00
9.00
E 0
E 0
9 cdm $^{-2}$
220 cdm $^{-2}$
4400 cdm $^{-2}$


Subject: GT (age - 67 years)
Pupil Diameter (mm)
5.50
4.50
3.50
2.50
1.50
Time (seconds)
1.00
3.00
5.00
7.00
9.00
E 0
E 0
9 cdm $^{-2}$
220 cdm $^{-2}$
4400 cdm $^{-2}$

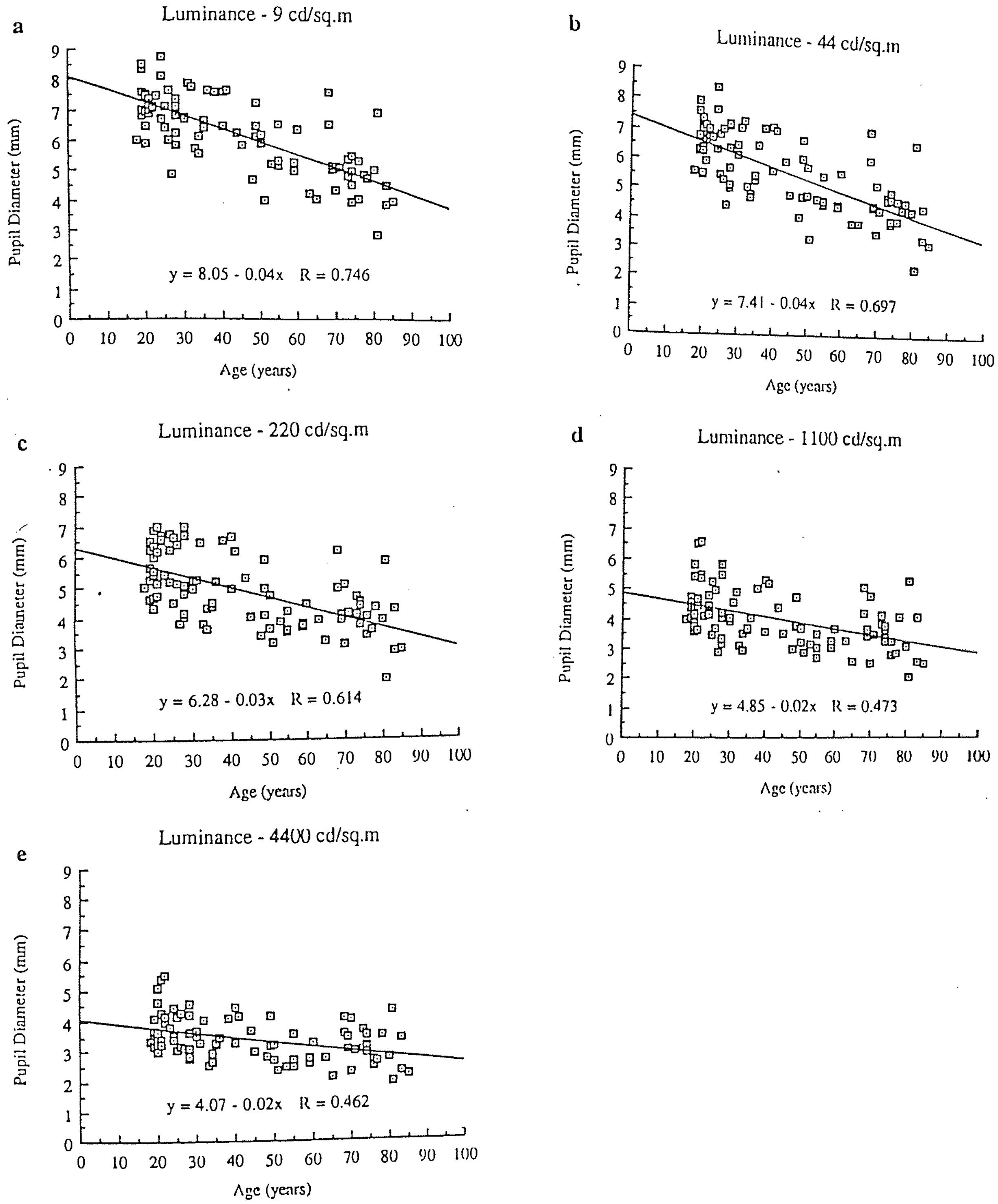

a
Luminance - 9 cd/sq.m
Pupil Diameter (mm)
Age (years)
y = 8.05 - 0.04x R = 0.746
b
Luminance - 44 cd/sq.m
Pupil Diameter (mm)
Age (years)
y = 7.41 - 0.04x R = 0.697
c
Luminance - 220 cd/sq.m
Pupil Diameter (mm)
Age (years)
y = 6.28 - 0.03x R = 0.614
d
Luminance - 1100 cd/sq.m
Pupil Diameter (mm)
Age (years)
y = 4.85 - 0.02x R = 0.473
e
Luminance - 4400 cd/sq.m
Pupil Diameter (mm)
Age (years)
y = 4.07 - 0.02x R = 0.462
0 1 2 3 4 5 6 7 8 9
0 10 20 30 40 50 60 70 80 90 100

Fig 2

Figure Legends

Figure 1 Typical pupil size data from a young subject (age 25 years) and an old (age 67 years) subject for 3 levels of luminance (9, 220 and 4400 cdm^{-2})

Figure 2 Scattergrams pupil diameter as a function of age for each luminance condition. Note the reduction in slope with increasing luminance.

Figure 3 Mean pupil size for a typical 20 year old and a typical 70 year old as a function of luminance. The data points have been calculated from the regression analyses of the data shown in figure 3 (error bars represent 95% confidence limits for the true mean pupil size).

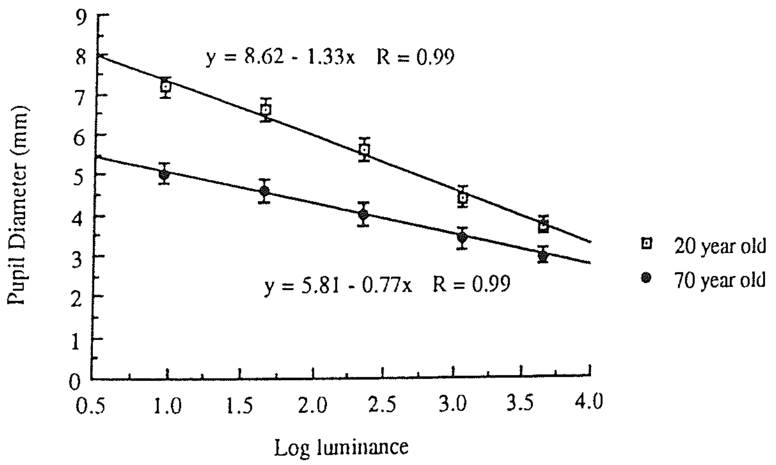


Fig 5.