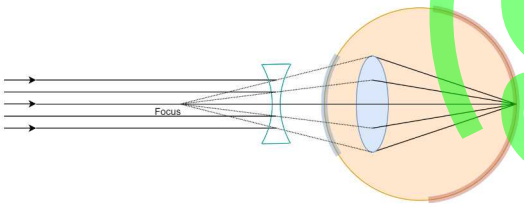

Breakthrough Adaptive Theory Proposing Emmetropization Requirements for Myopia

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0. Abstract

Current understanding is lacking when it comes to explaining many peculiar behaviours of physiologic Myopia. We aim to propose an alternative theoretical framework taking into account the observed interplay of multiple environmental and lifestyle factors for physiologic Myopia.

Careful physical characterization resulted in the breakthrough framework of Continuous Adaptation Theory (CAT) and its two refractive state equivalences that consider physiologic Myopia as refractive state resulting from adaptative responses of the eye. By extension, the same adaptive mechanism responsible for onset of Myopia (in emmetropic eyes) is predicted to be behind Myopia progression also. And the same could be utilised for stabilization of progressive Myopia and even Myopia reversal.

The breakthrough insights provided by our theory when implemented with behavioural interventions towards myopia management should provide first ever clinical observations of long-term axial shortening directly translating into substantial vision improvements.

Note: Additional Preliminary information accompanies this paper.

0.1 Keywords

Axial Shortening, Progression, Myopia Management, Emmetropization

0.2 Ethics declarations

The author declares no competing interests.

1. Introduction

Myopia – is a refractive error widely regarded as irreversible with a suspected multifactorial aetiology lacking any viable long-term solution[1]. Extreme axial elongation[2] resulting from severely high Myopia increases risk of vision threatening complications (even after appropriate refractive compensation) including but not limited to Open-angle glaucoma, cataract, retinal tears that can lead to retinal detachment, and macular degeneration (also termed myopic maculopathy)[3]. An estimated half of the world's population will be myopic by 2050 if the current trends continue[4].

There is an urgent need for developing interventions that can reverse/stabilize or at least slow down long-term rate of Myopia progression. This article describes breakthrough insights from adaptive characterization (resulting in the Continuous Adaptation Theory) of physiologic Myopia only. The governing hypothesis behind the adaptive approach is viability of axial shortening and emmetropization for Physiologic Myopia. The theory proposes that myopization results from simultaneous 'push-pull' interaction of near-work induced accommodative load (pull) when combined with underutilisation of distance vision (push). The role of light is to direct adaptive change from defocus possibly answering the decade long open question on 'how eyes deduce direction of adaptation from defocus?'.

2. Background

This article employs prefixes like *compensated* myopic/hyperopic eye or suffixes like a myopic/hyperopic/presbyopic eye *wearing prescription* to denote an eye using refractive interventions different from an eye without interventions. The mention of the word infinity or symbol ∞ should be taken to mean optical infinity at a distance of 10 m or greater (≤0.1 D). We have strived to provide terminologies and abbreviation whenever applicable at the beginning of each new section.

The aim of this article is to answer the following questions.

1. What are the factors/causes responsible for physiologic Myopia?
2. Why so far there is still lack of a well established aetiology for physiologic Myopia?
3. Why was common Myopia considered irreversible so far?
4. There are mounting evidences that seemingly contradict widely presumed irreversibility of Myopia and hint at the existence of a viable protocol that can result in evidence of emmetropization at work. Is a truly viable management protocol/method possible for physiological Myopia?

2.1 Methodology

Article selection reporting experimental results/observations used terms associated with primarily physiological Myopia and human eyes on PubMed. Special emphasis was on selecting articles reporting unusual or conflicting behavioural observations about Myopia. The presentation follows the natural order:

physiological myopia (onset and stabilization or progression) → proposed causes of Myopia → effects of myopia → viability/shortcomings of existing Myopia management methods. Characterizing physiological aspects of vision was done using a grounds up mixed mode approach involving ray optics to rule out suspected improper isolation of physiologic variables responsible for Myopia.

2.2 Physiologic Myopia and Pathologic Myopia

Physiologic Myopia is the proper inability to bring distant objects into focus (image formation behind the retina even after relaxing accommodation) compared to an emmetropic eye. All observed instances of myopic refractive error can be categorised under physiologic or pathologic/malignant/degenerative Myopia[5]. Even high degree of refractive error from physiologic Myopia (increasing risk of sequelae) must be distinguished from Pathologic Myopia alongside pathological complications that can accompany highly severe forms of physiologic Myopia[6]. Pathologic myopia is often associated with high myopia and complications of the fundus such as degeneration of the macula, optic nerve, or the peripheral retina. Nevertheless complications (for instance, posterior staphyloma) have been observed to occur in eyes without high myopia and even in emmetropic individuals[7].

For the scope of the article, Physiologic Myopia is strictly defined as Myopia without other ocular anomalies except axial elongation. This is important from the standpoint of consistent classification of Myopia – Myopia can be either termed physiological or pathological but not both in the sense that Physiological Myopia can develop pathological complications later on indicating differences in the underlying mechanism and possible control/management. The scope of this article is limited to characterizing Physiological Myopia only.

2.3 Animal models of Experimental Myopia and Form Deprivation

There is a large pool of studies documenting experimental myopia in animals. We expect only a subset of these observations to actually extend to the human eyes.

Both hyperopia and myopia resulted in young chicks when convex and concave lenses respectively were used as defocus indicating the capability of the eye to respond and direct axial changes in the opposite direction to compensate for the induced lens. Also observed was the disproportionately stronger response of myopic defocus compared to same duration of hyperopic defocus as long as the cycle time wasn't too frequent (< 30 minutes)[8]. Once external defocus was removed, induced experimental Myopia slowed and then reversed towards emmetropia suggesting that the built in mechanism is able to detect and swiftly adapt to changes in external stimulus. The same was observed for a higher primate (rhesus macaques) as well[9].

Efforts to induce Form Deprivation Myopia were successful even after Optic Nerve Section (ONS) indicating that the eye possesses internal mechanisms that can still direct axial changes (this mechanism may also act as a fall back)[10]. This is further supported from evidences regarding hemi-retinal form deprivation influencing local axial changes in infant monkeys and chicks before eye-growth is completed.

The study on infant rhesus macaques concluded that effects of form deprivation on refractive development in primates are mediated by presumably retinal mechanisms integrating visual signals in a spatially restricted manner[11]. It can be stated that the aforementioned temporally adaptive observations are a consistent feature across multiple species that include higher primates (extending similar possibility for humans as well) and that retina acts as the primary initiator for most of these localized refractive changes.

2.3.1 Changes in the eye due to physiologic Myopia

Hyperopic defocus using minus lenses leads to the observation of choroid thinning (causing the retina to shift backward) increasing AL compensating for the introduced defocus (in this case, resulting in Myopia). Choroidal and scleral thinning was observed to be most prominent at the posterior pole compared to the equatorial regions of the eye[12]. Discussing the exact pathways and mechanisms behind these changes is beyond the scope of this article.

Human eyes starts forming around third week of gestation and the process is mostly completed by the tenth week[13]. Eyes continue to grow rapidly after birth to the age of one to two years, and then in a gradual manner until adult eyeball size is usually attained around onset of puberty. The primary goal is to match the eye's axial length with its optical components (emmetropization). Eye size and shape at birth influences subsequent eye growth but hasn't been observed to be associated with refractive error development[14].

The distinct nature of axial elongation in response to external environmental factors separately from eye growth is required to explain observations of focally controlled ocular growth in infant monkeys and chicks. The eye undergoes changes from superposition of growth and adaptive signals after birth [Josh Wallman and Jonathan Winawer, 2004]. Terming Axial elongation as eye growth actively conflicts with evidences pointing towards existence of an active emmetropization mechanism. Such a mechanism should be present and fully functional (although the time period over which it acts may differ) in Human eyes also influencing axial changes apart from eye growth[15]. Axial elongation due to Myopia results in a marked shape change (elongation) distinct from overall (globe) growth phase. Because of multiple such reasons, we will prefer to use the term axial change instead of axial growth in this article for outcomes of integration of visual signals. This also naturally absorbs the term axial shortening conflicting with the directional connotations of word growth and its mistaken connotations with bodily growth.

2.4 Multi factorial associations of Myopia

2.4.1 Genetics

For decades, investigations were primarily focused on figuring out the suspected genetic causes behind Myopia. There are multiple studies regarding Myopia's associations with Genetics. However, evidences are now mounting that at most, there can be genetic susceptibility towards physiological Myopia in the face of mostly missing heritable markers for physiological Myopia unlike the mostly hereditary/parental nature for cases of pathological Myopia[16]. This argument is further supported from environmental relation of common

Myopia including its negative association with outdoor activity and the recently discovered effect of sunlight[17] protecting from Myopia onset and progression.

2.4.2 Environmental and behavioural Associations with near work and outdoor exposure

When it comes to physiologic Myopia, its causes are commonly predicted to be a multifactorial interplay of environmental and lifestyle factors. Myopia shows strong correlations with urban lifestyle, higher education, along with intensive visual near-work (defined as eyes working at or near their accommodation limit) that comes with it including but not limited to reading, writing and time spent looking at digital displays whether on PC/Laptop or smartphones/tablets[18]. Myopia is not significantly associated with time spent doing near work after adjustment for other factors such as age, sex, ethnicity, parental myopia, school type, and outdoor activity. There were independent associations with closer reading distance (< 30 cm) and continuous reading (> 30 minute) leading the study authors to speculate intensity rather total duration of near work to be an influential factor for Myopia. The study additionally reinforces the need for targeted workplace measures to reduce occupational exposure and mitigations such as allowances for regular breaks from near work[19].

2.5 Myopia onset and its progression

The onset of Myopia is usually seen as setting the stage for progression of Myopia. This translates to a disease like presumed aetiology of Myopia where worsening Myopia is viewed as the natural course of its progression. This standpoint is mostly justified in the absence of any viable long-term methods demonstrating the ability to slow or stabilize Myopia progression or possibly reverse it (myopia control[20]).

That Axial elongation results from ‘uncontrolled growth’ of the eyes from causes yet undetermined is the most common explanation with justifications given mainly in the form of experimental studies failing to observe substantial outcomes. Studies investigating under-correction of refractive prescription saw enhancement instead of inhibition of myopia progression compared to the full correction group [[21], [22]].

Myopia onset is primarily observed in the early childhood and mostly stabilizing towards the mid twenties. However, both myopia onset and progression has been observed to happen at all ages. There are observations regarding adult onset/progression of Myopia after enrolling into college[23]. The COVID-19 pandemic also resulted in significant reports of Myopia onset and progression in both adults[24] and school aged children[25] as the result of lockdown confinement.

We have previously outlined how environmental and behavioural factors show substantial association with Myopia. The environmental associations of physiologic Myopia can’t be accounted by genetic considerations alone. The adaptive framework and the eyes as an organ dedicated towards visual perception means environmental factors optically affecting the eye such as object distance (resulting in accommodation), contrast, brightness/intensity (affecting the pupil) or their superposition are to be termed as physiological factors. Factors not optical, for instance: hereditary, birth defects/congenital and

environmental factors different from physiological ones mentioned above such as, toxins, trauma, and other unidentified factors internal to the eye are to be clubbed under pathological factors.

That Myopia result from changes to the equilibrium of homeostatic control mechanisms present inside the eye has been postulated for decades[26, 27]. These observation in light of the nature of changes accompanying axial elongation 2.3.1 suggest that an adaptive mechanism might be at work for physiological Myopia alongside concepts of equilibrium, feedback, and control required to describe it. This adaptive standpoint requires treating Myopia progression (shifting of equilibrium) separately from stabilized myopia. That Myopia onset/progression has been observed to happen at all ages is a strong indication that Myopia management is also feasible ideally at all ages including beyond childhood.

2.5.1 Myopia control and management methods

Myopia control/management refers to interventions[28] concerned with stabilization/reversal of Myopia only and must be distinguished from existing modes of refractive intervention such as lenses, contacts and surgical procedures whose primary goal is to compensate for defocus (subjective refraction[29]). In this context, compensation is more appropriate term than correction when it comes to refractive interventions. There can be no fundamental physical difference between refraction induced by glasses, contacts or refractive surgeries from the standpoint of optics.

The scope of this article is restricted to the observation that none of the existing methods can be considered as truly and significantly affecting the outcome of physiologic Myopia, i.e., axial changes via the route of emmetropization. As of now there is still no widely accepted method directly targeting/affecting long-term structural consequences of axial elongation due to Myopia which is consistent with the fact that exact aetiology of physiological myopia is still elusive so far[30].

Two most commonly used myopia management treatments Ortho-K and Atropine treatment do not account for or directly address the environmental association of Myopia outlined previously. These widely used management options also frequently suffer from rebound effects[31, 32]. The frequent observations of rebound myopia after cessation of treatment shows that these management strategies do not address the underlying processes and environmental variables affecting axial elongation and should not be treated as such.

Of special note is the recent promising advancement in the form of light therapies reporting significant axial shortening beyond measurement error. RLRL[33] (Repeated Low-level Red Light) and High Environmental Illuminance therapies[34] have shown promise for Myopia management. Light therapies emulate the safety and efficacy model of daytime outdoor exposure and its protective effect against Myopia onset/progression[35, 36]. However, we have yet to come across reliable signs of significant emmetropization happening from existing variants of light therapies.

3. Refractive characterization of the eye

Refractive characterization of a myopic/hyperopic/presbyopic eye requires Ray optics. The preliminary material included with this article serves as an in-depth introduction for the same. This article builds upon and uses characterization of the Ideal Lens System (ILS from now on) along with the phenomena of shift in observation range from introduced defocus or screen distance changes utilizing Relative Dioptre Scale for visualisation.

3.1 Lumped Lens optical consideration of the eye

A labelled diagram[37] of the human eye is given below for reference in Figure 1.

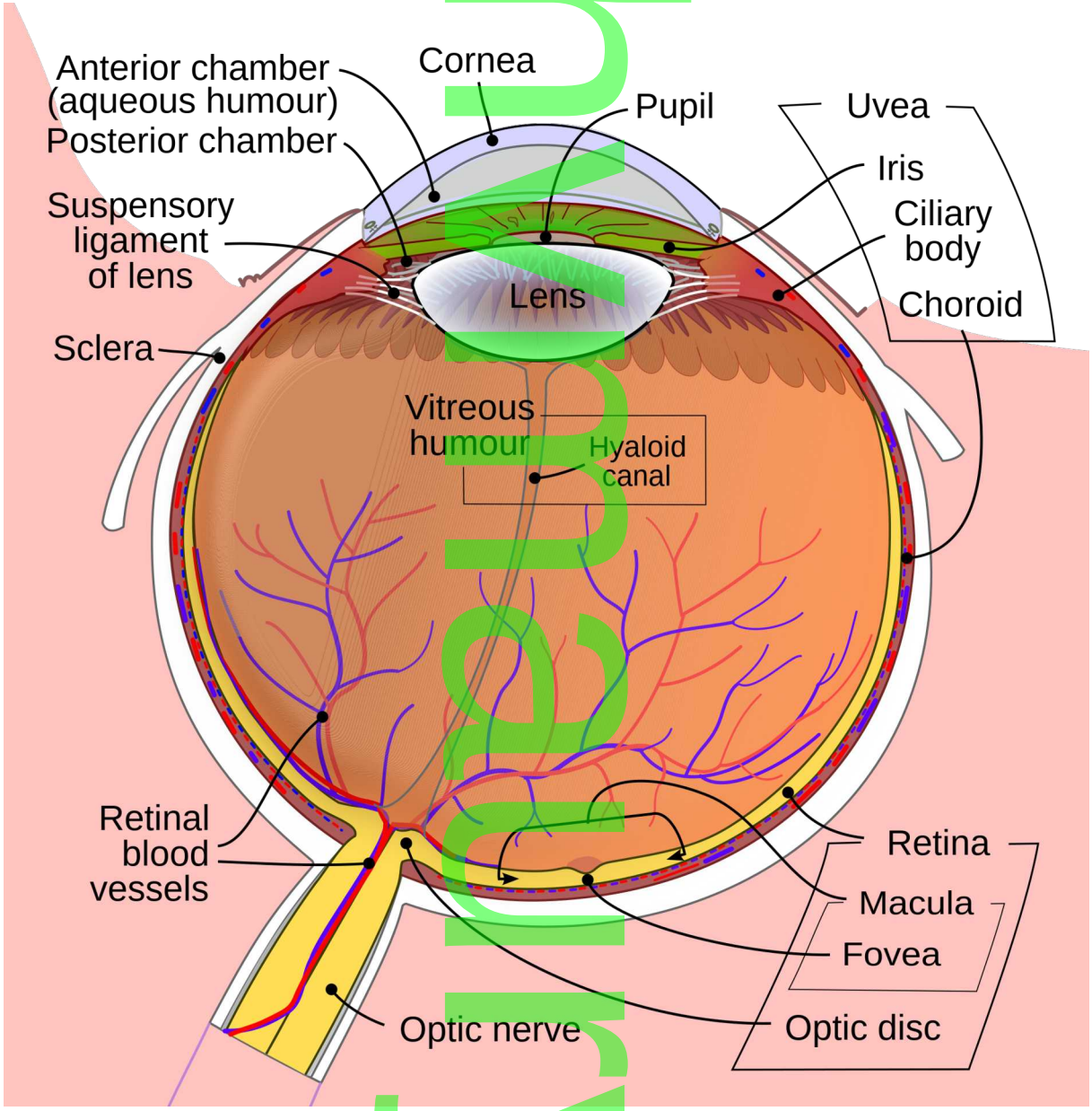

Figure 1 Labelled diagram of the human eye. It shows the lower part of the right eye after a central and horizontal section.

The role ocular components play inside the eye are explained in the order in which a light ray entering the eye traces its path towards photoreceptors on the retina.

Cornea → Aqueous humor → Eye lens → Vitreous humor → Photoreceptors on the Retina

The Pupil is a hole in the Iris acting like aperture from ILS. The aqueous & vitreous humors act as an optical medium for light travel – any non-destructive/physiological changes to the index of the refractive media results in power changes, leaving us with remaining ocular components of the eye as:

Cornea → Eye lens → Photoreceptors on the Retina

The cornea and the eye lens can be viewed as two fixed and variable power optical element with the retina acting as an image sensor. The cornea, the eye lens, and the mediums surrounding them combined together converge light rays onto a spot on the retina forming an inverted image just like the ILS[38].

The primary goal of this article is quantifying observation range changes due to refractive errors. Instead of taking the traditional approach which has historically been attempts to precisely model the complex ocular components, we have chosen to study simpler systems like the ILS for the eye. For the purpose of quantifying image formation, we would like to introduce the concept of 'lumped lens' having combined refractive power of cornea and eye lens together with the accommodation capabilities of eye lens. The retina acts as the image screen. The imaginary distance of retina from the optical centre of this lumped lens will be referred throughout this article as Retinal Distance (RD in short) and the same can be regarded as the screen distance equivalent like the ILS for the eye. Any external defocus/refractive intervention (in the form of glasses, contacts etc.) has to take into account the Vertex distance and other applicable lens placement factors from the optical centre of the lumped lens.

3.2 Observation range of an Emmetropic eye

While the far-point of an emmetropic eye can be ideally fixed at ∞, a representative value is required as the near-point of an emmetropic human eye. For this article, we will assume this to be 25 cm for simplicity without loss of generalisation. It represents the closest distance an adult emmetropic eye should be able to focus continually without immediate fatigue/discomfort under daily circumstances. This value has been represented with a red dashed vertical line at the +4 D mark on the RDS. An elder person might not be able to observe objects this close due to presbyopia. Throughout this article, the word emmetropic without any prefix will refer to *an emmetropic eye without presbyopia* (Accommodation ability of 4 D or greater).

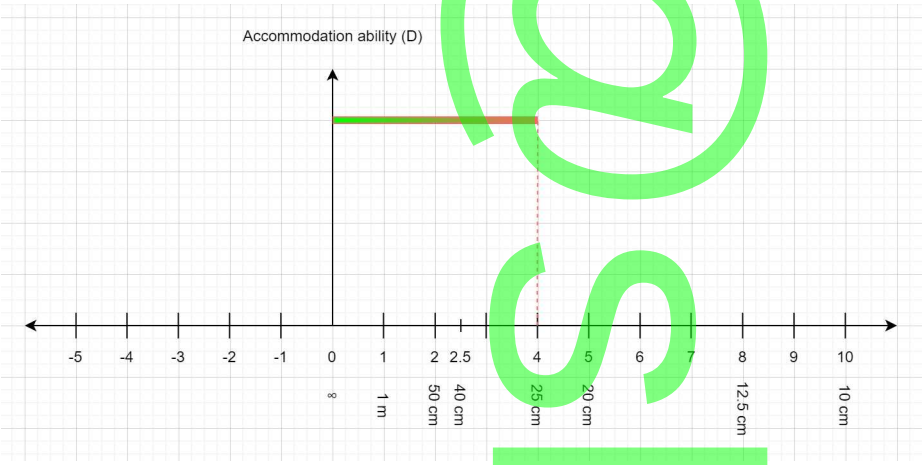

Figure 2 The observation range (25 cm up to ∞) of an emmetropic eye on the RDS

Because accommodation is facilitated by the ciliary muscle, the left end of observation range corresponds to relaxation (focusing at far-point) while the right end corresponds to reaching the limit of ciliary muscle contraction. We have chosen to divide the observation range into two distinct regions as shown in Figure 3 assuming a neutral point.

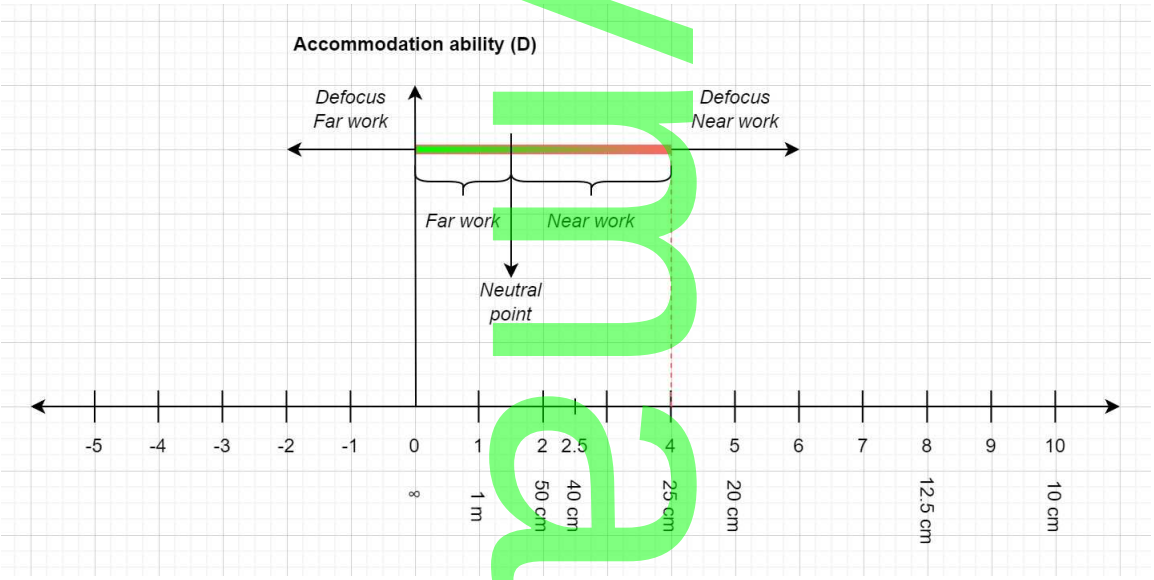

Figure 3 Observation range demarcation in the presence of a neutral point

The neutral point divides the observation range into two subsets – corresponding to far-work beyond the neutral point [d_{far}, $d_{neutral}$) and Near-work closer than the neutral point ($d_{neutral}$, d_{near}]. Outside the observation range, defocus far work can be defined as (-∞, d_{far}) and defocus near work as (d_{near}, ∞). These classifications apply regardless of observation range changes.

3.3 Myopia/Hyperopia

For refractive error, a best possible refractive compensation[39] can be usually determined resulting in a compensated observation range ideally close to an emmetropic eye (Figure 2). This best compensated observation range will be referred to as pseudo-emmetropic observation range for the rest of this article.

The refractive compensation can then be 'subtracted' considering the vertex distance from the pseudo-emmetropic observation range giving the originally uncompensated observation range of the eye. Simply put, knowing the properly compensated observation range of a myopic/hyperopic eye, its actual observation range can be determined. Astigmatism, floaters, and aberrations due to retina/refractive media affect final image quality even with best possible refractive compensation in place. Visual acuity/resolution is a property primarily associated with the retina different from defocus[40].

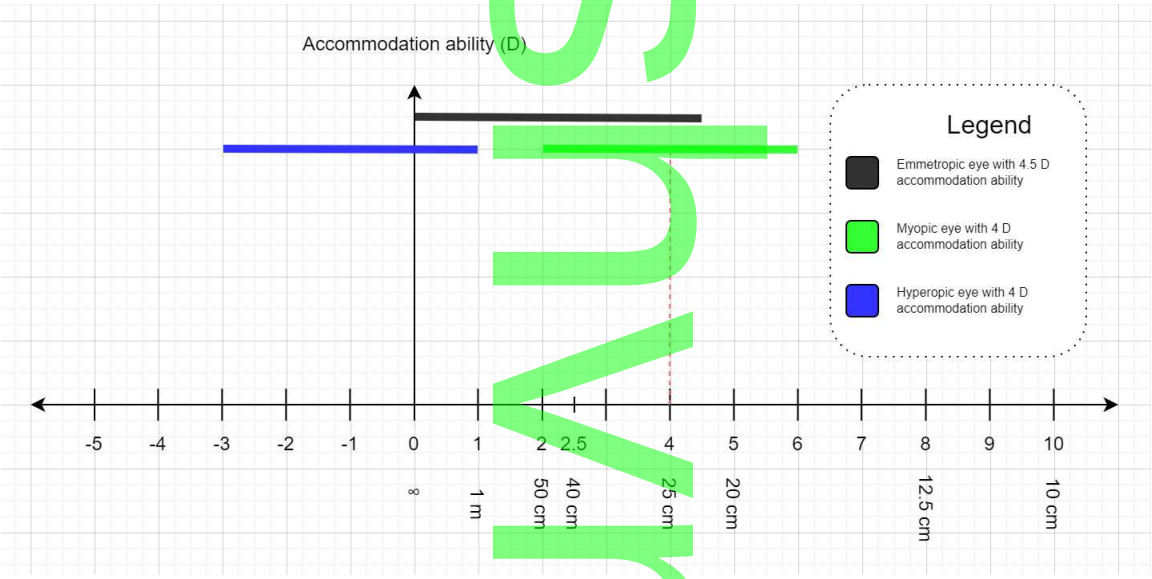

Figure 4 Representing Myopic and Hyperopic observation ranges on the RDS

It can be stated that physiologic **Myopia** (green) is a refractive error in which the eyes' far point (the maximum distance at which the eye can **focus**) is closer than and no longer located at optical infinity.

Similarly, physiologic Hyperopia (blue) is a refractive error in which the far point is situated 'well beyond' optical infinity resulting in accommodation need for focusing at infinity. Hyperopia is much less common than Myopia. Hyperopia/far-sightedness primarily results from axial changes to the eyeball such that images of closer objects are formed behind the retina. Prebyopia unlike Myopia/Hyperopia involves changes to the accommodation ability of the eye. Presbyopia can be also represented on the RDS.

In the lumped lens consideration, both physiologic Myopia/Hyperopia result from changes to the lumped lens and the retina. It should be now intuitive to understand how appropriate refractive compensation can restore pseudo-emmetropia in both cases. It should also become obvious how Myopic eyes need hyperopic shift in observation range for emmetropization and vice-versa.

3.4 Focusing vs. Exposing and Actual vs. Apparent focus

Having already differentiated between image distance and screen distance earlier for ILS, one can extend this distinction in the context of exposing and focusing for the eyes too. This is required to describe for instance, the probable description of an eye **focused** at infinity but **exposed** to a nearby white wall.

An eye (or any optical system) can be exposed to all possible physical distances but focused only within its the constraints of its observation range. Exposure outside observation range results in defocus. The defocus due to Myopia/Hyperopia results from *exposing* eyes to distances farther/closer their respective far/near-point outside their observation range.

This distinction between focusing and exposing is important to describe what actually happens due to refractive interventions. We will refer to focusing after refractive interventions as *apparent* focus in order to distinguish it from *actual* focusing without refractive intervention. The term **apparent focusing** refers to focusing involving combination of eye with refractive intervention while **actual focusing** refers to unassisted focusing involving only the eyes. Refractive interventions in this context can be said to act as mapping between actual and apparent observation ranges of the eye.

A diagram explaining this for Myopia is given in Figure 5:

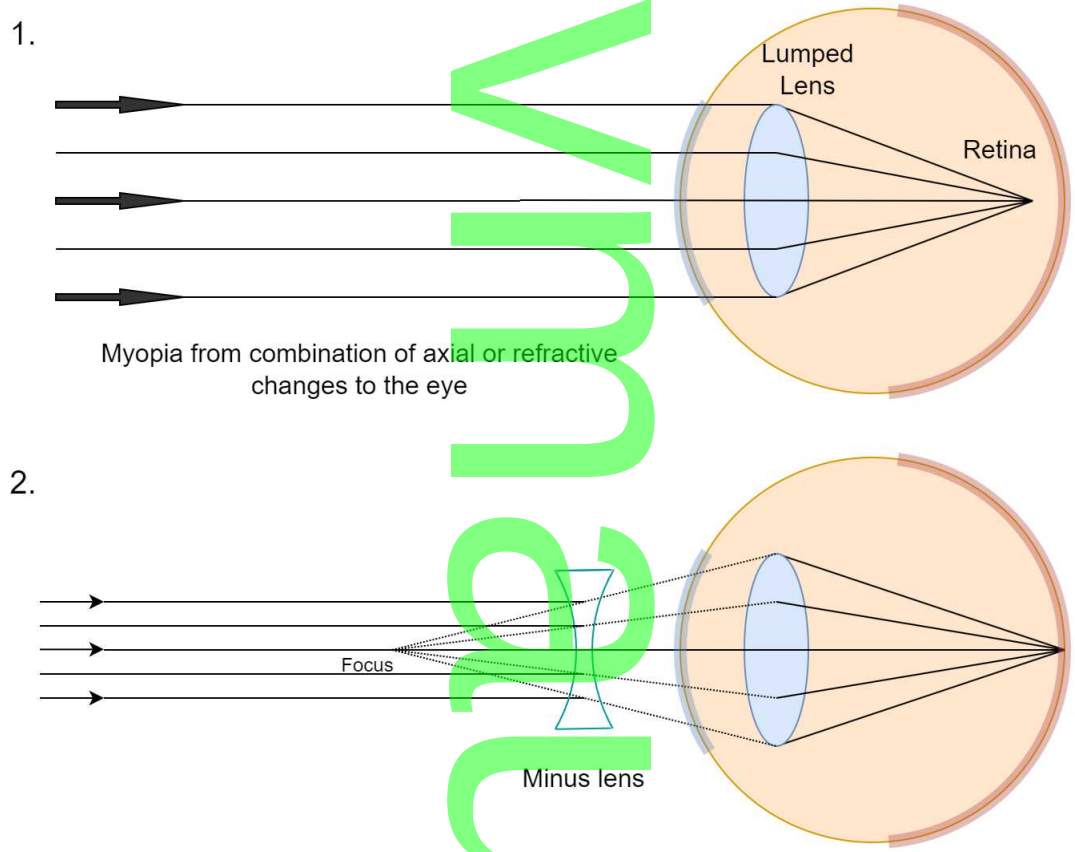

Figure 5 A diagram showing how refractive intervention compensate for Myopia.

In Ray optics speak, the introduced refraction introduces additional divergence to the incoming light rays shifting the resulting image plane to coincide with the retinal plane. It is intuitive to visualize how the compensated myopic eye is actually focused at a distance closer than the apparent focusing distance. It is obvious that for ***apparent*** focus, a myopic eye must ***actually*** focus at a distance closer than the said

distance. For a hyperopic eye to achieve apparent focus at the same distance, it must actually focus farther than the distance in question.

3.5 Changes to Accommodation-convergence reflex from Myopia

Human eyes form a stereoscopic pair for depth perception which necessitates the presence of convergence[41]. Convergence is basically simultaneous tilt in axis of both eyes towards the object point in focus. This article is limited to convergence aspects and behaviour related to Myopia.

For an adult emmetropic eye focusing on an object equidistant from both eyes, the relation between convergence angle θ and the accommodated power of eye is governed by $\theta = \sin^{-1}\left(\frac{IPD \times Accommodation\ Power}{2}\right)$, where IPD (InterPupillary Distance) has been used as distance between axes of both eyes. The angle between the respective image planes depicted in blue happens to be the sum of convergence angle measured from parallel axes of both eyes (Figure 6).

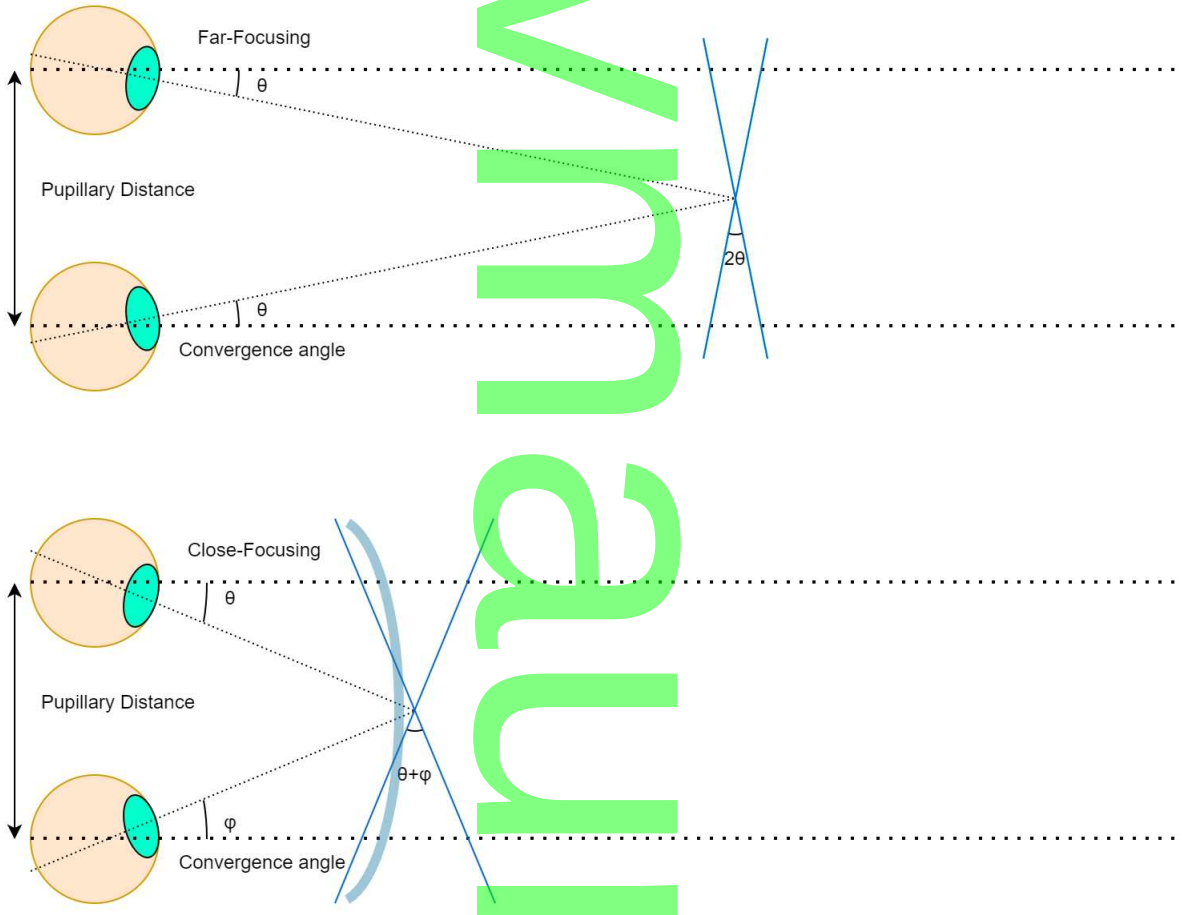

Figure 6 Depiction of convergence with observed distance compared to observing at infinity. Note the increasing angle between the perceived image planes shown in blue as focusing distance gets closer.

Using avg. Value of IPD (63 mm) gives 1.8°±0.1° of convergence angle for each eye per Dioptre of Accommodation. For symmetric focusing at 25 cm (+4 D accommodation), the eye needs to converge by ~

7.2°. The increase in angle between the perceived image planes due to stereoscopic fusion as focusing distance comes closer should also be noticed.

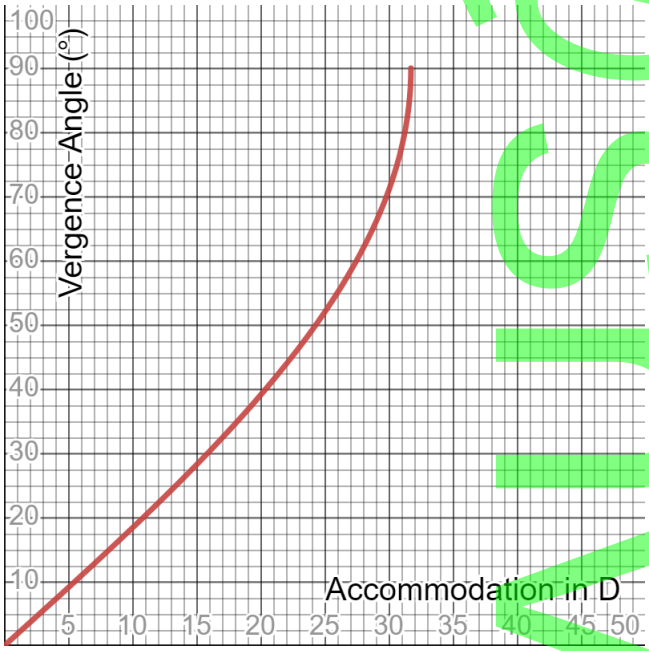

Figure 7 A plot of convergence angle with accommodation (IPD: 63 mm)

As can be seen from Figure 7, the reflex acts in a linear fashion even beyond the usual accommodation ability for the eye (+4 to +5 D). It is not a mere coincidence that the range of ciliary accommodation lies mostly within the contraction range of extraocular muscles responsible for convergence. Extraocular muscles responsible for convergence start hitting their limits at close-up distances characteristic of severe myopia and the same is reflected in definitions of severe Myopia.

For an emmetropic eye with the far-point at infinity, the reflex ideally acts at all observable distances. The same applies to a pseudo-emmetropic eye also with best possible refractive compensation. For an uncompensated Myopic eye with its far-point no longer at infinity, accommodation begins only when convergence 'reaches' distances closer than the far-point. For distances beyond the myopic far-point, eyes remain in a relaxed state. This can be termed as introduction of **convergence lag** for Myopia[42]. In both cases, it can be said that the reflex starts acting only when the observed distances reach closer than the far-point of the eye whether myopic/emmetropic.

The roughly cylindrical nature of converged image plane distortion with its axis normal to the line joining both eyes suggests its association with astigmatism. It predicts presence of baseline levels of astigmatism in population primarily involved with significant near-work. It remains to be investigated how this particular form of cylindrical image plane distortion affects ocular biometry. It is possible that fully compensating for this form of astigmatism can result in discomfort and further progression of astigmatism. Astigmatism of this form is best left slightly uncompensated unless it perceptibly affect vision.

It is possible that subsequent conflict and recalibration of the accommodation-convergence reflex plays a crucial role influencing reports of initial discomfort period associated with sometimes major changes in refractions. The common observation of discomfort stabilizing in the span of few days hints that the convergence reflex also gets recalibrated within this time-frame.

4. The Continuous Adaptive Theory (CAT)

The fundamental idea underlying the framework of CAT is that refraction of the eye and hence the ocular components maintaining it as outlined earlier are in equilibrium. This refractive equilibrium can be disturbed and consequently shifted by physiologic environmental factors.

4.1 Variable time-scale adaptive processes of the eye

Decoding the adaptive nature of the eye involves figuring out how the various adaptive mechanisms inside the eye communicate delivering focused images at the retina [Josh Wallman and Jonathan Winawer, 2004]. There are only two ways corresponding to two independent variables in which the focusing distance of the ILS can be changed/shifted: due to focal length or screen distance changes. The same applies to the Lumped Lens optical consideration for the human eye.

A lot has been already described about accommodation in multiple texts. Accommodation happens to be a very short-term (almost instantaneous) response. The ciliary muscle is relaxed without accommodation. A high-quality video of accommodation in action[43] can be accessed here: https://youtu.be/1yIpyitm6eE

Long-term axial changes (requiring time-scales of months and longer) as a result of Myopization[44] mostly involve changes to the cornea (changes to the corneal curvature and ACD[45]) and the thinning of posterior sclera with physical distancing of the retina[46].

Hypothesis H1: Predicts the existence of a medium-term intermediate bridging processes between already well known short-term accommodation and long-term axial changes.

Because physical displacement of the posterior part of retina already happens as the axial component of Myopia, it is only reasonable to expect existence of a process resulting in changes to the focal length of the lumped lens (refractive component of myopia). H1 implies the existence of a biological mechanism capable of compensating changes brought by this intermediate process into observed long-term axial changes to the retina and cornea. Besides evidences pointing at presence of active emmetropization, this hypothesis is further strengthened from the continuous structures of iris, the ciliary body and the choroid (uvea).

This medium-term shift has been observed to result in changes to both ciliary body and choroid thickness[47]. Intermediate changes to the ciliary body corresponding to ciliary muscle state should result in refractive shifts in relaxed and accommodated power of the eye lens. The cornea changes refraction in the long-term in order to alleviate these changes. While extensive details are hard to come by, we speculate that observations reporting ciliary body thickening[48, 49] indicate presence of myopic ciliary shift.

Also probable is that thickness changes to the choroid happen in tandem acting as a precursor for displacement of retina and corresponding scleral shape changes. We suspect changes in ciliary body and choroid to be in place before long term axial changes can be made to the cornea and retina respectively. The role of choroidal thickness in observations exhibiting inverse association with AL changes already hints about this possibility being correct.

4.2 Observation range changes during Myopization

The eye experiences continuous changes to its observation range while becoming myopic. The accommodation ability of the eye can be assumed to be roughly constant during myopization. By comparing the observation range of a Myopic eye with an emmetropic eye, it can be stated that a myopic eye continuously gains additional close-range focusing capability while *sacrificing* capability to observe distant objects as shown in Figure 8.

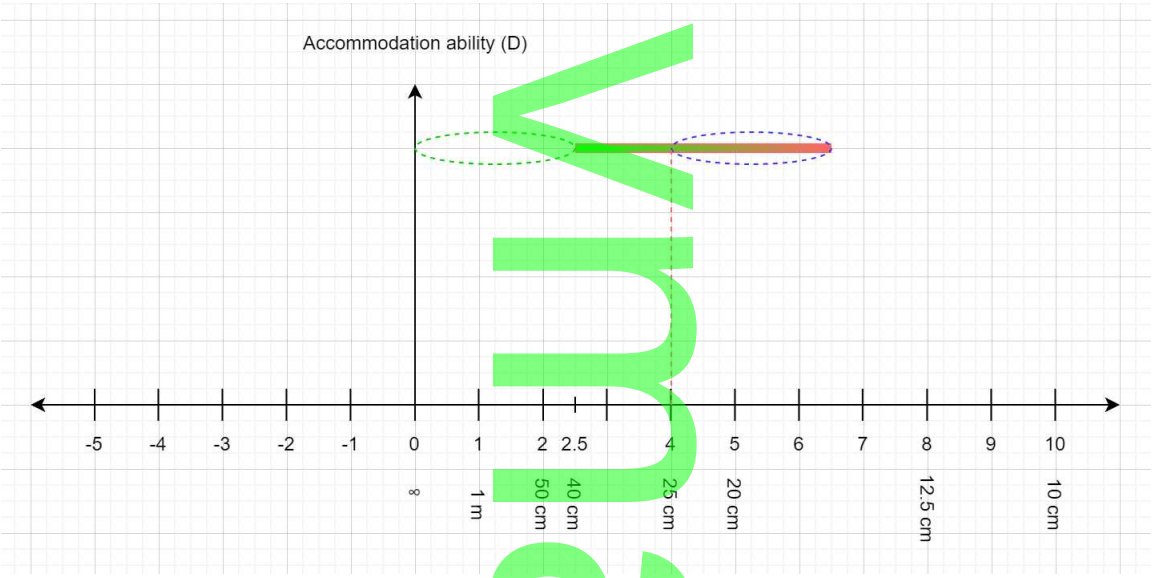

Figure 8 Compared to an emmetropic eye, the gained close-range observation capability by a Myopic eye (2.5 D) is shown with an blue oval while its sacrificed observation range is shown with a green oval.

The blue oval denotes gained observation capability between myopic and emmetropic near-points while the green oval denotes lost observation capability between myopic far-point and infinity (its emmetropic counterpart). Shifting of observation range in this manner is in agreement with existing associations of myopia and hints that both might constitute a simultaneous requirement. Myopia is associated with both near-work incidence and lack of regular outdoors exposure (not the same as near-work).

Hypothesis H2: The observation of Myopization process resulting in the eye gradually gaining extra close-range capability while sacrificing capability to observe distant objects can be explained as shift in refractive equilibrium brought by near-work loading promoted by under-utilisation of distant vision capability.

The simultaneous ‘push-pull’ analogy for shifting of observation range makes this clearer. It hints that an eye undergoes axial changes in order to relieve accommodative load from near work. Due to limits on the

extent of ciliary accommodation ability, under-utilisation of observation range extreme (distance focusing capability in this case) permits for an even stronger adaptive response. For myopia, accommodative load due to near work can be said to exert a 'pull' while under-utilisation of distant vision capability exerts a 'push' on the observation range. A Push or pull in isolation is insufficient to affect observation range resulting in an equilibrium shift.

H2 explains the first of the many unexplained mysteries of Myopia: Why it is observed that a population does not experiences Myopia even with significant near-work incidence[50]? It gives an answer in the form of sufficient utilisation of distant vision capability keeping in check adaptation from accommodative load due to near-work. We invite researchers to verify the physical implications of this explanation. It also explains why near-work correlates[51] with Myopia but can't be the only factor. It means under-utilisation of distant vision capability (not same as near-work) also contributes towards Myopia[52]. It additionally implies that eyes additionally respond to relieve accommodative load in addition to existing observations of eyes responding to superposition of growth signals, defocus, and pathological factors even. The scope of CAT is self-restricted to physiological factors only.

4.3 Influence of light and the problem of deducing adaptive direction from defocus

The pupil of the iris[53] evolved as an aperture control mechanism to regulate the amount of light entering the eye. [Pupil size[54] in adults usually varies from 2 to 4 mm in diameter in bright light to 4 to 8 mm in the dark.] In this context, environmental light intensity relatively affects the pupil size in two ways: pupil constricted (bright) and pupil dilated (dim/dark) lighting.

The lumped lens consideration implies that the dilated pupil's shallower Depth of Field should result in additional accommodation in dim lighting in order to maintain the same focus distance. However, even overly relaxed DOF calculations hint that pinhole effect alone is not enough to explain the dramatic improvements in vision that takes place during daytime. It hints that the iris must somewhat mechanistically affect the ciliary muscle relaxation with constricting 'tug'. This prediction too is supported from the continuous structure of iris and ciliary body as part of uvea.

4.3.1 Pupil constricted lighting conditions and evolution

During the course of evolution, the eye evolved[55] from a simple light sensing structure to an absurdly complex and specialized visual organ as observed in humans and higher primates. The scope of this article is extremely limited to pointing out the role of sun as the only primal light source influencing and directing evolution of organs such as eyes. If one connects the dots further, it can be understood that human eyes too show heightened sensitivity to the spectrum and intensity offered by bright but indirect (diffused) sunlight. This basically means the best example for aforementioned pupil constricted lighting environment is the one

of indirect sunlight. For the purpose of this article, indirect diffuse exposure to sunlight will be defined as the sun not present in the field of vision – whether reflected or directly visible.

4.3.2 Reasons behind existence of a Form Deprivation response

It is very well known observation at this point that near-work under pupil dilated lighting is associated with Myopia[56]. We have previously outlined the established body of studies on Myopia being the 'default' behaviour of animal eyes when subjected to form deprivation in dim environments[[57],[58] and [59]]. Form deprivation has also been successfully induced in higher primates (Rhesus Macaques[60]) as well which leads to a simple implication that the same exists in the human eyes as well.

Form deprivation also makes evolutionary sense as component of the myopization process maintaining refractive equilibrium with emmetropization. Put simply, without existence of myopization process there would be no possibility of eyes correcting hyperopia. The case for existence of such processes is further strengthened from the varied uncorrected refractions of eyes at birth. Such an adaptive process has to exist because the eye can be born hypermetropic or myopic both and has to overcome it accordingly during emmetropization.

Hypothesis H3: It is predicted that pupil dilated lighting during near-work accelerates myopization by activating FDM pathways[61] along with the processes alleviating accommodative load on the ciliary. Form deprivation is nothing but myopization response to blur.

It hints that possible efforts towards inducing emmetropization could be rendered ineffective by the dominant nature of the FDM pathway under pupil dilated lighting. The activation of FDM pathway might explain why myopic defocus results in Myopization in pupil dilated lighting instead of the observed and expected emmetropization response as observed animal models. It basically implies that pupil constricted lighting is basically a requirement if one wants to observe emmetropization from myopic defocus.

We've previously outlined how adaptive requirements from accommodative load and under-utilisation of distant vision capability together shift the refractive equilibrium towards Myopia. In this context, less than adequate lighting levels can be said to speed up the rate of Myopization by parallel activation of the FDM pathway. Lighting as a factor happens to be the last remaining puzzle piece for our understanding of physiological factors affecting Myopia[62]. This might also explain why highly myopic people experiencing Myopia progression can show sensitivity to bright lighting environment which normally do not affect emmetropic individuals. Lower light levels also result in reduction of information, implying increased susceptibility towards alignment errors and visual aberrations thereby making Myopization inherently 'inferior' in this regard.

4.4 Equivalences in observation range and shifting behaviour of an emmetropic eye and an eye compensated for Myopia

The similarities between an emmetropic eye and an eye compensated for Myopia can be broken into two separate equivalences. These physical equivalences emerge from the optical equivalence of refraction (bending of light rays).

4.4.1 Observational equivalence of far-point

The apparent far-point of a pseudo-emmetropic (best compensated myopic/hyperopic) eye is refractively equivalent to the actual far-point of an emmetropic eye. This equivalence can't be extended to the near-point due because of the variability in accommodation ability (for instance, presbyopia).

It is trivial to show that the apparent far-point of a myopic eye with proper refractive compensation lies at infinity. One can term this as 'clamping' of actual far-point due to refraction intervention as shown in Figure 9.

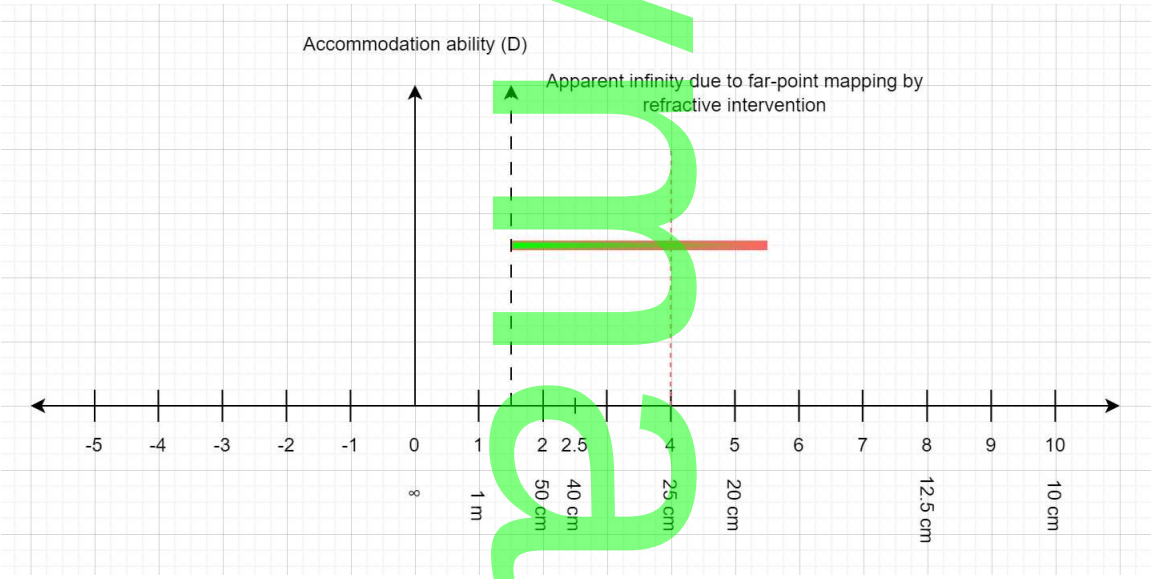

Figure 9 Clamped far-point of a Myopic eye (1.5 D) by refractive intervention

4.4.2 Behavioural/Equilibrium Equivalence of observation range shift

A myopic shift affects the observation range in the same way whether it happens to an emmetropic eye (onset of Myopia) or previously myopic eye (Myopia progression). This equivalence naturally extends for hyperopic shift in equilibrium also.

5. Discussions

5.1 Severity of refractive errors and risks enhancement from presbyopia

From the standpoint of Ray Optics, plus (+) sign for degree of Myopia encodes the truly 'compensating' behaviour refractive interventions with the opposing (-) sign have on the myopic observation range.

High Myopia is defined at 5.0 D spherical equivalent or more. [WHO] Other literature define High Myopia to start at 6.0 D spherical equivalent or more. Myopia being mostly axial in nature affects observation range mainly due to SPH defocus. In the pursuit of rigour, we will treat SPH and CYL components separately. The position of near and far point compared to an emmetropic eye should ideally indicate the severity of myopia/hyperopia. We propose defining refractive state severity on the basis of lack of overlap between the actual observation range and its pseudo-emmetropic counterpart shown in Figure 10. The overlap factor has been taken as the value for threshold Myopia (≥ 0.5 D according to WHO).

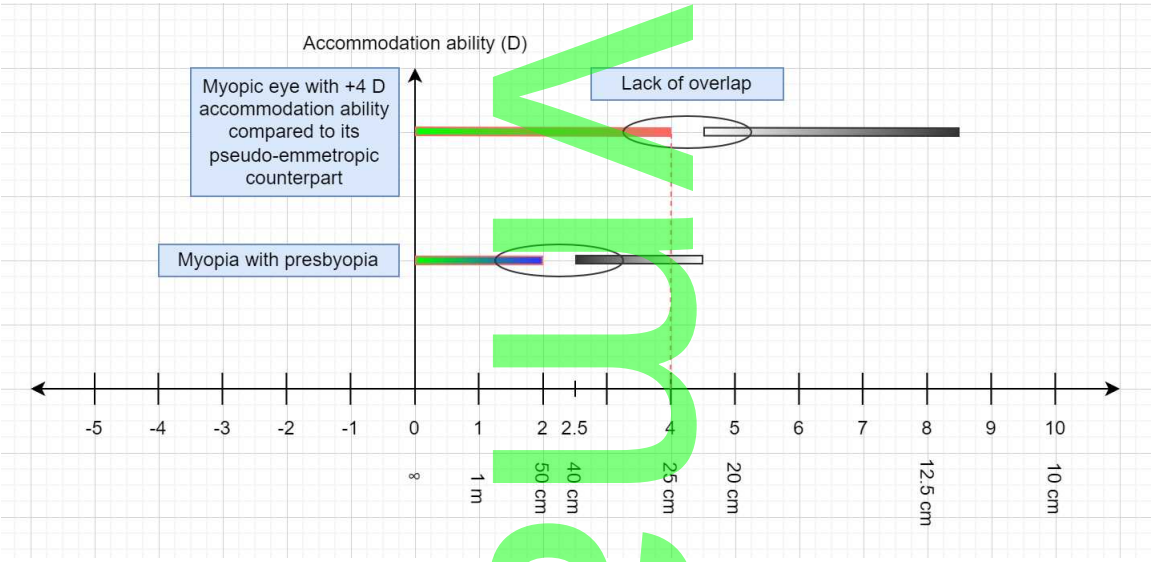

Figure 10 The 'overlap' criteria for determining severity of Myopia. The coloured observation range represents the pseudo-emmetropic observation range after best possible refractive compensation.

The following arguments favour our overlap criteria for severity of refractive states:

1. Encodes the observation that a person satisfying the criteria is not capable of focusing at any 'reasonable' working distance without refractive intervention. Conversely, low myopes can focus closer than their far-point comfortably without refractive compensation because of this overlap.
2. Yields equivalent classification as the existing scientific consensus values for Myopia.
3. Predicts an increase in risk with age due to onset of Presbyopia. A borderline severe case of Myopia in adulthood can become severe myopia with age signifying increased risks.

4. Severity of Myopia depends on factors affecting observation range which may or may not be affected by refractive errors like astigmatism. This is the primary reason behind avoiding spherical equivalents for this article and isolating astigmatism separately.

Severe Myopia indicates the difficulty faced by eye's extraocular muscles when focusing close to its near-point (for highly severe myopia, even the far-point may be beyond reach of comfortable convergence without refractive intervention).

5.2 Continuous Adaptation Theory

5.2.1 Refractive equilibrium and its implication from equivalences

These equivalences basically guarantee the similarity between the refractive equilibrium of a stabilized myopic eye and that of an emmetropic eye. Refractive state is stabilized in both because myopization is in equilibrium with emmetropization. This basically predicts that factors resulting in onset of physiologic Myopia in an emmetropic eye should be responsible for its progression in a compensated Myopic eye as well. Myopia progression is nothing but 'onset of Myopia' in myopic eye already compensated for Myopia. It also has a parallel implication that an eye with stabilized Myopia shows behaviour closer to an emmetropic eye than an eye experiencing active Myopia progression. This can be extended to state that the eye has no way of knowing its absolute state and is aware of changes relative to imposed stimulus only.

For shifting of this equilibrium point towards hyperopic adaptation, myopic defocus is needed because ciliary muscle is relaxed for distant work implying absence of accommodative load. Myopic defocus emerges as a necessary but not sufficient[63] requirement for inducing emmetropization. We have already pointed out the role played by pupil constricted lighting as being useful towards overcoming FDM pathway for emmetropization. It should also offer an explanation so as to why truly physiologic hyperopic progression unlike Myopia progression is rarely observed[64].

The equivalences alone signify the urgent need to revisit and isolate the behaviour shown by stabilized Myopia from progressive Myopia in pertinent literature and explains why efforts to gather insights about Myopia from studies on refractive state alone failed to yield actionable insights to date.

The breakthrough insights from these two equivalences are given below (Table 1):

Table 1: Equivalences between a pseudo-emmetropic eye and an emmetropic eye

Myopic eye wearing best possible refractive compensation (pseudo-emmetropic eye)	**Emmetropic eye**
Failure to observe Myopia reversal with best possible refractive compensation even after distance work	No observed hyperopia (shifting of far-point beyond infinity) even after (in-focus) distance work

The case for reversibility of Physiologic Myopia

Myopic shift observed as Myopia progression	Myopic shift observed as Onset of Myopia
Some population reports stabilized myopia even with significant near-work habits.	Some population reports no myopia even with significant near-work habits.
Apparent Far-point is at infinity	*Actual* far-point is at infinity

The refractive state of a physiological myopic/hyperopic eye is as '*valid*' as an emmetropic eye from the standpoint of CAT. These application of these equivalences with the lack of specific anomalies inside the eye should serve to distinguish physiological Myopia from pathological Myopia. Physiological myopia is not some disorder or disease but rather just a state. This is necessary from the self-consistency of our adaptive framework and the resulting behavioural equivalences.

5.2.2 Proposed mechanism behind physiologic Myopia

Section 4.1 describes how short-term, medium term and long-term processes together are responsible for maintaining the refraction of an eye in accordance with its visual environment. We have also described how the observation range of an emmetropic eye gradually changes during Myopization in section 4.2.

The onset of Myopia has been mainly predicted to result from the ciliary muscle 'tiring' out during strenuous near-work (see pseudomyopia/NITM[65]). This accommodative load on the ciliary results in a small defocus translating into the myopic adaptation in the long-term. Doing near-work closer to the focusing limit of the ciliary muscle should theoretically bring faster exhaustion of the ciliary. Defocus near work predictably results in superposition of defocus response in addition to extreme accommodation load.

Without 'suitable' interventions, the ciliary body starts developing changes in order to alleviate this accommodative load. It is expected that a person with myopic ciliary shift possesses markedly better capability of sustaining near work for a longer time period along with suppression of near-work induced load signalling. Myopic shift in the ciliary could also result in discouragement towards future utilisation of distance vision capability in the form of excessive tear formation, rapid uncontrolled blinking, increased sensitivity towards bright lighting and signalled discomfort (HARE[66]) thereby establishing a subtle feedback loop.

Under-utilisation of distant vision capability in the presence of ciliary body changes then initiates long-term axial changes in order to alleviate this myopic shift. Subsidence of external factors causing myopization results in equilibrium being established again with the ciliary body gradually returning to its normal state **preserving** the axial state resulting in observed stabilization of Myopia.

We've already mentioned that a component of astigmatism should result from increasing angle between image planes due to closer observation distances in section 3.5. Another component of astigmatism is

expected to result from anisotropic changes that these ocular components can undergo during myopization.

514 The 'recalibration' of the accommodation-convergence reflex as convergence lag mentioned earlier is also predicted to happen alongside myopia.

516 5.2.3 Predicted requirements for Emmetropization

If physiologic myopia is indeed a consequence of adaptation, it should be possible to introduce a shift in

518 equilibrium in the opposite direction for reversing Myopia. To summarise our findings, section 4.2 covers why accommodative load from near-work coupled with under-utilisation of distant vision capability should

520 result in Myopization. Section 4.3 outlines why defocus in pupil dilated lighting conditions accelerate Myopia using FDM pathways. Section 4.4 establishes refractive equivalence between behaviour shown by

522 a best compensated myopic eye and an emmetropic eye. A pseudo-emmetropic eye and an eye with very low Myopia should differ only in their ability to focus at distant objects.

524 For emmetropization, we need to determine adaptive 'duals' of the factors responsible for Myopization. Implementation of these duals needs to be augmented with management of near work induced

526 accommodative load causing myopization in the first place. These findings are tabulated in Table 2.

Table 2: Establishing duals of physiological factors required for myopization

Factors resulting in Myopization	**'Duals' for inducing Emmetropization**
Accommodative load from near-work resulting in adaptive requirement.	Exposure to Myopic defocus (exposure beyond myopic far-point)
Under-utilisation of the distance vision capability	Near-work management to reduce accommodative load causing Myopization in the first place.
Myopization is accelerated under pupil dilated lighting due to parallel activation of FDM pathway	Emmetropization requires pupil constricted lighting in order to overcome the activation of FDM pathway

528 These duals give the first ever breakthrough insights into physical requirements for emmetropization. They expand our explanatory framework that can now explain why earlier attempts[67] utilising reduced

530 prescription to observe reduction in Myopia mostly failed due to lack of proper isolation of variables.

The distances beyond far-point (myopic defocus) that need to be exposed to under pupil constricted lighting

532 lie inside the green oval for a myopic eye shown in Figure 8. We will refer to this as ADV (short for Actual Distance Viewing). The ideal Pupil constricted lighting is indirect sunlight as on a clear sunny day. Because

hyperopic adaptation requires pupil constricted lighting, it should also be slightly faster (Superior) due to the availability of more information.

5.2.4 Role of Genetics in the context of adaptive nature of physiologic Myopia

The Genetics of myopia is frequently associated with myopic individuals having more chances of a myopic parent. After accounting for the possibility that myopic children can share most of the same physiological environment with their parents, it is unclear how much of a role genetics actually play towards progression of physiologic Myopia. It must also be noted that most of the studies on parental Myopia additionally fail to strictly differentiate between progressive and stabilized myopia[68, 69, 70] in accordance with the equivalences in section 4.4. These equivalences outline the urgent need to fully isolate physiological variables from pathological ones. We expect definitive trends to emerge when progressive Myopia is properly isolated from stabilized Myopia in studies investigating parental origins of Myopia.

It is highly probable that the genetic susceptibility part for physiologic myopia can have something to do with the relative sensitivity of the Myopization pathways.

5.2.5 Strength and Limitations of CAT

The strength of our theory lies in proposing a consistent aetiology using an adaptive equilibrium model for Myopia explaining onset/progression and even the to date observed ‘irreversibility’ consistent with all existing observations. The resulting equivalences succinctly explain why studies on stabilized Myopes have so far been an exercise in futility due to their similarity with emmetropes. CAT is also the only theory describing myopia so far consistent with the theory of evolution of eyes as a visual organ.

At the same time we want to stress that the simple lens model on which CAT builds upon can’t account for difference between peripheral and central components of vision or predict other factors that can play a role towards towards Myopization of the human eye.

Because of the way CAT re-defines pathological Myopia from physiological Myopia in terms of reversibility, the theory naturally breaks down for pathological Myopia due to unpredictable alterations to the underlying adaptive mechanism responsible for maintaining refractive equilibrium of the eye.

5.2.6 The informal Law of physiological Myopia

Given time and effort, a person with physiological Myopia should be able to emmetropize at par or better than their current abilities with best possible refractive compensation.

This law encapsulates our bold prediction from CAT signifying the error correcting, superior nature of hyperopic adaptation.

5.3 Changes to the Field of View from Axial Changes

FoV depends on the screen distance which in the case of Lumped Lens consideration is taken as the distance of the central part of the retina (RD) from the optical centre of the lumped lens. Axial elongation due to Myopia results in physical distancing of the posterior part of retina while the foveal region responsible for vision remains mostly unaffected at least for cases of non-severe Myopia.

The resulting FoV reduction can be estimated from *emmetropic AL ÷ myopic AL* assuming the proportionality of AL with Retinal Distance (RD). This works in a manner similar to how focal length changes affect FoV of the image in a camera. For instance, emmetropic AL of 23 mm and Myopic AL of 25 mm result in myopic FoV roughly 0.92 of the emmetropic FoV.

The closest study that considers FoV changes in highly myopic subject is the one done by {Yanming Chen; Ji Liu; Yining Shi} in the pathological domain[71]. It is reasonable on the basis of optics alone that effects of FoV reduction start resembling 'tunnel vision effect' with highly severe Myopia. This also implies that people managing to make significant Myopia reversal should experience widening of their FoV.

5.4 Predicting time taken for long-term axial changes

There are two approaches for predicting the time taken for long term axial changes. Both approaches should converge at similar estimates.

The first approach emerges from the consideration that both myopic and hyperopic adaptation are the outcome of same adaptive process. This means myopic and hyperopic adaptations should bear rough similarity on the order of time-scales on which they take place. By our prediction, time required for Hyperopic adaptation can be estimated from the data on Myopia progression[72]. The observed rate of hyperopic adaptation happens to be slightly faster than the progression rate of Myopia because it requires pupil constricted lighting with extra available information.

The second approach involves figuring out the relation between axial length of the eye with the retinal distance (RD) from the optical centre of the eye. The second approach is described in detail below.

In the emmetropic lumped lens consideration, the RD should also be equal to the focal length of the lumped lens when the eye is focused at infinity. The lens formula then gives the required shift in RD for focusing an object at the Myopic eye's far-point. To determine changes to retinal distance from AL measurements, we have assumed RD to be proportional to AL denoting the ratio RD/AL as β.

$$\text{Lens relation}: \quad \frac{1}{s} - \frac{1}{u} = \frac{1}{f}$$

$$\text{Here, elongated (myopic) RD serves as screen distance } (s) \text{ and emmetropic eRD serves as focal length } (f)$$

$$\frac{1}{RD} + \frac{1}{-u} = \frac{1}{f}$$

$$\text{emmetropic RD } (f) = \frac{-u \times RD}{-u + RD}$$

$$\text{if we assume RD / AL as } \beta \text{ then}$$

$$\text{Elongation in Axial Length } \Delta AL \text{ due to Myopia} = AL - \frac{f}{\beta} = \frac{\beta \times (AL^2)}{-u + \beta \times AL}$$

$$\text{For instance, a myopic eye wearing prescription of } -4\ D \text{ corresponding to a far-point of roughly } 25\ cm \text{ will give } u \text{ as } -25\ cm \text{ for the formula.}$$

If AL and degree of Myopia for a non-severe Myopic eye is known, this formula gives change in AL that must be necessary for myopia progression/emmetropization provided β remains constant. Measuring the long-term rate of AL changes then gives a rough estimate of the time period required for axial changes.

6. Conclusion (not complete)

The term 'Continous' in CAT basically denotes the continuos temporal integration of stimulus from both near and distance work by eyes. Figuring out this continuous integration of visual stimulus needed proper physical quantification of actual distance work and refractive clamping with the prediction of FDM pathway activation during pupil dilated lighting. This continuous integration is probably responsible for push-pull observation behind cause of Myopia too.

It predicts that stabilizing/reversing Myopia might involve imposing Myopic defocus in pupil constricted lighting so as to overcome FDM pathways activation in dim/dark lighting. The theory naturally hints at Light Therapy using pupil constriction as the only possible and physically viable long-term protocol for Myopia management. We expect the sheer predictive prowess of CAT to continue with rapid light therapy optimisations coupled with near-work interventions towards effective Myopia management.

The framework of CAT put forward in this article might very well be the first such explanation put forward characterizing physiological Myopia in a way that manages to consistently and convincingly explain nearly all clinically observed aspects of physiological Myopia including but not limited to its onset, progression and even its apparent irreversibility so far in clinical trials so far. Building on the suspected multi-factorial

aetiology of physiological Myopia, the theory with its two equivalences successfully explains failing to understand Myopia on the inability to properly isolate the underlying physiological factors.

An eye doing long-duration near-work but also sufficiently utilising distance vision capability should only be signalling eye-strain from long-duration near-work without becoming Myopic. It also hints that emphasis towards proper utilisation of distance vision capability forms an essential requirement for management of Myopia.

An important consequence of the CAT is that it does away with the 'eye-growth' dichotomy and simultaneously explains many contradictions in the commonly accepted age-bound theory for Myopia progression and stabilization during mid-twenties. This hints that physiologic Myopia stabilization happening during mid-twenties must be linked to changes brought by environmental and lifestyle factors from attaining adulthood and conscious improvements in viewing habits including eye-strain awareness during long duration near-work. It also makes it trivial to explain why some myopes can still experience continued 'Myopia progression' throughout their adult lives.

The framework of CAT naturally accounts for and predicts eyes trying to adapt continuously towards various visual stimulus that can be encountered during the day – which implies that changes from emmetropization should get somewhat 'compensated' by myopization due to 'ordinary work' during the rest of the day. This temporal integration hints at less than expected rate of recovery. The adaptive nature of the process also implies that the requirements for Myopia reversal should be far stricter than that required for Myopia stabilization. This is the 'dual' of observing a population subset with significant near-work habits not becoming Myopic. It also implies existence of a population subset experiencing stabilization of Myopia but not reversal.

6.1 Summing up the Continuous Adaptive Theory (CAT) for physiological Myopia

A tabulation of the predicted differences between myopization vs emmetropization is being provided below:

Table 3: Physiological factors required to induce adaptation

Function	Onset/Progression of Myopia	Emmetropization (Duals)
Visual stimulus 'pulling' the adaptive equilibrium	Near work induced accommodative load	Myopic defocus under pupil constricted lighting so as to overcome FDM pathway
Visual stimulus 'pushing' the adaptive equilibrium	under-utilisation of distance vision capability	Near-work management and periodic breaks as signalled by

		the eye to alleviate accommodative load.
Accelerator Light levels	Pupil dilated utilising FDM pathways	Pupil constricted so as to overcome the FDM pathways
Accommodative shift in the ciliary/feedback loop causing shift in Observation Range (far-point and near-point)	Myopic	Hyperopic
Secondary refractive errors	Results in aberrations and progression of refractive errors like astigmatism	Corrects aberrations and refractive errors
Field of View	Shrinks	Expands
Time Interval	Existing Myopia progression rate	faster than Myopia progression due to extra light information

6.2 Key takeaways

The author recognise the tediously slow and time intensive nature (taking months and years) for the Myopia reversal process outlined in this article. Still, we are firmly convinced that the results outlined are still of enormous utility towards maintaining post-refractive surgery outcomes and preventing Myopia progression until faster and better optimised routes are discovered. We expect that long-term commitment along with various habitual and lifestyle interventions are required to properly implement physical requirements for emmetropization. It is theoretically very simple but practically very difficult.

Although this article provides a protocol for satisfying necessary requisites for observing stabilization and/or reversal of physiologic Myopia, the article should not be taken as against wearing glasses/contacts or refractive interventions in general. The aim of this article is to reduce dependence on glasses.

6.3 Further research

Proposing precise set of requisites that must be satisfied for reversing physiological Myopia presents a massive unexplored opportunity in front of the scientific community.

1. Optimal nature of myopic defocus under pupil constricted lighting that promotes fastest rate of emmetropization.

2. Whether insights mentioned in this article can actually be extended for investigating possible Myopization in Hyperopes.
3. Further optimisation of lighting environment and distant calibration target requirement for ADV.
4. Experimental studies trying to observe form-deprivation hyperopia under pupil constricted lighting.
5. Detailed investigation into the role played by mechanistic interaction between iris and ciliary.
6. Corporate and lawmaker's role towards enabling effective management of physiologic Myopia.

7. Appendix: Myopia Management Implementation acc. to CAT

The obvious end-goal for any theory capable of consistently and convincingly explaining peculiarities shown by physiologic myopia should be the ability to arrive at a physically viable method causing reversal of Myopia. The following sections describe the implementation details for the same using CAT.

Most if not all of the implementation details regarding Myopia management in this section are the result of limited scale experimentation spanning more than a year including the time spent documenting and writing this article. It would have been near-impossible otherwise to gather important insights from theoretical deliberations alone.

7.1 Saturation time for emmetropization and near-work management

The question of what should be the ideal time for exposure to myopic defocus emerges from peaking of AL reduction (saturation from now on) around 50 minutes. [Delshad, S., Collins, M.J., Read, S.A. et al. The time course of the onset and recovery of axial length changes in response to imposed defocus, 2020[73]]

"The first statistically significant reduction in axial length occurred after 40 minutes of exposure to myopic defocus, with a mean reduction of −8 ± 9 μm ($p = 0.017$). This change peaked shortly after, reaching a maximum axial length reduction of −10 ± 8 μm at 50 minutes ($p = 0.001$)."

We recognise that the article in question is not a long-term study on axial changes. But even then, the observation of saturation behaviour and its expected duration being somewhere close to an hour should apply. The peaking of AL changes in itself is an obvious indicator that the eye takes periodic breaks. The time to achieve saturation naturally increases if done in smaller time intervals. Myopes willing to maximize benefits should aim for an observation time > saturation time. For preliminary trials, the tentative duration of exposure time to maximize saturation in the absence of any prior long-term experimental data can be taken close to an hour (more than 50 min). They should be encouraged to determine long-term saturation time on their own from the signals given by their eyes.

Opposite to myopization, promoting emmetropization demands managing accommodative loading due to near-work as much as possible. This forms the 'additional requirement' part required for reversing myopia

than just stabilising it (Section 5.2.3). Accommodative load can be managed in two ways – reducing the time or increasing the distance at which near-work is done.

The former can be achieved by reducing amount of near-work. It is obviously the most effective but largely impractical approach. It also establishes the importance of taking regular breaks as indicated by the eye and doing distance work during breaks. The already established recommendation[74] in the form of 20-20-20 rule is handy in this regard. The second approach refers to mitigations that minimize accommodation. This can be done by physically or refractively increasing the distance at which near-work is done.

7.2 Implementation of ADV

Having described the saturation and near-work management aspects in the previous section 7.1, we will now elaborate the physical requirements for ADV – combination term for myopic defocus under bright outdoor indirect sunlight inducing emmetropization as outlined under section 5.2.3.

7.2.1 Duration and regime requirements

Due to the lack of any previous experimental data regarding the time interval between ADV sessions, we suggest that myopes should attempt ADV sessions until saturation described in section 7.1 consistently on a daily basis. Effective Myopia management requires augmenting daily ADV sessions with refractive intervention and near-work management guidelines for the rest of the day.

7.2.2 Prescriptive compensation for Myopic defocus requirements

The lack of prior large-scale experimental data also implies that the ideal value of myopic defocus for ADV is in dire need for determination. It is very probable that a ‘saturation’ criteria for defocus could also exist resulting in the eyes hitting an emmetropization strength limit once defocus is beyond certain threshold.

This leads us to suggest that non-severe myopes should be tentatively able to attempt ADV with no prescriptive compensation at all. This implies not wearing any glasses or contacts resulting in a greatly simplified implementation because doing ADV without refractive interventions directly stimulates emmetropia (ensuring direct exposure to final state of emmetropization). Myopes experiencing unital difficulties should gradually taper their refractions utilising their former prescriptions.

7.2.3 Distance viewing requirements

As it stands, ADV requires regular (daily) exposure of entire visual field for saturation time period to distant contrasting calibration ‘targets’ under myopic defocus in indirect sunlight. The idea behind exposing entire visual field to distant calibration ‘targets’ emerges from the concept of conveying maximum information to the retina. One needs to exclude viewing the Sun directly because the Sun is a point object in the visual field even if one ignores the harms[75] direct sunlight exposure has on the eyes. It is imperative for the myopes to keep the Sun behind them at all times to minimize risk of harmful UV exposure.

Regarding observation of distant sunlit objects, myopes should place no demands or special emphasis in the way distant objects are being observed. They should strive to observe naturally in a relaxed manner without squinting, forcing or stressing their eyes in any manner. Myopes can attempt slow walking, standing, or sitting still while performing ADV according to their convenience. This should not differ from the way an emmetropic or a refractively compensated (pseudo-emmetropic) person normally observes objects at a distance. The best analogy we can give is similar to trying to read a distant signboard or resolving fine details presented by a distant structure. We expect contrasting patterns in both vertical and horizontal meridians to be useful and implore researches to optimise target object requirements and explore such synthetic target patterns for ADV.

Figure 11 Image demonstrating close to ideal calibration target for ADV

An image showing ideal ADV environment satisfying our criteria is shown in Figure 11. The Sun in clear sky is behind the observer in this image and most of the objects are more than 20 m away with the farthest being more than 100 m away resulting in a good calibration target. The difference between an object at 4 m compared to an object located at 20 m is 0.2 D, a distinction important for fairly low myopia.

Because the lighting requirement is for the eyes only, being under direct sunlight or doing it from a shaded place doesn't matter. The outcomes are independent from whether the body is exposed to Sunlight or not. People residing in hot climatic conditions should attempt ADV from a cool and shaded place to combat the sweltering heat outside. Swamp (desert) coolers are effective in this regard.

It remains to be seen how the strategic requirements posed by ADV pans out for myopes living in inclement climatic conditions receiving little sunlight during the year. Artificial lighting that recreate the bright daylight environment might prove useful according to recent suggestions. [NBK470669: "In countries where the intensity of outdoor light is generally lower, because of air pollution or short duration

of natural daylight – such as Canada or Scandinavia in the winter, or Beijing year-around – sunlight therapy could be supplemented in the form of SAD lights (approved and used for Seasonal Affective Disorder)"]

7.3 Refractive intervention guidelines for Myopia management

We have already established experimentally that observing objects closer than the myopic far-point while wearing prescription requires focusing at a closer distance compared to viewing directly. This directly translates to extra accommodation requirement for viewing the same distance using refractive compensation intended for Myopia. This should also imply that glasses for non-severe Myopia can be worn on a need basis – only for visual requirements farther than the myopic near-point. As myopia reversal progresses, this far-point should shift closer to ∞ reducing dependence on glasses.

In accordance with our duals established in section 5.2.3, proper refractive interventions can ensure that the subject's quality of life remains relatively unaffected from the requirements of managing Myopia while simultaneously minimizing near-work load on ciliary muscle.

For Myopia management, worn glasses are the equipment of choice because they are easy to wear and remove in accordance with varying refractive demands during the day; cheaper, reliable, safer for the eyes, allowing easier management in the long run compared to contacts.

Within few weeks of daily ADV sessions, it should be expected for an eye to gradually start experiencing difficulties both while wearing their former normal prescription during the day (resulting from reduction in refraction) and in the form of subtle aversion from near-work. This should result from the gradual disruption of myopic feedback loop during the initial weeks of ADV sessions. The suggested course of action is to implement refractive interventions in the order in which they become necessary. Myopes should introduce changes one at a time and that too only when indicated by the eye so as to maintain fall back.

The disruption of myopic feedback loop from ADV sessions also means that refractive demands of the eye become somewhat complicated. As such situations arise, the signalled comfort of the eyes towards worn prescription should be prioritized. The eyes usually signal immediate discomfort for both over and too much under-correction and the same should be avoided. As long as the worn prescription is kept within this narrow range of comfort according to the signals given by the eyes, we expect emmetropization to dominate.

This concept of refractive intervention is an important aspect of myopia management and requires strictly individual implementation because of the varying near-work requirements of myopes, their present refractive state and preferences/tolerance to defocus. The adaptive nature of the eye makes it obvious that the refractive compensation requirements from the standpoint of reducing accommodative load for a system as dynamic as the human eye can not be accomplished using SVS. For the ease of understanding, we have tabulated these guidelines in the table below.

Table 4: Tentative Refractive compensation guidelines for near-work management

Working distance	Daylight (outdoors on a sunny day)	Evening/Night
For ADV until saturation	Without wearing prescription	N/A
Other distance work	Full Prescription preferably with UV protection	Full Prescription
work at a distance just beyond the myopic far-point	under-prescription	under-Prescription
Near-work done at a distance closer than the myopic far-point	Non-severe Myopes are able to observe objects closer than their myopic far-point comfortably without prescription	
Life-critical task such as driving, operating heavy industrial machinery and other dangerous work regardless of time and distance	Best Possible Refractive compensation ensuring full visual capability to prevent incidents and to comply with applicable local laws	

These guidelines are only meant as a starting point for the trial implementation for our Myopia management method resulting in a slightly more complicated answer for the commonly asked question in myopia – "When should I wear glasses?". It is expected that the eye's refractive demand will change during the course of the trial as emmetropization progresses. The evaluation criteria always remains the fastest and safest reversal of Myopia and we fully expect some of these tentative guidelines to fail or get superseded by further experimental data.

7.3.1 Blue Light Blocking lenses

Coming to the type of lenses used, we suggest ordinary lenses without any special coating such as blue light blocking filters because of the reasons given below:

1. Increased costs of lenses that will need to be replaced eventually in the near future as emmetropization continues.
2. Provides no clinically substantiated protection against Myopization as evident from multiple research attempts into investigating their benefits[76].

3. Nearly every recent computing device with a display already has an inbuilt blue-light reduction/night-comfort feature. [Windows Night Light[77] and Apple Night Shift[78]]. The intended physical purpose of blue-light glasses is already achieved at the source level for modern computing devices.

4. Blue light lenses can not replace the utility and eye-protection offered by sunglasses under direct outdoor sunlight.

7.4 The proposed mechanism for emmetropization

Section 5.2.2 already covers our attempts at characterizing how myopization takes place.

This section attempts to describe the mechanism of Myopia reversal based on our observations upon year long implementation of the method described in the preceding sections. For lower degree of Myopia, subject's experience reduce to only a subset of what has been described in this section.

The initial days of ADV sessions should be relatively uneventful with slow spontaneous onset of brief moments of sharp vision (referred to as clear flashes from now on) vanishing immediately after blinking with long reset time (minutes to hours) between consecutive clear flashes. This suggests that just like Myopization, the ciliary is the fastest to respond preparing for emmetropization.

Within weeks of regular ADV sessions, besides a perceptible increase in clarity, clear flashes become both more frequent while lasting longer. This development alone with the occurrence of significant clear flashes coincident with outside exposure to daylight should be enough to conclusively debunk the prevailing hypothesis that these clear flashes result from formation of tear film[79] on the cornea or due to the diurnal variation in vision[80]. ADV can also result in transient intervals of blurrier than usual vision on some days. We suspect that it might signify the eye undergoing repair/restructuring.

It can be naturally deduced from the anatomy of the eye that clear flashes because of their instantaneous nature must arise due to increase in focal length of the eye lens. In the case of Myopia, adaptive pull can be said to arise from accommodative load on the ciliary muscle. However, the opposite of this is incorrect because the ciliary muscle is not 'tired or exhausted' in its relaxed state – hence the overshoot in 'negative accommodation[81]'. It also explains the commonly reported instances of 'ciliary spasms' in myopic people observing spontaneous brief flashes of clear vision under pupil constricted lighting when not wearing their glasses.

Within weeks, emmetropization forces the establishment of a feedback loop opposite to the previously described myopic feedback loop – resulting in enhanced sensitivity to eye-strain/aversion towards near-work. Experiencing discouragement from near work serves as a reliable indicator that emmetropization is underway. For a person experiencing active myopia progression, this happens after disruption of existing myopic shift and establishment of hyperopic ciliary shift.

After regular ADV sessions spanning over longer time-frames (months), myopes should start experiencing a perceptible level of visual clarity brought automatically when venturing outside on a sunny day – a telltale marker of hyperopic ciliary shift. Long-term axial changes soon follow to compensate this hyperopic response of the ciliary as long as near-work management is maintained. Measurable reduction in retinal distance starts happening once this stage is reached. This stage should continue translating into improvements to baseline vision with time until emmetropia is achieved.

Successful observation of hyperopic ciliary shift would cement the bi-directional bridging nature of the precursor p long-term axial changes for both myopic and hyperopic adaptations (Hypothesis H1). This alone should be sufficient to confirm that the predicted[82] *active emmetropization mechanism* is not different from the process described in this article inducing Myopia or Hyperopia in accordance with the imposed visual stimulus. The process of Emmetropization naturally involves ocular re-calibration for distance vision and translates into eventual changes to the eyeball shape in the long-term (months). Some myopes can also report feeling changes to the extraocular eyeball muscles both during and after ADV sessions.

It is equally important to mention that most of the aforementioned clarity gains during ADV sessions vanishes swiftly under pupil dilated lighting. This behaviour from the eyes could be looked as a source of frustration upon witnessing the clarity gained during the day vanishing in the night. This observation is so important from the standpoint of light's role in influencing adaptive behaviour of the eye that we predict that it should result from the mechanistic interaction of the iris restricting 'headroom' for negative accommodation (responsible for clear flashes), explaining the loss of clarity under pupil dilated lighting. This can be termed as restrictive effect of the dilated pupil for ciliary relaxation under dim lighting. This mechanistic interaction of the iris with the ciliary should be also associated with why observation of FDM as the default behaviour of the eye[83].

7.5 Precautions, Safety and myope selection requirements

7.5.1 Implementation Criteria

Managing Myopia according to our method requires active integration into daily lifestyle and myopes should be willing to devote the (an hour or two) of their daily time towards achieving saturation requirements for ADV besides following guidelines for the rest of the day.

The lack of any prior widespread experimental data means heavy reliance on precautions as a first line of safety. We insist on limiting the first run of trials to **Non-severe** young adults only having good ocular health history without any adverse event. They should also be screened for presence of musculoskeletal disorders. Further information from the outcome of the preliminary trials on non-severe myopics should be useful towards narrowing down additional requirements for severe myopes.

It is recommended that the myopes exercise caution during the initial transition period of the trial, starting with 'less brighter' objects first and take regular breaks until acclimatisation is completed within the first

week. We expect the majority of myopes to experience excessive-tearing and strong aversion signals from the eyes in the form of eye-strain and minor headache during the beginning of the trial due to the aforementioned sensitivity of a myopic eye towards bright light. It is also recommended that observation duration too should be gradually ramped up towards saturation over the course of multiple days under constant monitoring so as to prevent the possibility of any adverse complications from over exertion.

7.5.2 Safety of ADV:

The only part of our method inducing any significant change to the eye comes from ADV. ADV should have a risk profile similar to onset/progression of Myopia because the same adaptive process responsible for Myopia should result in hyperopic adaptation towards emmetropization also.

We would also like to point out positive sentiments of experts about outdoor therapies like ours that involve High Environmental Illuminance trials: ["Outdoor-light therapy may offer the ideal treatment for myopia. Not only does encouraging children to play outside combat other major health concerns – such as childhood obesity, juvenile diabetes, and depression – but also, light therapy presents little to no serious health concerns or side-effects compared to those of other available myopia-treatments."1]

There are multiple studies demonstrating safety profile and tolerance of eyes towards light therapies with light levels far higher than that of indirect sunlight for Myopia management[84]. No serious complications have been reported in RLRL's (Repeated Low-Level Red Light) studies with periods from 6 months up to 2 years. There is even a 12-month study reporting improved accommodative function after RLRL treatment[85].

7.5.3 Important Warning for personal safety and compliance with applicable laws/regulations:

Myopes need to be made strictly aware of the potential life-threatening dangers of doing critically important work involving life at risk without wearing best possible refractive correction. Put simply, safety of personal and other's lives while driving during low-light such as night-time or working in dangerous circumstances including but not limited to operating construction, industrial, or heavy-machinery/equipments should always be prioritized and best possible refractive compensation must always be worn.

Myopes are expected to use fair judgement and not jeopardise their own and other's lives for Myopia management. Because ADV involves observing defocus from Myopia and significant reduction in visual acuity is involved, it is only imperative that personal safety must be prioritised and ADV should always be attempted in a safe environment.

8. References

1. Carr BJ, Stell WK. The Science Behind Myopia. 2017 Nov 7. In: Kolb H, Fernandez E, Nelson R, editors. Webvision: The Organization of the Retina and Visual System [Internet]. Salt Lake City (UT): University of Utah Health Sciences Center; 1995-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK470669/

2. Pugazhendhi S, Ambati B, Hunter AA. Pathogenesis and Prevention of Worsening Axial Elongation in Pathological Myopia. Clin Ophthalmol. 2020 Mar 18;14:853-873. doi: 10.2147/OPTH.S241435. PMID: 32256044; PMCID: PMC7092688.

3. Haarman AEG, Enthoven CA, Tideman JWL, Tedja MS, Verhoeven VJM, Klaver CCW. The Complications of Myopia: A Review and Meta-Analysis. Invest Ophthalmol Vis Sci. 2020 Apr 9;61(4):49. doi: 10.1167/iovs.61.4.49. PMID: 32347918; PMCID: PMC7401976.

4. Holden BA, Fricke TR, Wilson DA, Jong M, Naidoo KS, Sankaridurg P, Wong TY, Naduvilath TJ, Resnikoff S. Global Prevalence of Myopia and High Myopia and Temporal Trends from 2000 through 2050. Ophthalmology. 2016 May;123(5):1036-42. doi: 10.1016/j.ophtha.2016.01.006. Epub 2016 Feb 11. PMID: 26875007.

5. Grosvenor T. A review and a suggested classification system for myopia on the basis of age-related prevalence and age of onset. Am J Optom Physiol Opt. 1987 Jul;64(7):545-54. doi: 10.1097/00006324-198707000-00012. PMID: 3307441.

6. https://icd.who.int/browse11/l-m/en#/http://id.who.int/icd/entity/1666440799

7. Kyoko Ohno-Matsui, Pei-Chang Wu, Kenji Yamashiro, Kritchai Vutipongsatorn, Yuxin Fang, Chui Ming Gemmy Cheung, Timothy Y. Y. Lai, Yasushi Ikuno, Salomon Yves Cohen, Alain Gaudric, Jost B. Jonas; IMI Pathologic Myopia. Invest. Ophthalmol. Vis. Sci. 2021;62(5):5. doi: https://doi.org/10.1167/iovs.62.5.5.

8. Winawer J, Zhu X, Choi J, Wallman J. Ocular compensation for alternating myopic and hyperopic defocus. Vision Res. 2005 Jun;45(13):1667-77. doi: 10.1016/j.visres.2004.12.013. PMID: 15792842.

9. Earl L Smith III, Li-Fang Hung, The role of optical defocus in regulating refractive development in infant monkeys, Vision Research, Volume 39, Issue 8, 1999, Pages 1415-1435, ISSN 0042-6989, https://doi.org/10.1016/S0042-6989(98)00229-6.

10. McFadden SA, Wildsoet C. The effect of optic nerve section on form deprivation myopia in the guinea pig. J Comp Neurol. 2020 Dec 1;528(17):2874-2887. doi: 10.1002/cne.24961. Epub 2020 Jun 26. PMID: 32484917; PMCID: PMC7541599.

11. Smith EL 3rd, Huang J, Hung LF, Blasdel TL, Humbird TL, Bockhorst KH. Hemiretinal form deprivation: evidence for local control of eye growth and refractive development in infant monkeys. Invest Ophthalmol Vis Sci. 2009 Nov;50(11):5057-69. doi: 10.1167/iovs.08-3232. Epub 2009 Jun 3. PMID: 19494197; PMCID: PMC2778320.

12. Coviltir V, Burcel M, Cherecheanu AP, Ionescu C, Dascalescu D, Potop V, Burcea M. Update on Myopia Risk Factors and Microenvironmental Changes. J Ophthalmol. 2019 Oct 31;2019:4960852. doi: 10.1155/2019/4960852. PMID: 31781378; PMCID: PMC6875023.

13. Ludwig PE, Lopez MJ, Czyz CN. Embryology, Eye Malformations. [Updated 2022 Apr 5]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK482496/

14. Lim LS, Chua S, Tan PT, Cai S, Chong YS, Kwek K, Gluckman PD, Fortier MV, Ngo C, Qiu A, Saw SM. Eye size and shape in newborn children and their relation to axial length and refraction at 3 years. Ophthalmic Physiol Opt. 2015 Jul;35(4):414-23. doi: 10.1111/opo.12212. Epub 2015 May 10. PMID: 25958972.

15. Wildsoet CF. Active emmetropization--evidence for its existence and ramifications for clinical practice. Ophthalmic Physiol Opt. 1997 Jul;17(4):279-90. PMID: 9390372.

16. Milly S. Tedja, Annechien E. G. Haarman, Magda A. Meester-Smoor, Jaakko Kaprio, David A. Mackey, Jeremy A. Guggenheim, Christopher J. Hammond, Virginie J. M. Verhoeven, Caroline C. W. Klaver, for the CREAM Consortium; IMI – Myopia Genetics Report. Invest. Ophthalmol. Vis. Sci. 2019;60(3):M89-M105. doi: https://doi.org/10.1167/iovs.18-25965.

17. Naqvi SAH, Rehman ZU, Nazir T, Rizwan A, Raza H, Obaid N. Sunlight Exposure: A Protective Role in the Development of Myopia. J Coll Physicians Surg Pak. 2021 Sep;31(9):1126-1128. doi: 10.29271/jcpsp.2021.09.1126. PMID: 34500538.

18. Dutheil F, Oueslati T, Delamarre L, Castanon J, Maurin C, Chiambaretta F, Baker JS, Ugbolue UC, Zak M, Lakbar I, Pereira B, Navel V. Myopia and Near Work: A Systematic Review and Meta-Analysis. Int J Environ Res Public Health. 2023 Jan 3;20(1):875. doi: 10.3390/ijerph20010875. PMID: 36613196; PMCID: PMC9820324.

19. Jenny M. Ip, Seang-Mei Saw, Kathryn A. Rose, Ian G. Morgan, Annette Kifley, Jie Jin Wang, Paul Mitchell; Role of Near Work in Myopia: Findings in a Sample of Australian School Children. Invest. Ophthalmol. Vis. Sci. 2008;49(7):2903-2910. doi: https://doi.org/10.1167/iovs.07-0804.

20. Smith MJ, Walline JJ. Controlling myopia progression in children and adolescents. Adolesc Health Med Ther. 2015 Aug 13;6:133-40. doi: 10.2147/AHMT.S55834. PMID: 26316834; PMCID: PMC4542412.

21. Chung K, Mohidin N, O'Leary DJ. Undercorrection of myopia enhances rather than inhibits myopia progression. Vision Res. 2002 Oct;42(22):2555-9. doi: 10.1016/s0042-6989(02)00258-4. PMID: 12445849.

22. Yazdani N, Sadeghi R, Ehsaei A, Taghipour A, Hasanzadeh S, Zarifmahmoudi L, Heravian Shandiz J. Under-correction or full correction of myopia? A meta-analysis. J Optom. 2021 Jan-Mar;14(1):11-19. doi: 10.1016/j.optom.2020.04.003. Epub 2020 Jun 2. PMID: 32507615; PMCID: PMC7752985.

23. Gebru EA, Mekonnen KA. Prevalence and Factors Associated with Myopia Among High School Students in Hawassa City, South Ethiopia, 2019. Clin Optom (Auckl). 2022 Mar 10;14:35-43. doi: 10.2147/OPTO.S308617. PMID: 35299899; PMCID: PMC8921835.

24. Kohmarn T, Srisurattanamethakul N, Watcharapalakorn A, Poyomtip T, Poolsanam C. Outbreak of COVID-19-Related Myopia Progression in Adults: A Preliminary Study. Clin Optom (Auckl). 2022 Aug 4;14:125-131. doi: 10.2147/OPTO.S374155. PMID: 35959467; PMCID: PMC9359493.

25. Wang J, Li Y, Musch DC, et al. Progression of Myopia in School-Aged Children After COVID-19 Home Confinement. JAMA Ophthalmol. 2021;139(3):293–300. doi:10.1001/jamaophthalmol.2020.6239

26. Josh Wallman, Jonathan Winawer Homeostasis of Eye Growth and the Question of Myopia 2004/08/19 doi: 10.1016/j.neuron.2004.08.008

27. Chakraborty, R., Ostrin, L.A., Benavente-Perez, A. and Verkicharla, P.K. (2020), Optical mechanisms regulating emmetropisation and refractive errors: evidence from animal models. Clin Exp Optom, 103: 55-67.

https://doi.org/10.1111/cxo.12991

28. Huang J, Wen D, Wang Q, McAlinden C, Flitcroft I, Chen H, Saw SM, Chen H, Bao F, Zhao Y, Hu L, Li X, Gao R, Lu W, Du Y, Jinag Z, Yu A, Lian H, Jiang Q, Yu Y, Qu J. Efficacy Comparison of 16 Interventions for Myopia Control in Children: A Network Meta-analysis. Ophthalmology. 2016 Apr;123(4):697-708. doi: 10.1016/j.ophtha.2015.11.010. Epub 2016 Jan 27. PMID: 26826749.

29. Kaur K, Gurnani B. Subjective Refraction Techniques. [Updated 2022 Dec 6]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK580482/

30. National Research Council (US) Committee on Vision. Myopia: Prevalence and Progression. Washington (DC): National Academies Press (US); 1989. Appendix D, The Etiology Of Myopia. Available from: https://www.ncbi.nlm.nih.gov/books/NBK235065/

31. Chuang AY. How to effectively manage myopia. Taiwan J Ophthalmol. 2017 Jan-Mar;7(1):44-47. doi: 10.4103/tjo.tjo_24_17. PMID: 29018754; PMCID: PMC5525606.

32. Vagge A, Ferro Desideri L, Nucci P, Serafino M, Giannaccare G, Traverso CE. Prevention of Progression in Myopia: A Systematic Review. Diseases. 2018 Sep 30;6(4):92. doi: 10.3390/diseases6040092. PMID: 30274355; PMCID: PMC6313317.

33. Xiong R, Zhu Z, Jiang Y, Kong X, Zhang J, Wang W, Kiburg K, Yuan Y, Chen Y, Zhang S, Xuan M, Zeng J, Morgan IG, He M. Sustained and rebound effect of repeated low-level red-light therapy on myopia control: A 2-year post-trial follow-up study. Clin Exp Ophthalmol. 2022 Dec;50(9):1013-1024. doi: 10.1111/ceo.14149. Epub 2022 Sep 7. PMID: 36054314; PMCID: PMC10086781.

34. Regan Ashby, Arne Ohlendorf, Frank Schaeffel; The Effect of Ambient Illuminance on the Development of Deprivation Myopia in Chicks. Invest. Ophthalmol. Vis. Sci. 2009;50(11):5348-5354. doi: https://doi.org/10.1167/iovs.09-3419.

35. Earl L. Smith, Li-Fang Hung, Juan Huang; Protective Effects of High Ambient Lighting on the Development of Form-Deprivation Myopia in Rhesus Monkeys. Invest. Ophthalmol. Vis. Sci. 2012;53(1):421-428. doi: https://doi.org/10.1167/iovs.11-8652.

36. Ho CL, Wu WF, Liou YM. Dose-Response Relationship of Outdoor Exposure and Myopia Indicators: A Systematic Review and Meta-Analysis of Various Research Methods. Int J Environ Res Public Health. 2019 Jul 21;16(14):2595. doi: 10.3390/ijerph16142595. PMID: 31330865; PMCID: PMC6678505.

37. Image: Rhcastilhos. And Jmarchn., CC BY-SA 3.0 <https://creativecommons.org/licenses/by-sa/3.0>, via Wikimedia Commons

38. Sánchez López de Nava A, Somani AN, Salini B. Physiology, Vision. [Updated 2022 Jul 7]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK538493/

39. Elliott DB. The good (logMAR), the bad (Snellen) and the ugly (BCVA, number of letters read) of visual acuity measurement. Ophthalmic Physiol Opt. 2016 Jul;36(4):355-8. doi: 10.1111/opo.12310. PMID: 27350181.

40. Ji Hyun Kim, Hye Sun Lee, Na Rae Kim, Gong Je Seong, Chan Yun Kim; Relationship Between Visual Acuity and Retinal Structures Measured by Spectral Domain Optical Coherence Tomography in Patients With Open-Angle

Glaucoma. Invest. Ophthalmol. Vis. Sci. 2014;55(8):4801-4810. doi: https://doi.org/10.1167/iovs.13-13052.

41. Linton P. Does vision extract absolute distance from vergence? Atten Percept Psychophys. 2020 Aug;82(6):3176-3195. doi: 10.3758/s13414-020-02006-1. PMID: 32406005; PMCID: PMC7381460.

42. Labhishetty V, Cholewiak SA, Roorda A, Banks MS. Lags and leads of accommodation in humans: Fact or fiction? J Vis. 2021 Mar 1;21(3):21. doi: 10.1167/jov.21.3.21. PMID: 33764384; PMCID: PMC7995353.

43. Goldberg D. Computer-animated model of accommodation and theory of reciprocal zonular action. Clin Ophthalmol. 2011;5:1559-1566 https://doi.org/10.2147/OPTH.S25983

44. van ALPHEN G. On emmetropia and ametropia. Opt Acta (Lond). 1961;142(Suppl):1-92. PMID: 13860704.

45. Bhardwaj V, Rajeshbhai GP. Axial length, anterior chamber depth-a study in different age groups and refractive errors. J Clin Diagn Res. 2013 Oct;7(10):2211-2. doi: 10.7860/JCDR/2013/7015.3473. Epub 2013 Oct 5. PMID: 24298478; PMCID: PMC3843406.

46. Jonas JB, Jonas RA, Bikbov MM, Wang YX, Panda-Jonas S. Myopia: Histology, clinical features, and potential implications for the etiology of axial elongation. Prog Retin Eye Res. 2022 Dec 28:101156. doi: 10.1016/j.preteyeres.2022.101156. Epub ahead of print. PMID: 36585290.

47. Lee SS, Alonso-Caneiro D, Lingham G, Chen FK, Sanfilippo PG, Yazar S, Mackey DA. Choroidal Thickening During Young Adulthood and Baseline Choroidal Thickness Predicts Refractive Error Change. Invest Ophthalmol Vis Sci. 2022 May 2;63(5):34. doi: 10.1167/iovs.63.5.34. PMID: 35616928; PMCID: PMC9150825.

48. Bailey MD, Sinnott LT, Mutti DO. Ciliary body thickness and refractive error in children. Invest Ophthalmol Vis Sci. 2008 Oct;49(10):4353-60. doi: 10.1167/iovs.08-2008. Epub 2008 Jun 19. PMID: 18566470; PMCID: PMC2994597.

49. Dinesh Kaphle, Katrina L. Schmid, Leon N. Davies, Marwan Suheimat, David A. Atchison; Ciliary Muscle Dimension Changes With Accommodation Vary in Myopia and Emmetropia. Invest. Ophthalmol. Vis. Sci. 2022;63(6):24. doi: https://doi.org/10.1167/iovs.63.6.24.

50. Low W, Dirani M, Gazzard G, Chan YH, Zhou HJ, Selvaraj P, Au Eong KG, Young TL, Mitchell P, Wong TY, Saw SM. Family history, near work, outdoor activity, and myopia in Singapore Chinese preschool children. Br J Ophthalmol. 2010 Aug;94(8):1012-6. doi: 10.1136/bjo.2009.173187. Epub 2010 May 14. PMID: 20472747; PMCID: PMC4041336.

51. Huang HM, Chang DS, Wu PC. The Association between Near Work Activities and Myopia in Children-A Systematic Review and Meta-Analysis. PLoS One. 2015 Oct 20;10(10):e0140419. doi: 10.1371/journal.pone.0140419. PMID: 26485393; PMCID: PMC4618477.

52. Lagrèze WA, Schaeffel F. Preventing Myopia. Dtsch Arztebl Int. 2017 Sep 4;114(35-36):575-580. doi: 10.3238/arztebl.2017.0575. PMID: 28927495; PMCID: PMC5615392.

53. Bloom J, Motlagh M, Czyz CN. Anatomy, Head and Neck, Eye Iris Sphincter Muscle. [Updated 2022 Jul 19]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK532252/l

54. Spector RH. The Pupils. In: Walker HK, Hall WD, Hurst JW, editors. Clinical Methods: The History, Physical, and Laboratory Examinations. 3rd edition. Boston: Butterworths; 1990. Chapter 58. Available from: https://www.ncbi.nlm.nih.gov/books/NBK381/

55. Nilsson DE. Eye evolution and its functional basis. Vis Neurosci. 2013 Mar;30(1-2):5-20. doi: 10.1017/S0952523813000035. PMID: 23578808; PMCID: PMC3632888.

56. Muralidharan AR, Lança C, Biswas S, Barathi VA, Wan Yu Shermaine L, Seang-Mei S, Milea D, Najjar RP. Light and myopia: from epidemiological studies to neurobiological mechanisms. Ther Adv Ophthalmol. 2021 Dec 19;13:25158414211059246. doi: 10.1177/25158414211059246. PMID: 34988370; PMCID: PMC8721425.

57. Marcus H.C. Howlett, Sally A. McFadden, Form-deprivation myopia in the guinea pig (Cavia porcellus), Vision Research, Volume 46, Issues 1–2, 2006, Pages 267-283, ISSN 0042-6989, https://doi.org/10.1016/j.visres.2005.06.036.

58. Zhou X, Lu F, Xie R, Jiang L, Wen J, Li Y, Shi J, He T, Qu J. Recovery from axial myopia induced by a monocularly deprived facemask in adolescent (7-week-old) guinea pigs. Vision Res. 2007 Apr;47(8):1103-11. doi: 10.1016/j.visres.2007.01.002. Epub 2007 Mar 9. PMID: 17350070.

59. Ji FT, Li Q, Zhu YL, Jiang LQ, Zhou XT, Pan MZ, Qu J. [Form deprivation myopia in C57BL/6 mice]. Zhonghua Yan Ke Za Zhi. 2009 Nov;45(11):1020-6. Chinese. PMID: 20137422.

60. Qiao-Grider Y, Hung LF, Kee CS, Ramamirtham R, Smith EL 3rd. Recovery from form-deprivation myopia in rhesus monkeys. Invest Ophthalmol Vis Sci. 2004 Oct;45(10):3361-72. doi: 10.1167/iovs.04-0080. PMID: 15452037.

61. Kim US, Mahroo OA, Mollon JD, Yu-Wai-Man P. Retinal Ganglion Cells-Diversity of Cell Types and Clinical Relevance. Front Neurol. 2021 May 21;12:661938. doi: 10.3389/fneur.2021.661938. PMID: 34093409; PMCID: PMC8175861.

62. Muralidharan AR, Lança C, Biswas S, Barathi VA, Wan Yu Shermaine L, Seang-Mei S, Milea D, Najjar RP. Light and myopia: from epidemiological studies to neurobiological mechanisms. Ther Adv Ophthalmol. 2021 Dec 19;13:25158414211059246. doi: 10.1177/25158414211059246. PMID: 34988370; PMCID: PMC8721425.

63. Chung K, Mohidin N, O'Leary DJ. Undercorrection of myopia enhances rather than inhibits myopia progression. Vision Res. 2002 Oct;42(22):2555-9. doi: 10.1016/s0042-6989(02)00258-4. PMID: 12445849.

64. Chukwuyem EC, Musa MJ, Zeppieri M. Prescribing Glasses For Children. [Updated 2023 Feb 4]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2023 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK585105/

65. Ciuffreda KJ, Vasudevan B. Nearwork-induced transient myopia (NITM) and permanent myopia--is there a link? Ophthalmic Physiol Opt. 2008 Mar;28(2):103-14. doi: 10.1111/j.1475-1313.2008.00550.x. PMID: 18339041.

66. Christopher J, Priya Y, Bhat V, Sarma G. Characteristics of Headache in Children Presenting to Ophthalmology Services in a Tertiary Care Center of South India. Cureus. 2022 Feb 1;14(2):e21805. doi: 10.7759/cureus.21805. PMID: 35251869; PMCID: PMC8890450.

67. García García M, Breher K, Ohlendorf A, Wahl S. To Correct or Not Correct? Actual Evidence, Controversy and the Questions That Remain Open. J Clin Med. 2020 Jun 24;9(6):1975. doi: 10.3390/jcm9061975. PMID:

32599775; PMCID: PMC7356996.

68. Yam JC, Tang SM, Kam KW, et al. High prevalence of myopia in children and their parents in Hong Kong Chinese Population: the Hong Kong Children Eye Study. Acta Ophthalmol. Epub ahead of print 24 January 2020. DOI: 10.1111/aos.14350.

69. Low W, Dirani M, Gazzard G, et al. Family history, near work, outdoor activity, and myopia in Singapore Chinese preschool children. Br J Ophthalmol 2010; 94: 1012–1016.

70. Lim DH, Han J, Chung TY, Kang S, Yim HW; Epidemiologic Survey Committee of the Korean Ophthalmologic Society. The high prevalence of myopia in Korean children with influence of parental refractive errors: The 2008-2012 Korean National Health and Nutrition Examination Survey. PLoS One. 2018 Nov 26;13(11):e0207690. doi: 10.1371/journal.pone.0207690. Erratum in: PLoS One. 2018 Dec 20;13(12):e0209876. PMID: 30475837; PMCID: PMC6261017.

71. Yanming Chen, Ji Liu, Yining Shi; Evaluation of visual field changes of high myopic eyes in a Chinese population at northwestern China.. Invest. Ophthalmol. Vis. Sci. 2015;56(7):2952.

72. Verkicharla PK, Kammari P, Das AV. Myopia progression varies with age and severity of myopia. PLoS One. 2020 Nov 20;15(11):e0241759. doi: 10.1371/journal.pone.0241759. PMID: 33216753; PMCID: PMC7678965.

73. Delshad, S., Collins, M.J., Read, S.A. et al. The time course of the onset and recovery of axial length changes in response to imposed defocus. Sci Rep 10, 8322 (2020). https://doi.org/10.1038/s41598-020-65151-5

74. Sheppard AL, Wolffsohn JS. Digital eye strain: prevalence, measurement and amelioration. BMJ Open Ophthalmol. 2018 Apr 16;3(1):e000146. doi: 10.1136/bmjophth-2018-000146. PMID: 29963645; PMCID: PMC6020759.

75. Chawda D, Shinde P. Effects of Solar Radiation on the Eyes. Cureus. 2022 Oct 29;14(10):e30857. doi: 10.7759/cureus.30857. PMID: 36465785; PMCID: PMC9709587.

76. Wong NA, Bahmani H. A review of the current state of research on artificial blue light safety as it applies to digital devices. Heliyon. 2022 Aug 15;8(8):e10282. doi: 10.1016/j.heliyon.2022.e10282. PMID: 36042717; PMCID: PMC9420367.

77. https://support.microsoft.com/en-us/windows/set-your-display-for-night-time-in-windows-18fe903a-e0a1-8326-4c68-fd23d7aaf136

78. https://support.apple.com/en-in/HT207570

79. Chang AY, Purt B. Biochemistry, Tear Film. [Updated 2022 Jun 11]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2022 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK572136/

80. Ulaganathan S, Read SA, Collins MJ, Vincent SJ. Daily axial length and choroidal thickness variations in young adults: Associations with light exposure and longitudinal axial length and choroid changes. Exp Eye Res. 2019 Dec;189:107850. doi: 10.1016/j.exer.2019.107850. Epub 2019 Oct 19. PMID: 31639338.

81. Raz A, Marinoff GP, Landzberg KS, Guyton DL. Substrates of negative accommodation. Binocul Vis Strabismus Q. 2004;19(2):71-4. PMID: 15180591.

82. Wildsoet CF. Active emmetropization--evidence for its existence and ramifications for clinical practice. Ophthalmic Physiol Opt. 1997 Jul;17(4):279-90. PMID: 9390372.

83. Zhihui She, Li-Fang Hung, Baskar Arumugam, Krista M. Beach, Earl L. Smith, The development of and recovery from form-deprivation myopia in infant rhesus monkeys reared under reduced ambient lighting, Vision Research, Volume 183, 2021, Pages 106-117, ISSN 0042-6989, https://doi.org/10.1016/j.visres.2021.02.004.

84. Rose KA, Morgan IG, Ip J, Kifley A, Huynh S, Smith W, Mitchell P. Outdoor activity reduces the prevalence of myopia in children. Ophthalmology. 2008 Aug;115(8):1279-85. doi: 10.1016/j.ophtha.2007.12.019. Epub 2008 Feb 21. PMID: 18294691.

85. Chen H, Wang W, Liao Y, Zhou W, Li Q, Wang J, Tang J, Pei Y, Wang X. Low-intensity red-light therapy in slowing myopic progression and the rebound effect after its cessation in Chinese children: a randomized controlled trial. Graefes Arch Clin Exp Ophthalmol. 2023 Feb;261(2):575-584. doi: 10.1007/s00417-022-05794-4. Epub 2022 Aug 17. PMID: 35976467.