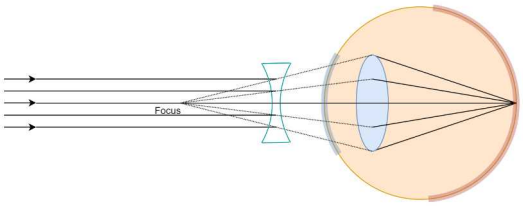

Breakthrough Adaptive insights into Emmetropization for Physiologic Myopia

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0. Abstract

Current understanding is both inconsistent and lacking when it comes to explaining various peculiar behaviours shown by physiologic Myopia. We aim to put forward a novel theoretical framework taking into account recent investigations into interplay of environmental and vision habits for physiologic Myopia.

The breakthrough Continuous Adaptation Theory (CAT) and its two refractive state equivalences approach physiologic Myopia as a shift in refractive equilibrium between two opposing processes - myopization and emmetropization. Physiologic myopia is the resultant of simultaneous ‘push-pull’ shift in equilibrium from near-work induced accommodative strain (pull) when combined with under-utilisation of distance vision (push). The role of light serves to direct adaptive change from the resulting blur due to defocus, possibly answering the decades long open question on ‘how eyes determine direction of adaptation from defocus?’.

By extension, it was shown that mechanism responsible for onset of Myopia (in emmetropic eyes) should be identical for Myopia progression also. And the same could be harnessed to stabilize progression and even reduce Myopia towards possible emmetropia. The breakthrough insights provided by our theory when implemented with appropriate behavioural interventions should provide first ever clinical observations of long-term axial shortening directly translating into conclusive and substantial Myopia reduction.

Note: Additional material accompanies this work. (Methods section and preliminary on Ray optics)

0.1 Conflict of Interest & Ethics declarations

The author declares no competing interests.

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0.2 Keywords

Axial Shortening, Progression, Myopia Control, Emmetropization

0.3 Significance Statement

The first ever proper breakthrough towards completely understanding factors behind physiologic Myopia.

1. Introduction

Myopia is a refractive error widely regarded as irreducible with a suspected multifactorial aetiology[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 (myopic maculopathy)[3]. An estimated half of the world's population is expected to be myopic by 2050 if the current trends continue unabated[4].

There is an urgent need for interventions that can stabilize or at least slow down long-term rate of Myopia progression. Existing methods for Myopia control have been observed to be incapable of directly affecting the primary consequence of Myopia which is posterior axial elongation.

This article is our attempt at describing breakthrough insights from adaptive equilibrium characterization of physiologic Myopia. The governing insight behind such an approach is the observed possibility of axial shortening and evidences pointing towards presence of active emmetropization mechanism in the eye. Our approach is in stark contrast with majority of existing approaches dominated by empirical guesses for physiologic Myopia.

2. Background

This article uses prefixes like *compensated* and suffixes like *wearing prescription* to denote an eye seeing with refractive interventions. The mention of the term infinity or symbol ∞ should be taken to mean optical infinity at a distance of 10 m or greater (≤0.1 D) instead of the usual 20 feet or 6 metre. We have strived to provide terminologies/define abbreviation at the beginning of each new section wherever applicable.

This article attempts to answer the following questions:

1. What are the primary factors responsible for physiologic Myopia?
2. Why so far there was lack of a well established cause for physiologic Myopia?
3. Why was common Myopia considered permanent/irreducible in nature so far?
4. There are mounting evidences that seemingly contradict widely presumed irreversibility of Myopia and hint at the existence of a viable intervention that can result in reduction of Myopia. The goal of this article is to arrive at a truly viable protocol/method for reducing physiologic Myopia.

The background summary follows the natural order: classification of myopia (physiologic vs pathologic) → physiologic myopia (onset and stabilization/progression) → observed associations of Myopia → Animal Models of myopia and its observations → viability/shortcomings of current Myopia control interventions.

2.1 Physiologic Myopia vs Pathologic Myopia? A strictly modular approach towards classification

Myopia is a refractive error resulting in 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 myopia can be classified under physiologic or pathologic/malignant/degenerative Myopia[5]. This basically means that the Myopia can result from either physiological or pathological factors.

Even high degree of refractive error due to physiologic Myopia (increasing risk of sequelae) needs to be strictly distinguished from Pathologic Myopia along with 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, signs/complications associated with pathologic myopia(for instance, posterior staphyloma) have been observed to occur in eyes without high myopia sometimes even in otherwise emmetropic individuals[7] [IMI Pathologic Myopia, May 2021].

For this article, Physiologic Myopia is strictly defined as Myopia in the absence of other ocular anomalies except axial elongation. This is important from the standpoint of consistent classification – Myopia can be either physiologic or pathologic (but not both) in the sense that highly severe Physiologic Myopia too can develop pathological complications later on indicating differences in the underlying mechanism. The benefits of this strict classification will be apparent later in the article.

The scope of this article is restricted to Physiologic Myopia only. The term Myopia from now on in this article should be taken to mean physiologic Myopia unless stated otherwise.

2.1.1 Myopia onset and its progression

Myopia onset is primarily observed in the early childhood and mostly stabilizes towards the mid twenties. However, both myopia onset and its progression has been observed to happen at all ages. This is confirmed by existing observations regarding adult onset/progression of Myopia after enrolling into college[8]. The COVID-19 pandemic also resulted in reports of Myopia onset and progression in both adults[9] and school aged children[10] associated with lockdown confinement.

The onset of Myopia is usually seen as setting the stage for progression of Myopia. This translates to a presumed aetiology of Myopia where worsening Myopia is viewed as the natural course of disease progression. This standpoint is mostly justified in the absence of to date viable long-term methods demonstrating the ability to slow or stabilize Myopia progression or possibly reduce it (see myopia control[11]). 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 so far failing to observe significant reduction in Myopia. For instance, studies isolating only under-correction as a variable saw enhancement instead of inhibition of myopia progression compared to the full correction group [12, 13].

2.2 Multi factorial associations of Myopia

2.2.1 Genetics

For decades, investigations were primarily focused on figuring out the suspected genetic causes behind Myopia. There are numerous studies investigating Myopia's associations with Genetics. However, evidences are now mounting that at most, there can be genetic susceptibility towards physiologic AKA nonsyndromic Myopia in the face of mostly missing heritable markers[14]. To quote the exact paragraph, "A known genetic factor has been implicated in genesis and development of syndromic myopia (such as Marfan syndrome or congenital stationary night blindness). Nonsyndromic myopia has no clear association with a genetic mutation; however, polymorphisms in different genes are associated with nonsyndromic myopia.".

This is unlike the mostly hereditary/parental nature for cases of syndromic/pathologic Myopia[15]. This argument is further supported from environmental connection of common Myopia including its negative association with outdoor activity and the recently discovered protective effect of sunlight[16] towards Myopia onset and progression.

2.2.2 Environmental and behavioural Associations with near work and outdoor exposure

Myopia shows major associations with environmental and behavioural factors which can't be explained 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 (deciding accommodation), contrast, brightness/intensity (affecting the pupil) or their superposition are to be termed as physiologic factors. Factors not optical in nature, for instance: hereditary, birth defects/congenital and environmental factors different from the ones mentioned above such as; toxins, trauma, and other unidentified factors internal to the eye are to be clubbed under pathological factors.

When it comes to physiologic Myopia, its causes are commonly predicted to be a multifactorial interplay of environmental and lifestyle factors with a component of genetic susceptibility. 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). It includes but is not limited to jobs involving handling small things (watchmaking, quality control, for instance), reading, writing and time spent looking at digital displays whether PC/Laptop or smartphones/tablets[17]. 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 cumulative duration

of near work to be the deciding factor for Myopia. This particular study additionally reinforces the need for targeted workplace measures to reduce occupational exposure and mitigations such as allowances for regular breaks from near work[18].

2.3 Animal models of Experimental Myopia and Form Deprivation

There is a large pool of studies inducing and 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 indicating the capability of the eye to respond and direct axial changes in the opposite direction to compensate for the defocus. Also observed was the disproportionately stronger response of eyes towards myopic defocus (inducing hyperopia) compared to same duration of hyperopic defocus (inducing Myopia) as long as the cycle time was kept more than 30 minutes[19]. Once external defocus was removed, induced experimental Myopia slowed and then reduced and in some cases even emmetropia was achieved suggesting that the built in mechanism is able to detect and swiftly adapt to changes in external stimulus. The same was observed in a higher primate (rhesus macaques) as well[20].

Efforts to induce Form Deprivation Myopia were successful even after Optic Nerve Section (ONS) indicating that the eye possesses internal mechanisms still capable of directing axial changes (this mechanism might also be acting as a fall back)[21]. 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[22]. It can be stated that the aforementioned temporally adaptive observations are a consistent feature across multiple species that include higher primates (predicting similar possibility for humans as well) and that retina acts as the primary initiator for majority of these localized changes.

2.3.1 Changes in the eye due to Myopia

Hyperopic defocus using minus lenses resulted in observation of swift choroidal thinning (causing the retina to displace backward) indicating AL compensation for the introduced defocus. Choroidal and scleral thinning was observed to be most prominent at the posterior pole compared to the equatorial regions of the eye[23]. Describing the exact pathways and mechanisms 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[24]. 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 power of its optical components in such a way that images of objects at infinity can be formed with relaxed accommodation (achieving emmetropia). Eye size and shape at birth influences

subsequent eye growth but hasn't been observed to be associated with refractive error development later in the life[25].

The distinctive 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. Eye respond to superposition of growth and adaptive signals after birth [Josh Wallman and Jonathan Winawer, 2004]. Terming Axial elongation as eye growth is contradictory with evidences pointing towards existence of an active emmetropization mechanism. Such a mechanism should be also present and fully functional (although the time period may differ) in Human eyes influencing axial length besides growth[26]. Axial elongation due to Myopia results in a marked shape change (elongation) distinct from overall (globe) growth. Because of the aforementioned reasons, we will prefer to use the term axial change (refers to both axial elongation and shortening) instead of axial growth. This also avoids irreversible connotations of the term growth and its mistaken associations with bodily growth in the context of eyes.

That Myopia results from changes from homeostatic control mechanisms present inside the eye has been documented for decades[27, 28]. These observation together with the nature of changes accompanying axial elongation 2.3.1 suggest that an adaptive mechanism might be at work for physiologic Myopia alongside concepts of equilibrium, feedback, and control theory required to properly characterize 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 reduction should also be possible ideally at ages beyond childhood.

2.4 Myopia control / management methods

Myopia control / management refers to interventions[29] concerned with stabilization/reduction of Myopia different from existing modes of refractive intervention such as lenses, contacts and surgical procedures whose primary goal is to compensate for defocus (after subjective refraction[30]). The term compensation is better suited than widely used correction in this regard. There can be no difference between refraction by glasses, contacts or refractive surgeries from an optical standpoint.

The scope of this article is restricted to the simple observation that none of the existing methods can be considered as truly and significantly affecting the primary outcome of physiologic Myopia. As of now there is still no widely accepted method directly targeting/affecting long-term consequences of posterior axial elongation[31].

The two most commonly used myopia control treatments Ortho-K and Atropine treatment do not account for or directly address the already outlined environmental association of physiologic Myopia. These widely used management options also frequently suffer from rebound effects[32, 33]. The frequent observations of rebound myopia after cessation of treatment shows that none of the current management strategies do not address the underlying processes and environmental factors behind Myopia.

Of special note is the recent promising advancement in the form of light therapies reporting significant axial shortening beyond measurement uncertainity. RLRL[34] (Repeated Low-level Red Light) and High Environmental Illuminance therapies[35] have shown promise for Myopia management. Light therapies aim to emulate response to daytime outdoor exposure and its established protective effect against Myopia onset/progression[[36], [37]]. However, we have yet to come across reliable signs of significant myopia reduction happening from existing light therapies. Further advancements are required before such therapies stand a chance at becoming the standard for Myopia management.

3. Materials and methods (supplied separately)

4. The Continuous Adaptive Theory (CAT)

The fundamental hypothesis underlying the framework of CAT is that ocular components deciding refractive state of the eye are under homeostatic AKA adaptive equilibrium.

The mechanism that makes the eye less myopic/further hyperopic will be referred to as emmetropization and its inverse as Myopization by our conventions. This should not be confused with the term emmetropia/emmetropic. The former is a process (denoting direction) while the latter indicates refraction of the eye being neither hyperopic nor myopic (denoting position). It also implies that for a hyperopic eye to become emmetropic, myopization must dominate and vice-versa for a myopic eye to achieve the same.

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 to 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: focal length or screen distance changes. This is made somewhat complicated by two separate ocular elements present inside the eye – the lens and the cornea.

A lot has been already described about accommodation in multiple texts. Accommodation happens to be a very short-term (almost instantaneous) response changing the focal length of the eye lens. The ciliary muscle is said to be unaccommodated when focusing for objects at the eye's far point. A high-quality video of accommodation in action[38] can be accessed here: https://youtu.be/1yIpyitm6eE

Long-term axial changes (happening on the time-scale of months and longer) due to Myopia[39] mostly involve changes to the cornea (changes to the corneal curvature and ACD[40]) and the thinning of posterior sclera accompanying physical distancing of the retina[41].

Hypothesis H1: Predicts presence of a medium-term intermediate bridging response between the well known short-term accommodation and long-term processes causing axial changes. H1 proposes that this intermediate response precedes observed long-term axial changes to the retina and cornea. Besides evidences already pointing at presence of active emmetropization, this hypothesis is strengthened further

from the continuous structures of iris, the ciliary body and the choroid (uvea). This medium-term shift should result in observed changes to both ciliary body and choroid.

Intermediate changes to the ciliary body affecting the ciliary muscle state should result in shifts in relaxed and accommodated power of the eye lens. The cornea then undergoes long-term changes in order to alleviate such ciliary shift. In the absence of extensive details, we speculate observations reporting ciliary body thickening[42, 43] indicate myopic ciliary shift. Thickness changes to the choroid happen in tandem acting as a precursor for displacement of retina and associated scleral shape changes. Observations describing inverse association[44] of choroidal thickness with posterior axial changes further strengthens our conviction. We expect these intermediate changes in ciliary body and choroid to be mostly in place before long term axial changes are made to the cornea and retina respectively.

4.2 Observation range changes during Myopia

The eye experiences continuous changes to its observation range while becoming myopic. The magnitude of accommodation of the eye during this period can be assumed to be roughly constant. It can be stated that a myopic eye continuously gains additional close-range focusing capability while *sacrificing* capability to observe distant objects compared to an emmetropic eye as shown in Figure 1.

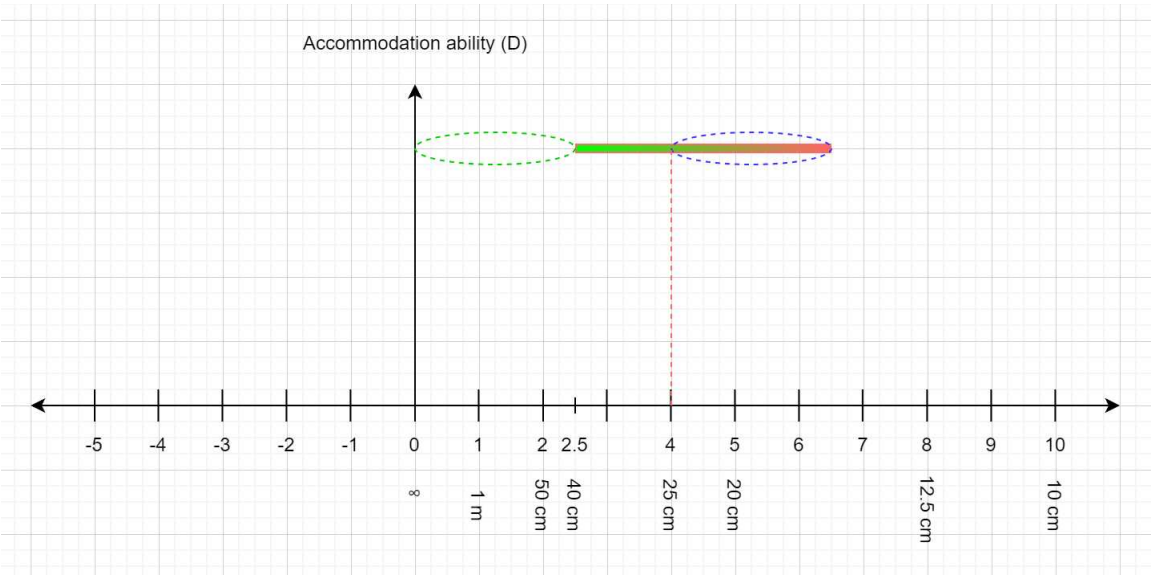


Figure 1 Compared to an emmetropic eye, the gained close-range observation capability by a Myopic eye (2.5 D) is shown with an blue dotted oval while its 'sacrificed' observation range is shown with a green dotted oval.

The blue dotted oval denotes gained observation capability between myopic and emmetropic near-points while the green dotted oval denotes lost observation capability between myopic far-point and infinity (its emmetropic counterpart). Physiologic Myopia is associated with extended duration of near-work and lack of regular outdoors exposure. This shifting of observation range is in agreement with well established associations of myopia and hints towards the possibility that both might constitute an essential requirement.

Hypothesis H2: Myopia 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 accommodative fatigue mediated defocus promoted by under-utilisation of distant vision capability.

The simultaneous 'push-pull' analogy for shifting of observation range makes this even clearer. It hints that the eye undergoes axial changes trying to relieve accommodative fatigue induced defocus[45]. Due to limits on the extension of ciliary accommodation ability, under-utilisation of observation range extreme (distance focusing capability for this case) permits for an even stronger response. For myopia, accommodative fatigue can be said to exert a 'pull' while under-utilisation of distant vision capability exerts a 'push'. The push criteria can also be termed 'permitting' criteria as in allowing the pull criteria to succeed in making myopic changes to the eye. A push or pull in isolation should be insufficient towards shifting refractive equilibrium.

An analogy in the form of car moving forward and application of brakes can be used. A car can't move if brakes are applied. Similarly, brakes can only stop a car but can't make it move again or reverse its direction of movement. In this context, releasing of brake is the 'permitting' criteria. Here, lack of regular outdoors exposure is insufficient to induce myopization but permits myopia.

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[46]? It provides an answer in the form of sufficient utilisation of distant vision capability keeping in check adaptation from accommodative fatigue. An eye doing long-duration near-work but also sufficiently utilising distance vision capability should indicate eye-strain from near-work without becoming Myopic in the long run. It also hints that proper utilisation of distance vision capability is an essential requirement for Myopia management.

We invite researchers to verify the physical implications of our explanation. It explains why near-work correlates[47] with Myopia but can't be the only factor. This implies under-utilisation of distant vision capability (not the same as near-work) is also a factor contributing towards physiologic Myopia[48].

4.3 Influence of lighting levels and the problem of deducing adaptive direction from defocus

The pupil of the iris[49] evolved as an aperture control mechanism to regulate the amount of light entering the eye. [Pupil size[50] in adults usually varies from 2 to 4 mm in diameter in brightly-lit environments to 4 to 8 mm in the dark.] In this context, environmental light intensity can be said to 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 requirement for near work in dim lighting in for same focus distance theoretically resulting in hyperopic defocus. Myopization then compensates for this defocus.

At the same time, it must be noted that, even very forgiving 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 'set-point' with its constricting 'tug'. This prediction too is supported from the continuous structure of iris and ciliary body as part of uvea and the same can be verified experimentally.

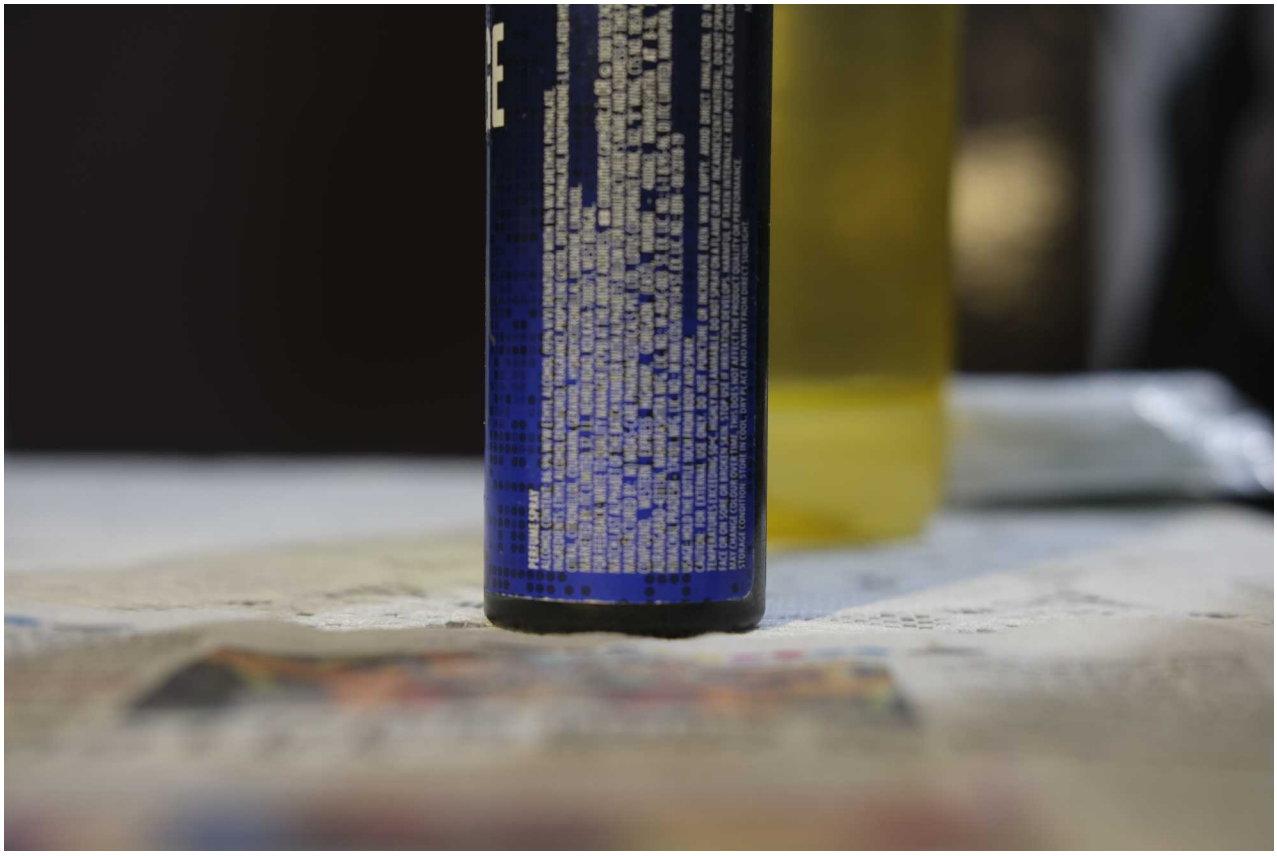
4.3.1 Pupil constricted lighting conditions and role of sunlight in evolution of eyes

Human eyes have evolved[51] from a simple light sensing structure to an absurdly complex and highly specialized organs dedicated to vision. The scope of this article is limited to pointing out the role of sun as the only primal light source influencing and directing evolution of eyes. Connecting the dots further, it can be understood that human eyes too must show selectivity to the intensity and (basically black body) spectrum of sunlight. This basically means the best example for aforementioned pupil constricted lighting environment is the one provided by indirect sunlight. For the purpose of this article, indirect exposure to diffuse sunlight will be defined as the sun not directly in the visual field – whether visible directly (incident) or specular reflection from mirror/water/snow.

4.3.2 Possible Reasoning behind Form Deprivation

It is very well known observation that near-work under dimly lit lighting environments is directly associated with Myopia[52]. There are multiple studies on Myopia being the 'default' behaviour of animal eyes when subjected to form deprivation in dim environments[[53],[54] and [55]]. Form deprivation has also been successfully induced in higher primates (Rhesus Macaques[56]) as well which leads to a simple implication that a similar response must exist for the human eyes as well.

We want to point out that from the standpoint of optics, there is a little difference between uniform blur produced by small amounts of hyperopic or myopic defocus. In other words, there is limited information conveyed by image formation alone without presence of other visual cues. The eye must rely on clues other than image formation alone in order to deduce this information.



These images are taken at 35mm focal length, f/4. Both images depict roughly equal amount of defocus blur in central text. The myopic/hyperopic focal plane can be easily determined by checking the lowermost clear portion of the image.

The above observation alone implies that the mechanism inside the eye responsible for adaptive changes are much more 'sophisticated in nature' than previously described. Form deprivation as a component of myopization also makes evolutionary sense maintaining refractive equilibrium with emmetropization process. Much debate has taken place discussing whether Form deprivation Myopia and lens-induced Myopia are different. However, our arguments instil confidence that the mechanisms are same indeed[57]. Without an opposing myopization process there would be no mechanism inside eyes to correct hyperopia. This explanation is further strengthened from the skewed distribution of refraction towards hyperopia for eyes at birth. Such an adaptive process has to exist because the eye can be born hyperopic or even myopic in some cases and has to adapt accordingly towards emmetropia.

Hypothesis H3: It is predicted that pupil dilated lighting during near-work accelerates myopization by activating FDM pathways[58] combined with processes alleviating accommodative fatigue on the ciliary. Form deprivation Myopia is nothing but an essential aspect of myopization process directly responding to blur signals from defocus (lens-induced myopia).

It hints that possible efforts towards inducing emmetropization could be rendered ineffective/countered by the dominant nature of the FDM pathway under pupil dilated lighting. The activation of FDM pathway might explain why myopic defocus in primate eyes results in further Myopization under pupil dilated lighting instead of the expected emmetropization response as observed in other animal models.

We've previously outlined how accommodative fatigue and under-utilisation of distant vision capability together shifts the refractive equilibrium towards Myopia. In this context, less than adequate lighting levels speeds Myopization rate by parallel activation of the FDM pathway alongside myopization component responding to accommodative fatigue. Lighting levels as a factor happens to be the last remaining puzzle piece for our understanding of physiological factors behind Myopia[59]. This might also explain why highly myopic people experiencing active Myopia progression can show sensitivity to bright lighting environment which normally does not affects emmetropic individuals. Lower light levels also hamper availability of information, increasing chances of developing alignment errors and visual aberrations thereby making Myopization inherently 'inferior' in this regard.

4.4 Refractive Equivalences for Physiologic Myopia

The similarities between an emmetropic eye and an eye compensated for Myopia can be broken into two equivalences. These result from simple equivalence of refraction.

4.4.1 Observational equivalence of far-point

The apparent far-point of a pseudo-emmetropic (best compensated myopic/hyperopic) eye is equivalent to the actual far-point of an emmetropic eye at infinity. This equivalence can't always be extended to the near-point due to the variation in accommodation ability and/or presbyopia.

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 refractive intervention as shown in Figure 2.

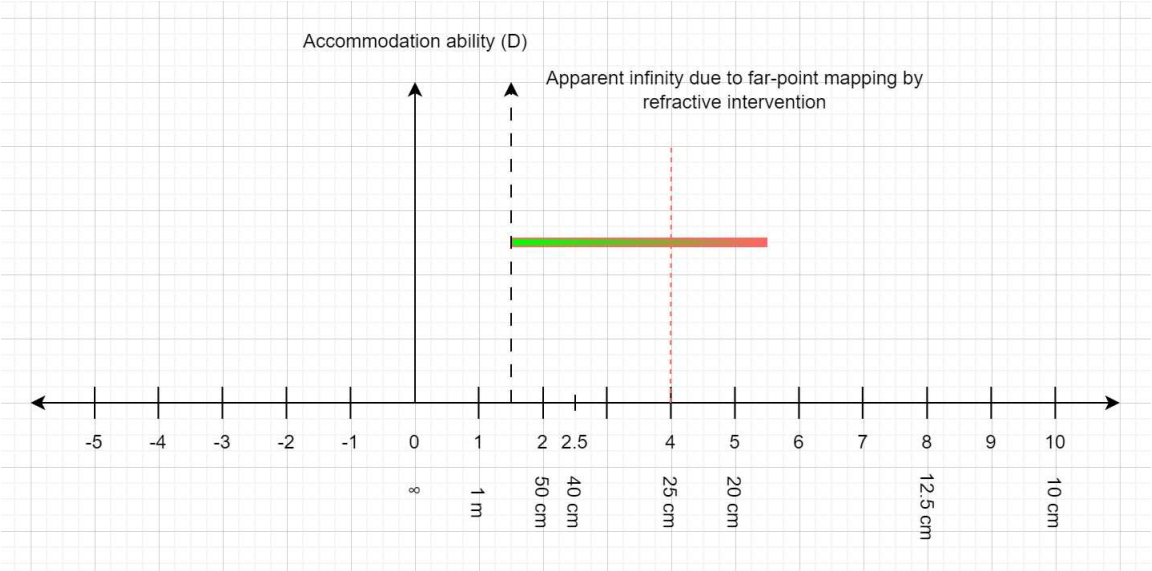


Figure 2 Clamped far-point of a Myopic eye (1.5 D) by refractive intervention

4.4.2 Behavioural/Equilibrium Equivalence of observation range shift

A shift affects the observation range in the same way whether it happens to an emmetropic eye (onset of Myopia) or an already myopic eye (Myopia progression). This equivalence naturally extends for hyperopic shifts in equilibrium also. This basically ensures that any viable method resulting in reduction of Myopia should also result in development of hyperopia in emmetropic eyes.

5. Results/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. It must be noted that the degree of refractive error of the eye is independent from refractive compensation.

Table 1: True Sign of Refractive state compared to required refractive compensation for pseudo-emmetropia

Refractive State	Sign denoting the true degree	Sign of Prescription/Refractive Compensation to achieve

		pseudo-emmetropia
Myopia	+	-
Emmetropia	0 (neither positive nor negative)	0/Plano/not required
Hyperopia	-	+

High Myopia is defined at 5.0 D spherical equivalent or more [WHO]. Other literature define High Myopia starting at 6.0 D spherical equivalent or more. Myopia being mostly axial in nature mainly affects observation range. The position of far point compared to an emmetropic eye ideally indicates the severity of hyperopia/myopia. 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 3. The overlap factor has been taken as the value for threshold Myopia (≥ 0.5 D according to WHO).

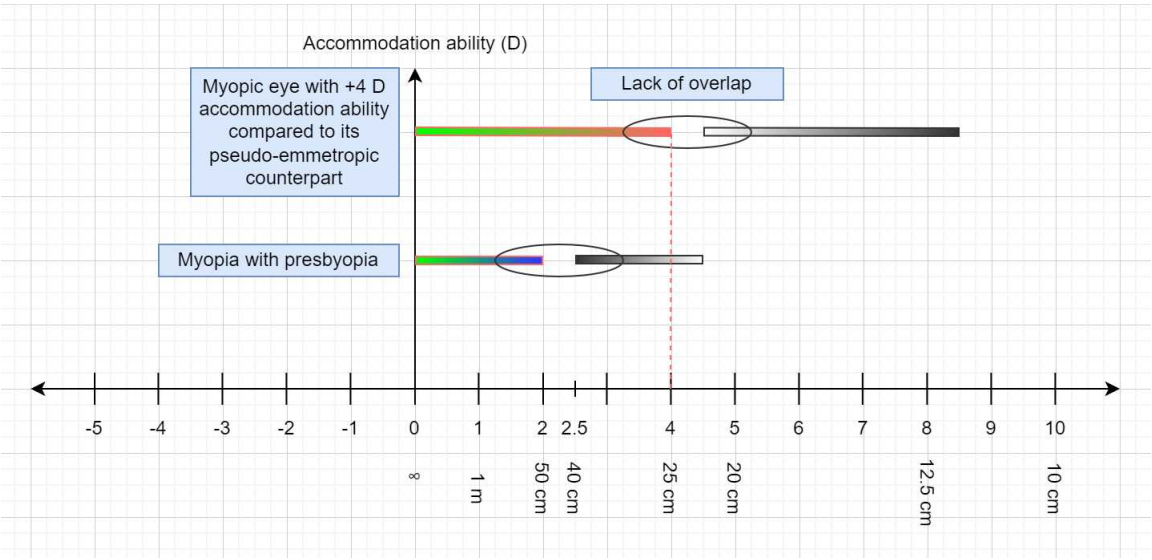


Figure 3 The 'overlap' criteria for determining severity of Myopia. The coloured observation range represents the pseudo-emmetropic observation range after best possible refractive compensation.

The following arguments favour our overlap criteria for severity determination:

1. Encodes the fact 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 intervention 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 turn into 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 presence of astigmatism. This is the primary reason behind avoiding spherical equivalents for this article and treating astigmatism separately.

Severe Myopia is also indicative of 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 proper refractive intervention).

5.2 Changes to Accommodation-convergence reflex from Myopia

Human eyes form a stereoscopic pair for depth perception which necessitates the presence of convergence[60]. 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 4).

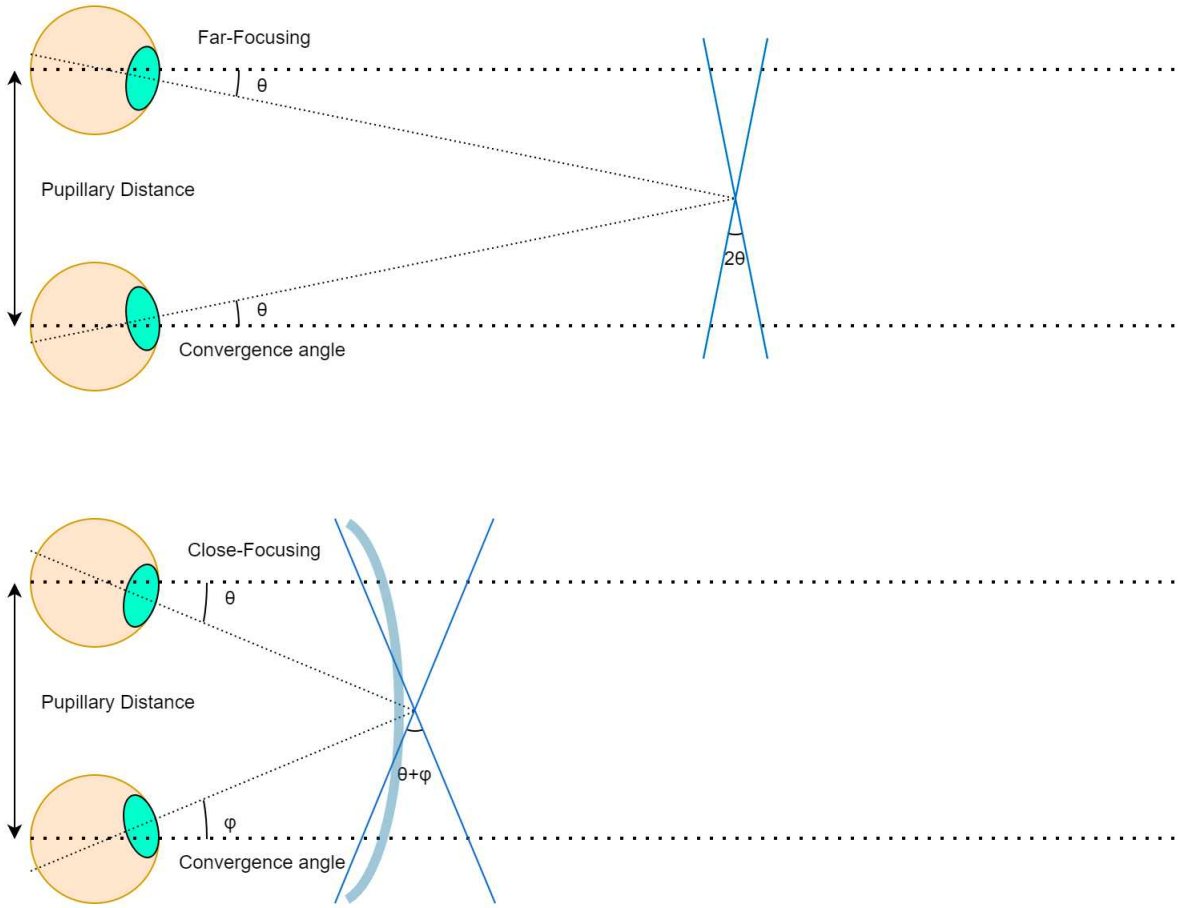


Figure 4 Depiction of convergence with observed distance compared to observing at infinity. Note the increasing angle between the perceived image planes shown in blue as focusing distance gets closer.

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.

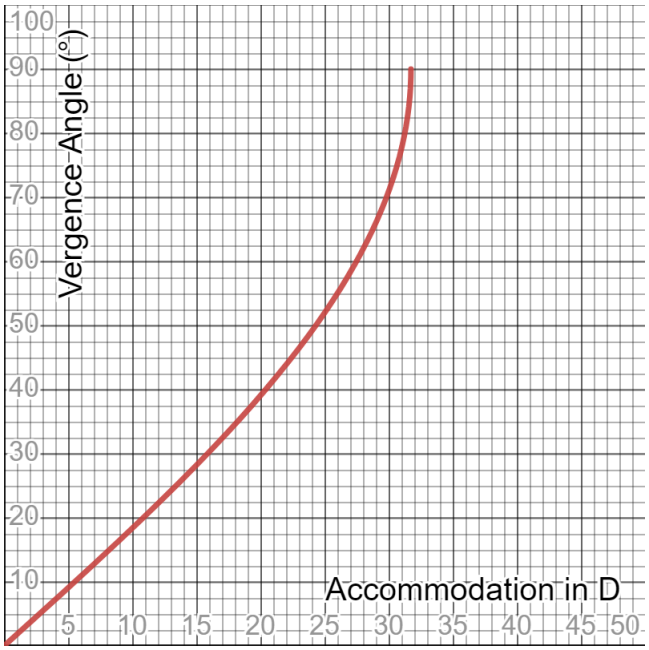


Figure 5 A plot of convergence angle with accommodation (IPD: 63 mm)

As can be seen from Figure 5, the reflex acts in a mostly 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 starts only when convergence 'reaches' distances closer than the far-point. For distances beyond the myopic far-point, eyes remain unaccommodated. This can be termed as introduction of **convergence lag** for Myopia[61]. 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 connection with astigmatism. It predicts presence of baseline levels of astigmatism in population primarily involved with significant near-work. It remains to be properly investigated how this particular form of cylindrical image plane distortion affects ocular biometry. It is possible that fully compensating for this form of astigmatism may result in discomfort and further astigmatism (progression). 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.

5.3 Implications for refractive equilibrium from refractive equivalences

The equivalence outlined in section 4.4.1 basically guarantee the similarity between the refractive equilibrium of a stabilized myopic eye and that of an emmetropic eye. Refractive state is in stable equilibrium because myopization is in equilibrium with emmetropization in both (stabilized myopic and emmetropic eye) predicting that requirements for an emmetropic eye to not experience onset of myopia should be the same for stabilization of Myopia. Myopia progression is nothing but 'onset of Myopia' in a myopic eye. Even in the lack of a widely agreed upon cause for Myopia, these equivalence impose the weaker condition that predicts the cause behind Myopia progression to be the same as onset of Myopia.

It also has a parallel implication that an eye with stabilized Myopia shows behaviour that is closer to an emmetropic eye compared to an eye experiencing active Myopia progression (changing equlibrium).

For shifting of this equilibrium point towards hyperopia, myopic defocus is required because ciliary muscle is relaxed for distant work implying absence of accommodative fatigue on the hyperopic side. Myopic defocus emerges as a necessary but not sufficient[62] requirement for inducing emmetropization. We have already pointed out the role of pupil constricted lighting towards overcoming FDM pathway for emmetropization. It should also offer an explanation so as to why physiologic hyperopic progression unlike Myopia progression is rarely observed[63].

The equivalences alone signify the urgent need to revisit and properly 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 conclusive insights to date.

The breakthrough insights from these two refractive equivalences are summarised below in Table 2:

Table 2: 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 reduction with best possible refractive compensation even after distance work	No observed hyperopia (shifting of far-point beyond infinity) even after (in-focus) distance work
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 myopic/hyperopic eye is as '*valid*' as an emmetropic eye from the standpoint of CAT. These equivalences combined with the lack of specific retinal complications/anomalies inside the eye should serve to distinguish physiologic Myopia from pathologic Myopia. Physiologic myopia is not some disorder or disease. It is consequence of the same ordinary process responsible for maintaining refractive state of all healthy human eyes. This is necessary from the self-consistency of our adaptive framework and the resulting behavioural equivalences.

5.4 Genetics, heredity and physiologic Myopia

According to our theoretical framework, physiologic Myopia is the result of shift in observation range brought on by two opposing processes under dynamic equilibrium responding to temporal integration of visual signals. Any influence of genetics on these processes won't considerably alter the processes themselves – rather the rate at which they can affect the eye and consequently the set-point of equilibrium. This is the primary reason why there can only be genetic susceptibility component for physiologic Myopia unlike the well-established mostly hereditary nature of pathologic Myopia.

The heredity of myopia is frequently described as myopic individuals having more chances of a myopic parent. After accounting for the possibility that myopic children share mostly similar environment with their parents, it becomes unclear how much of a role heredity actually play towards progression of physiologic Myopia. It must also be noted that most of the existing studies on parental Myopia additionally fail to strictly isolate progressive and stabilized myopia[64, 65, 66] 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.

5.5 Proposed mechanism behind physiologic Myopia

Section 4.1 describes how short-term, medium term and long-term processes are together 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 Myopia in section 4.2.

The onset of Myopia has been mainly predicted to result from the ciliary muscle 'tiring' out during threshold near-work (also see pseudomyopia/NITM[67]). This accommodative fatigue on the ciliary introduces imperceptible levels of hyperopic defocus whose further occurence the eyes then try to compensate by becoming myopic in the long term. Doing near-work closer to the focusing limit brings

faster exhaustion of the ciliary muscle. Defocus near work predictably results in superposition of defocus response in addition to extreme accommodation strain.

It additionally implies that eyes can 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 in this article is self-restricted to physiological factors only.

In the absence of 'suitable' interventions, the ciliary body starts developing changes adapting for the accommodative fatigue. 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 strain 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[68]) 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 myopia results in equilibrium being established again. The ciliary body gradually returns 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 5.2. Another component of astigmatism is expected to result from anisotropic changes that the ocular components can undergo during Myopia. The 'recalibration' of the accommodation-convergence reflex as convergence lag mentioned earlier is also predicted to happen alongside myopia.

5.6 Predicted requirements for Emmetropization

If physiologic myopia is indeed a consequence of adaptation, it should be possible to introduce a shift in equilibrium in the opposite direction towards emmetropia. To summarise our findings, section 4.2 covers why accommodative strain from near-work coupled with under-utilisation of distant vision capability should result in progression of Myopia. Section 4.3 outlines why defocus in pupil dilated lighting conditions accelerates Myopization using FDM pathways. Section 4.4 establishes refractive equivalence between behaviour shown by 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.

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 accommodative fatigue causing myopization in the first place. These findings are tabulated in Table 3.

Table 3: Establishing duals of physiological factors required for myopization

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

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[69] utilising reduced 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 pupil constricted lighting lie inside the green oval for a myopic eye shown in Figure 1. We will refer to this as ADV (short for Actual Distance Viewing). The ideal Pupil constricted lighting is taken to be indirect sunlight on a clear sunny day. Because hyperopic adaptation happens under pupil constricted lighting, it should also be slightly faster (Superior) due to the availability of more information.

This hints that commonly observed phenomenon of 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 implies that changes from emmetropization should get somewhat countered by myopization due to 'ordinary work' during the rest of the day. This temporal integration aspect hints at less than ideal real world rate of recovery. The refractive state of an eye undergoing myopia reduction is expected to follow a stair-step function with regular regressions below baseline shown in Figure 6. The time difference between each dip (scale exaggerated for clarity) is the rolling window (can

also be called emmetropization window) over which temporal integration takes place. This rolling window itself is some natural multiple of days. For most eyes, it should vary from 2-4 days.

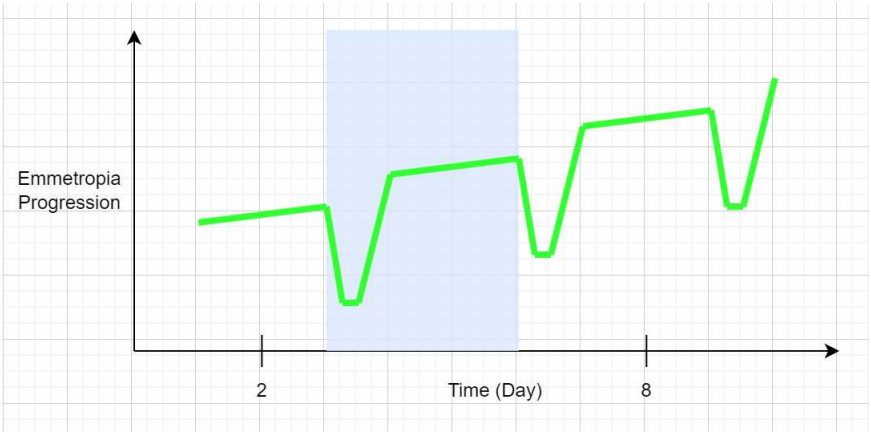


Figure 6: The plot of Refraction vs time

The adaptive nature of the process also implies that the requirements for Myopia reduction must be stricter than that required for myopia stabilization only. This is the 'dual' of observing a population subset with significant near-work habits not becoming Myopic.

5.7 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} for pathologic Myopia[70]. It can be argued on the principles of optics alone that effects of shrinking FoV should resemble 'tunnel vision effect' with highly severe Myopia. This also implies that people managing to make significant Myopia reduction should experience resultant FoV expansion.

5.8 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 outcomes of the 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 extgension, time required for Hyperopic adaptation can be estimated from the data on Myopia

progression[71]. The observed rate of hyperopic adaptation happens to be slightly faster than Myopia progression 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 $\propto$ AL denoting the ratio RD/AL as β.

$$\textit{Lens relation}:$$
$$\frac{1}{s}-\frac{1}{u}=\frac{1}{f}$$
$$\textit{Here, elongated (myopic) RD serves as screen distance } (s)$$
$$\textit{and emmetropic eRD serves as focal length } (f)$$

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

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

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

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

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

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 unchanged. Measuring the long-term rate of AL changes then gives a rough estimate of the time period required for axial changes.

5.9 Strengths and Limitations of CAT

The strengths of CAT lies in proposing an adaptive equilibrium model for Myopia explaining onset/progression and even the to date observed irreducibility. The resulting equivalences succinctly explain why studies on stabilized Myopes have so far been mostly an exercise in futility due to them being equivalent to their emmetropic counterparts. CAT is also the only theory so far describing myopia consistent with the theory of evolution of eyes as a visual organ.

At the same time we want to stress that the simplistic model on which CAT builds upon can't account for difference between peripheral and central components of vision or account for other non-physiological factors that can possibly contribute towards Myopia of the human eye. Because of the way CAT re-defines pathologic Myopia from physiologic Myopia, the theory naturally breaks down for pathologic Myopia due to unpredictable alterations to the underlying adaptive mechanism maintaining refractive equilibrium.

6. Conclusions

This article is an attempt at high level characterization of physiologic Myopia. The framework of CAT put forward in this article might very well be the first such explanation managing to consistently and convincingly explain nearly all clinically relevant aspects of physiologic Myopia including but not limited to its onset, progression and even its seemingly irreducible nature so far in human subjects.

The first and foremost of the many conclusions from CAT is that the vast majority of the observed evidences favour our explanation that physiologic Myopia exhibits behaviour similar to that of a process under active refractive equilibrium.

In other words, emmetropization $\rightleftharpoons$ myopization for eyes experiencing no shift in refractive state with time. One of these two processes has to dominate towards causing a shift in equilibrium. For an eye undergoing active myopia onset/progression, myopization must be dominating over emmetropization. The opposite must be true for reduction in myopia.

This behaviour also reliably establishes that the eye can never be in know of its absolute refractive state. All an eye can determine is relative changes (defocus) basis quality and intensity of image formation on retina and initiate changes according to the visual environment. The theory also firmly establishes adaptive nature of axial elongation and its distinct nature from actual ocular growth that gets completed after puberty.

The theory naturally hints that implementing pupil constricted lighting coupled with myopic defocus is the one and only physically viable long-term solution for physiologic Myopia management. We expect the sheer predictive prowess of CAT to continue with rapid optimisations coupled with near-work interventions for truly effective Myopia management soon.

6.1 Summing up the Continuous Adaptive Theory (CAT)

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

Table 4: Physiological factors requirements for processes dominating refractive equilibrium

Equilibrium shift by the process	Myopization (Onset/Progression of Myopia)	Emmetropization (Myopia reduction)
Visual stimulus 'pulling' the adaptive equilibrium	Near work induced accommodative strain resulting	Myopic defocus under pupil constricted lighting so as to

	in fatigue induced defocus. This is exacerbated in pupil dilated lighting environment.	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 strain. (under-utilisation of near vision capability)
Accelerator Light levels	Pupil dilated utilising FDM pathways	Pupil constricted so as to overcome 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 (inferior)	Corrects aberrations and refractive errors (Superior)
Field of View	Shrinks	Expands
Time Interval	Existing Myopia progression rate	faster than Myopia progression due to extra light information

6.2 The informal Law of physiologic Myopia

Given time and efforts, a person with physiologic Myopia should be able to emmetropize at par or better than their current visual abilities with best possible refractive compensation. 578

This law encapsulates our bold prediction from CAT signifying the error correcting, superior nature of emmetropization. 580

6.3 Key takeaways

The author recognises the tediously slow and time intensive nature (taking months and years just like myopia progression) for myopia reduction outlined in this article. Still, we are firmly convinced of its enormous utility towards preventing Myopia progression and maintaining post-refractive surgery outcomes until faster and better routes are uncovered. We expect that long-term commitment along with habitual and lifestyle interventions are required to for emmetropia - a theoretically simple but practically difficult task.

6.4 Further research

Predicting precise set of requirements that must be satisfied for reducing physiologic Myopia presents a massive unexplored opportunity in front of the scientific community.

1. Optimal degree and form of myopic defocus under pupil constricted lighting that safely maximizes the rate of emmetropization. Further optimisation of lighting environment and distant calibration target requirement for ADV.
2. Whether insights from this article can be used for possible Myopization in Hyperopes towards emmetropia.
3. Experimental studies trying to observe form-deprivation hyperopia under pupil constricted lighting.
4. Further investigation into the role played by mechanistic interaction between iris and ciliary in the context of emmetropization process.
5. Corporate and lawmaker's role towards popularising Myopia prevention guidelines for near work jobs.

7. Appendix: Protocol/Method for observing reduction in myopia towards possible emmetropia

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 resulting in verifiable reduction of Myopia. The following sections describe the implementation details for the same based on 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 the ideal time for exposure to myopic defocus emerges from observation of peaking of AL reduction (termed as saturation from now on) around 50 minute mark[1].

"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 chunks. Myopes willing to maximize benefits should ideally aim for an observation time > their 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, myopia reduction demands managing accommodative strain due to near-work as much as possible. This forms the 'additional requirement' part for reducing myopia instead of only stabilising it (Section 5.6). Accommodative strain 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 mostly 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[72] in the form of 20-20-20 rule is handy in this regard. The second approach refers to mitigations that reduce accommodation. This can be achieved 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 previous section 7.1, we will now elaborate the physical requirements for ADV – our acronym for combining myopic defocus under bright outdoor indirect sunlight inducing emmetropization as outlined under section 5.6.

7.2.1 Duration and regime requirements

Due to the lack of any previous experimental data regarding the time requirement 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.

1 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

7.2.2 Refractive intervention guidelines for Myopic defocus during ADV

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 possible for a 'saturation' criteria for defocus to exist resulting in the eyes hitting a limit beyond a certain threshold.

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

7.2.3 Requirements for distance viewing

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[73] direct sunlight exposure has on the eyes. It is imperative to keep the Sun behind at all times to minimize risk of harmful UV exposure (exposure = intensity×duration).

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 objects in a casual, relaxed manner without squinting, forcing or stressing their eyes in any manner. This should be identical to the way an emmetropic or a refractively compensated (pseudo-emmetropic) person normally observes objects at a distance. The best analogy is like trying to read a distant signboard or resolving fine details presented by a distant structure. Myopes can attempt slow walking, standing, or sitting as per convenience. We expect contrasting patterns in both vertical and horizontal meridians to be useful and implore researches to optimise and explore synthetic distant target patterns for ADV.

Figure 7 Image demonstrating close to ideal calibration target for ADV

An image showing ideal ADV environment satisfying our criteria is shown in Figure 7. 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 comprising 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 very low levels of 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 during hot weather conditions should attempt ADV from a cool and shaded place to combat the sweltering heat outside and vice-versa. Swamp (desert) coolers are effective during summers 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 throughout 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. 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 reduction progresses, this myopic far-point should recede towards ∞ reducing dependence on glasses.

In accordance with our duals established in section 5.6, proper refractive interventions can ensure that the subject's quality of life remains relatively unaffected from the daily requirements of managing Myopia while simultaneously minimizing accommodative strain on the ciliary.

For Myopia management, worn glasses emerge as a clear choice because they are easy to wear and remove in accordance with varying refractive demands during the day; cheaper, reliable, safer for the eyes, and allow 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 full scale prescription during the day (resulting from reduction in refraction) and subtle aversion from near-work. This should result from gradual disruption of myopic feedback loop during 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 options.

The disruption of myopic feedback loop from ADV sessions also means that refractive demands of the eye becomes somewhat complicated. As such situations arise, the signalled comfort of the eyes towards worn prescription should be prioritized. Eyes can usually signal immediate discomfort for both over and too much under-compensation and the same must 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 myopia reduction to continue.

This concept of refractive intervention is an important aspect of myopia management and requires strictly individual implementation because of the varying near-work requirements, their current degree of Myopia and preferences/tolerance to defocus. It is obvious that proper refractive compensation requirements from the standpoint of reducing accommodative strain for a system as dynamic and adaptive as the human eye can not be accomplished using Single Vision Spectacles (SVS). For the ease of understanding, we have summarised these guidelines in the table below.

Table 5: Tentative Refractive compensation guidelines for near-work management

Working distance	Daylight (outdoors on a sunny day)	Evening/Night
For ADV until saturation (not	Without any form of refractive	N/A

applicable for high myopia)	compensation	
Other distance work	Prescription as per comfort preferably with UV protection/Sunglasses	Prescription just shy of full based on eye comfort
Distance work just beyond the myopic far-point	Under-prescription as per comfort	Prescription just shy of full based on eye comfort
Near-work done at a distance closer than the myopic far-point (only possible for below high myopia)	Below high Myopia, people should be 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 best compensated visual acuity to prevent incidents and to comply with applicable laws	

These tentative guidelines are only meant as a starting point for the trial implementation resulting in a slightly more complicated answer for the commonly asked question in myopia – "When should one wear glasses?". It is expected for the eye's refractive demand to change with myopia reduction progress. The evaluation criteria always remains the fastest and safest reduction of Myopia and we fully expect some of these tentative guidelines to fall out of favour or get superseded by further experimental insights.

7.3.1 Avoidance of Blue Light Blocking lenses

Coming to the type of lenses used, we suggest simple/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 myopia reduction progresses.
2. Provides no clinically substantiated protection against Myopization as evident from multiple research attempts into investigating their benefits[74].
3. Nearly every recent computing device with a display already has an inbuilt blue-light reduction/night-comfort feature. [Windows Night Light[75] and Apple Night Shift[76]]. The intended

physical purpose of blue-light glasses is already achieved at the source level for nearly all modern computing devices.

4. Blue light lenses are not a substitute for the utility and eye-protection offered by sunglasses under direct outdoor sunlight.

7.4 The proposed mechanism behind myopia reduction

Section 5.5 already covers our attempts at characterizing how myopization takes place.

This section attempts to describe the mechanism of Myopia reduction based on our observations upon year long implementation of the very same method described in the previous sections. For much lower degree of Myopia, subject's experience should be 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 clarity in 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 body is the first to undergo changes according to H1.

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 pinhole effect or from formation of tear film[77] on the cornea. Besides diurnal variation in vision[78], ADV can sometimes result in transient intervals of blurrier than expected 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 result from increase in focal length of the eye lens. In the case of Myopia, adaptive pull can be said to arise from accommodative strain 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 term overshoot or 'negative accommodation[79]' is more apt. However, the muscle eventually gets tired and can not maintain its 'clear flash' state for long durations. It also explains the commonly reported instances of 'twitching clarity' in myopic people experiencing brief flashes of clear vision transitioning into pupil constricted lighting while not wearing their glasses.

Within weeks, active emmetropization should result in the establishment of a feedback loop opposite to the already described myopic feedback loop – resulting in enhanced sensitivity towards accommodative strain/aversion from near-work. Discouragement from near work serves as a reliable indicator that emmetropization is taking place. For a person experiencing active myopia progression, this happens due to establishment of hyperopic ciliary shift after undoing existing myopic ciliary shift.

After regular ADV sessions spanning over longer time-frames (months), myopes should be able to experience perceptible increase in visual acuity automatically when venturing outside on a sunny day – a telltale indication of hyperopic ciliary shift. Long-term axial changes soon follow to compensate this hyperopic response of the ciliary as long as under-utilisation of near vision continues. Measurable reduction in RD starts happening soon after this stage is reached. This should continue translating into improvements to baseline vision with time until emmetropia is achieved.

Confirmation of observation of hyperopic ciliary shift would cement its bi-directional bridging nature for long-term axial changes along with choroidal thickness changes for both myopic and hyperopic adaptations (Hypothesis H1). This alone should be sufficient to confirm that the predicted[80] *active emmetropization mechanism* is not different from the process described in this article inducing Myopia or Hyperopia in accordance with the imposed visual stimulus. Emmetropization naturally entails ocular re-calibration for distance vision and will result into eventual changes to the eyeball shape in the long-term (months). Some myopes can also report changes felt to the eyeball both during and after ADV sessions.

It is equally important to mention that most of the aforementioned clarity gains after ADV session 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. 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 hyperopic shift and clear flashes), explaining the loss of clarity under pupil dilated lighting. This can be termed as restrictive effect of the dilated pupil for negative accommodation. This mechanistic interaction of the iris with the ciliary should be also associated with Myopization[81].

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 must be willing to devote the (an hour or two) of their daily time towards achieving saturation requirements for ADV besides following near work management guidelines for the rest of the day.

The lack of any prior widespread experimental data means heavy emphasis 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 without any adverse event history and screened for the presence of musculoskeletal disorders. Insights from preliminary trials on non-severe myopics should prove useful towards narrowing down additional precautions for trials on severe myopes.

It is important that all myopes exercise caution during the initial beginning period of the trial, starting with 'less brighter' scenery first and take regular breaks until photosensitivity diminishes within the first few weeks. 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 beginning due to the aforementioned photosensitivity. 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 undue stress.

7.5.2 Safety of ADV:

The only part of our method causing any significant change to the eye results 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 also.

We would also like to point out positive sentiments of vision scientists 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

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Controversies around RLRL treatment:

There are multiple studies promising safety profile and tolerance of eyes towards light therapies with light levels far higher than that of indirect sunlight for Myopia control[82]. 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[83]. Update: However, A recent study reports retinal damage in a 12 year old female after 5 months RLRL LASER exposure[84]. This possibly means that indirect full spectrum sunlight remains the only light source with an excellent safety profile as of now.

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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 compensation. 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 adhered to strictly.

Myopes are expected to use fair judgement and not jeopardise their own and other's lives. Because ADV involves 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.

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

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