

Physiologic statokinetic dissociation is eliminated by equating static and kinetic perimetry testing procedures

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In the present study, we measured the extent of statokinetic dissociation (SKD) in normal observers and then equated the psychophysical tasks into a two-interval forced choice (2IFC) procedure. In Experiment 1, we used the Humphrey visual field analyzer in static perimetry and automated kinetic perimetry modes to measure contrast sensitivity thresholds and the Goldmann manual kinetic perimeter to measure isopters. This was carried out using a Goldmann size II target. Goldmann kinetic perimetry was performed manually with both inward (peripheral to center) and outward (center to periphery) directions of movement to deduce an “average” isopter. This revealed the presence of SKD when superimposed upon the map of static contrast threshold results. There was no evidence of any contribution of examiner technique or instrument-specific differences to SKD. In Experiment 2, we determined the psychometric curves plotting proportion seen as a function of stimulus eccentricity with static and kinetic stimuli with a 2IFC procedure and method of constant stimuli. In an additional experiment, we also showed that subjects were able to reliably discriminate whether a stimulus was static, moving inward, or moving outward, and hence, comparisons could be made between static and kinetic perimetry tasks. Overall, by making the task objective and reducing criterion bias, eccentricity thresholds were equated across static and

kinetic perimetry methods; hence, no evidence of SKD was seen. We suggest SKD is inherent to the differences in methodology of threshold measurement in conventional static and kinetic perimetry and individual criterion bias.

Introduction

A common method of assessing visual function in both experimental and clinical settings is to measure sensitivity to luminance contrast. Indeed, the detection and representation of the spatial layout of the visual scene is fundamentally defined by variations in contrast across the visual field (Marr, 1982). Contrast sensitivity in the clinical setting is typically assessed using perimetric technologies that quantify the ability of the observer to detect a spot of light presented to different locations across the visual field. This feature of perimetric testing is advantageous because it can provide an indication of both local and global patterns of visual loss, such as those occurring in ocular or neurological disease (Jampel et al., 2011; Traquair, 1939; Weinreb & Kaufman, 2009). However, subjective responses might be problematic as criterion biases

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affect the ability of the observer to report the stimulus (Khuu & Kalloniatis, 2015a; Phu, Kalloniatis, & Khuu, 2016).

The hill of vision (HoV) is the topographical representation of sensitivity across the visual field. It can be assessed with a stationary (static perimetry) or a moving target (kinetic perimetry), and in practice, the clinical standard instruments for these are standard automated perimetry (SAP) and Goldmann manual perimetry, respectively. Although SAP instruments utilize proprietary hardware and software, the thresholds obtained using such instruments are a common way of characterizing the HoV in the clinic and the laboratory. However, there are significant differences between how static and kinetic techniques assess the HoV. In SAP, a spot of light of fixed size (Goldmann size III) is briefly presented (100–200 ms) at a number of fixed locations in the visual field (Heijl, Lindgren, & Olsson, 1987; Katz, Quigley, & Sommer, 1995; Khuu & Kalloniatis, 2015b). The contrast required to detect the target (provided as an attenuation measurement of incident light in dB) is measured using a “thresholding technique,” and in SAP, staircase methods in combination with adaptive algorithms modulate the physical contrast of the target between presentations based on the observer’s subjective response (McKendrick, 2005). Hence, the shape of the HoV can be interpolated in the dB change from central to peripheral locations (Khuu & Kalloniatis, 2015b).

On the other hand, kinetic perimetry techniques use a target of fixed size and contrast that is moved (automatically or manually) across the visual field until the observer subjectively reports that the stimulus becomes perceptually visible or disappears from view (Niederhauser & Mojon, 2002). Repeating this procedure along different angular meridians produces a two-dimensional contour or isopter, which represents spatial locations at which contrast sensitivity is equal (“isocontrast”; Niederhauser & Mojon, 2002; Sloan, 1961).

Although both static and kinetic perimetry purportedly assess the HoV, discordance in contrast sensitivity measurements between these two procedures has been reported. This has been referred to as “statokinetic dissociation” (SKD; Gandolfo, 1996; Pineles et al., 2006; Riddoch, 1917; Rowe, Noonan, & Manuel, 2013; Schiller et al., 2006; Zappia, Enoch, Stamper, Winkelmann, & Gay, 1971). SKD was first described by Riddoch in 1917 (hence, Riddoch’s syndrome), who noted that patients with occipital lobe lesions were able to detect an object moving in the blind field but were unable to detect a static target. Although the neural specificity of damage was not exactly reported, Riddoch’s syndrome shares similarities with “blindsight,” in which moving objects in the blind visual field (from damage to the primary visual cortex)

are detected often without visual awareness, i.e., anosagnosia (Zeki & Ffytche, 1998). The detection of a moving stimulus in the blind field is thought to be mediated by preserved connections from a normal retina to prestriate areas, such as the superior colliculus, which feed to motion-selective cortical areas, such as the middle temporal area, bypassing damaged areas responsible for the detection of contrast and retinotopic coding, such as the primary visual cortex. However, this explanation for Riddoch’s syndrome and blindsight is debatable, and a number of alternative hypotheses have been proposed (Cowey, 2010).

SKD has also been reported in normal observers, termed *physiologic SKD* (Hudson & Wild, 1992; Osako, Osako, Hashimoto, & Okano, 1997; Safran & Glaser, 1980) as well as in those with visual loss arising from retinal or anterior visual pathway disease (rather than exclusively arising from higher cortical lesions; Casson, Osako, Johnson, & Hwang, 1991; Charlier, Defoort, Rouland, & Hache, 1989; Finkelstein & Johnson, 1989; Gandolfo, Rossi, Ermini, & Zinigran, 1995; Safran & Glaser, 1980; Tsutsui, Ichihashi, & Kimura, 1984; Wedermeyer, Johnson, & Keltner, 1989; Yabuki, Sakai, Suzumura, Endo, & Matsuo, 1989; Zappia et al., 1971). In normal observers, physiologic SKD has been defined as discordance between the position of the kinetic isopter of a fixed contrast stimulus found using a one-way method of limits (MoL) with the spatial position of a target when its threshold is measured using static perimetry, which has been taken to indicate greater relative sensitivity to a kinetic stimulus (Hudson & Wild, 1992; Osako et al., 1997). Although both Riddoch’s syndrome and physiologic SKD are hypothesized to reflect methodological differences between static and kinetic procedures, local adaptation and stimulus habituation due to repeated presentations at the same location in static perimetry when using custom test paradigms examining only a few test locations or spatial summation with a moving target (Hudson & Wild, 1992; Osako et al., 1997), differing neural mechanisms behind the detection of static and motion stimuli have also been suggested (Safran & Glaser, 1980).

In the present study, we consider the possibility that it is the differences in the methodological and psychophysical procedures employed to measure contrast sensitivity in static and kinetic perimetry that might contribute to physiologic SKD, i.e., that static and kinetic procedures simply estimate different points on a psychometric curve relating contrast detection with the spatial location of the stimulus (Hudson & Wild, 1992). In kinetic perimetry, for a stimulus of fixed size the proportion of times detected progressively increases, following an “ogive” function as it is presented nearer to central vision with its isopter limits delineated subjectively. On the other hand, for static

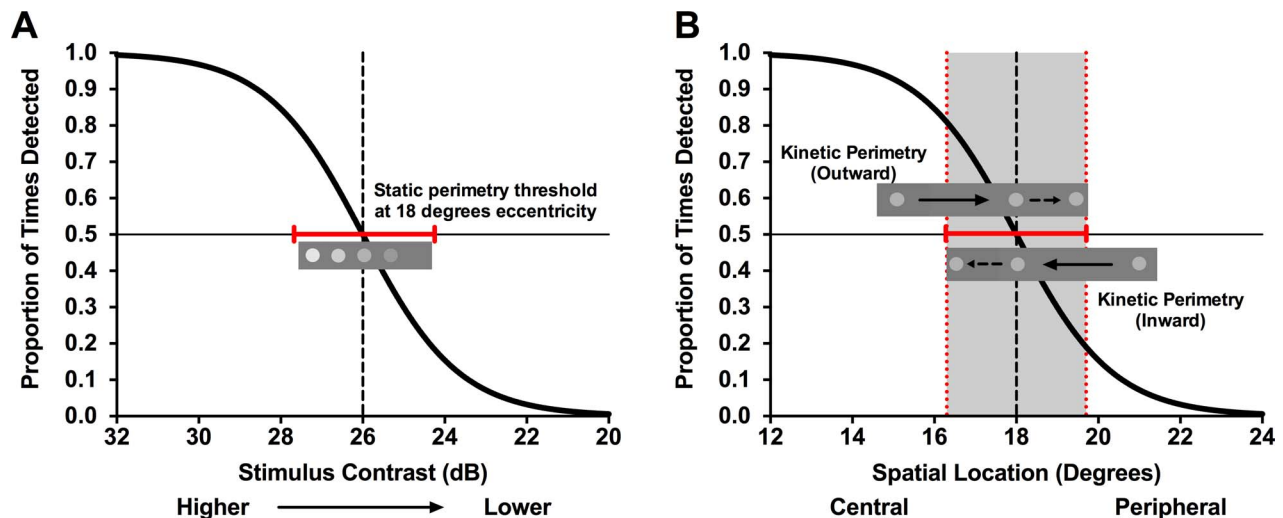


Figure 1. An idealized schematic showing ogive functions for static and kinetic perimetry tasks. (A) A contrast sensitivity threshold is obtained using a static stimulus at a nominal eccentric location (18° eccentricity) in the visual field. The stimulus contrast is varied systematically (depicted by circles of varying levels of gray), honing into a contrast threshold denoted by the dashed vertical line. The red horizontal bar indicates variability in static threshold estimation. (B) A stimulus of fixed contrast (e.g., the contrast threshold obtained from panel A) is moved from a nonseeing part of the visual field (peripheral) to seeing (central), i.e., inward, until the observer indicates that it is seen and, conversely, from seeing to nonseeing (outward). The idealized point of threshold detection should correspond to the 0.5 proportion seen, i.e., correlating with the location of the isocontrast static threshold (18°). However, due to the variability of the kinetic task, this may in reality be at any location bounded by the red dotted lines (the isocontrast region, shaded in the same representative gray of the circles' contrast level), which represent the inner and outer isopter limits for inward and outward moving targets, respectively. The black dashed arrows indicate overshoot of the estimated isopter limits.

perimetry, the contrast of the stimulus is modulated until it is just detectable, which coincides with the 50% correct judgment point at a particular spatial location. The more subjective nature of the kinetic perimetry task and the fact that because it does not directly estimate the contrast threshold (by changing the contrast of the stimulus) means the isopter location *is not restricted* to the point at which the stimulus is just detectable, whereby stimulus uncertainty is greatest (i.e., 50% correct judgment at the static threshold point), but rather at a spatial location at which stimulus uncertainty is reduced. This is therefore dependent upon a subject's individual response criteria. Iopter locations may also be affected by factors such as operator skill, reaction time, and stimulus speed.

To test the hypothesis that methodological differences might contribute to the extent of physiologic SKD, we conducted two separate studies in which the detectability of static and kinetic stimuli were measured and compared. In Experiment 1, we measured isopter locations using a two-way MoL, using both inward- and outward-moving stimuli. These procedures identified the location of inner and outer isopters and the "isocontrast" area enclosed by the isopters. Although contrast sensitivity change across the HoV does not occur in a stepwise fashion, we defined the isocontrast region in the present study to indicate the boundaries at which an observer reports perception of a kinetic target

of fixed size and luminance. We predicted that these isopters signify the spatial region in which the stimulus presumably transitions from being visible to invisible as a function of spatial location (Figure 1). We also determined at which point within the isocontrast region lies the spatial point with the same static contrast sensitivity threshold, hypothesizing that individual variation might be the true physiologic SKD.

In Experiment 2, we directly quantified the detectability of the kinetic stimulus by presenting it to fixed locations within the isocontrast region at smaller eccentricity steps. Here, method of constant stimuli (MoCS) with a two-interval forced choice (2IFC) procedure was used to quantify the detectability of fixed-contrast kinetic and static stimuli at different spatial locations in the form of a psychometric curve in a more objective manner. We predicted that the detectability of the target should gradually change with stimulus location as in Figure 1. If physiologic SKD were due to subjective differences in measuring static and kinetic contrast sensitivity, then equating the testing conditions and removing criterion dependency would mean that both static and kinetic psychometric functions would be the same. On the other hand, if physiologic SKD is representative of an actual disparity between detection of static and kinetic stimuli, then the psychometric function will have its point of subjective

equivalence shifted leftward or rightward, indicating a bias in contrast sensitivity in certain directions.

Experiment 1: Comparison between static and kinetic contrast thresholds using clinical perimetry

The purpose of Experiment 1 was to quantify the extent of SKD in normal observers by directly determining the concordance in spatial location of the contrast threshold point quantified using static perimetry and the kinetic isopter location. We used the Goldmann and the Humphrey visual field analyzer (HFA) perimeters. Our reason for using proprietary hardware is to ensure direct comparison and relevance to previous studies investigating SKD in clinical and laboratory settings, which have primarily used these devices (Hudson & Wild, 1992; Kalloniatis & Khuu, 2016; Khuu & Kalloniatis, 2015a, 2015b; Phu et al., 2016; Schiller et al., 2006; Wong & Sharpe, 2000).

These measurements allowed us to measure the SKD and, for the first time, define the spatial extent of isocontrast area as previous studies have only measured one isopter moving in one direction (typically from unseen to seen; Hudson & Wild, 1992; Wong & Sharpe, 2000). The isocontrast region may therefore provide a snapshot of the psychometric function where the perception of a fixed contrast target perceptually transitions from being visible to invisible. This also allows the determination of the extent to which the kinetic isopter location coincides with the static threshold point (i.e., when the static threshold is equal to the contrast of the kinetic target; Figure 1).

Methods

Observers

Seven healthy observers (four males and three females, age 20–56 years) participated in the study. Two were authors on the study (NA-S, MK), and all other observers were naïve to the aims of the study. All had normal or corrected-to-normal visual acuity (refractive errors were within ± 6.00 DS and ± 3.00 DC), normal ophthalmic examination, and normal visual fields. Observers gave their informed consent prior to participation. Ethics approval was given by the relevant University of New South Wales Ethics Committee, and the experiment followed the tenets of the Declaration of Helsinki.

Stimulus and procedures

Static visual fields were measured using the HFA 30-2 test pattern with the full threshold procedure. The Goldmann size II target was used for all testing as isopters produced in kinetic perimetry with this size are mostly contained within the central 30° and thus coincide with the test region of the 30-2 test pattern (Sloan, 1961). In addition to the 77 points associated with the 30-2 test pattern, the “custom test” function of the HFA was utilized to add a number of points outside of this test region when a Goldmann size II target was used to further test peripheral asymmetric isopters falling outside of the central 30° (Figure 2). In total, 105 points were measured. The full threshold paradigm was used as it is the only thresholding algorithm on the HFA that can be used with a size II stimulus. Thresholds were measured at least three times for each observer and then geometrically averaged to obtain an estimate of the contrast detection threshold at each location. Fluctuations were engaged, and so some locations had more than three thresholds. Testing was performed with one eye with natural pupils (the other eye was patched).

Data was collected over a number of testing sessions to reduce the effects of fatigue. For clarity, all data were converted to right-eye orientation. Refractive correction was provided using the HFA trial frame and appropriate refractive and presbyopic correction as calculated by the instrument. No observer’s fixation losses, false positives, or false negatives exceeded 15%.

Kinetic perimetry

The Goldmann perimeter was used to measure kinetic perimetry isopters, using Goldmann test size II (0.23° diameter) with the contrast filter set to 1b. Because the Goldmann perimeter and HFA have different luminance ranges, the output dB values from these instruments are not directly comparable. To overcome this issue, the equivalent dB contrast value of the kinetic stimulus translated to the HFA was determined. This was achieved by measuring the luminance of the target and its background on the Goldmann device using a photometer (Pritchard Photo Research PR-880), deriving the Weber fraction of the stimulus. This procedure was repeated on the HFA for a range of test dB values, and the Weber values from these devices compared. Accordingly, the filter used on the Goldmann perimeter for kinetic testing in the present study was approximately equal to 24 dB for size II on the HFA.

The target stimulus was manually moved across the visual field by an experienced operator at a speed of approximately 3° per second. The speed of the stimulus

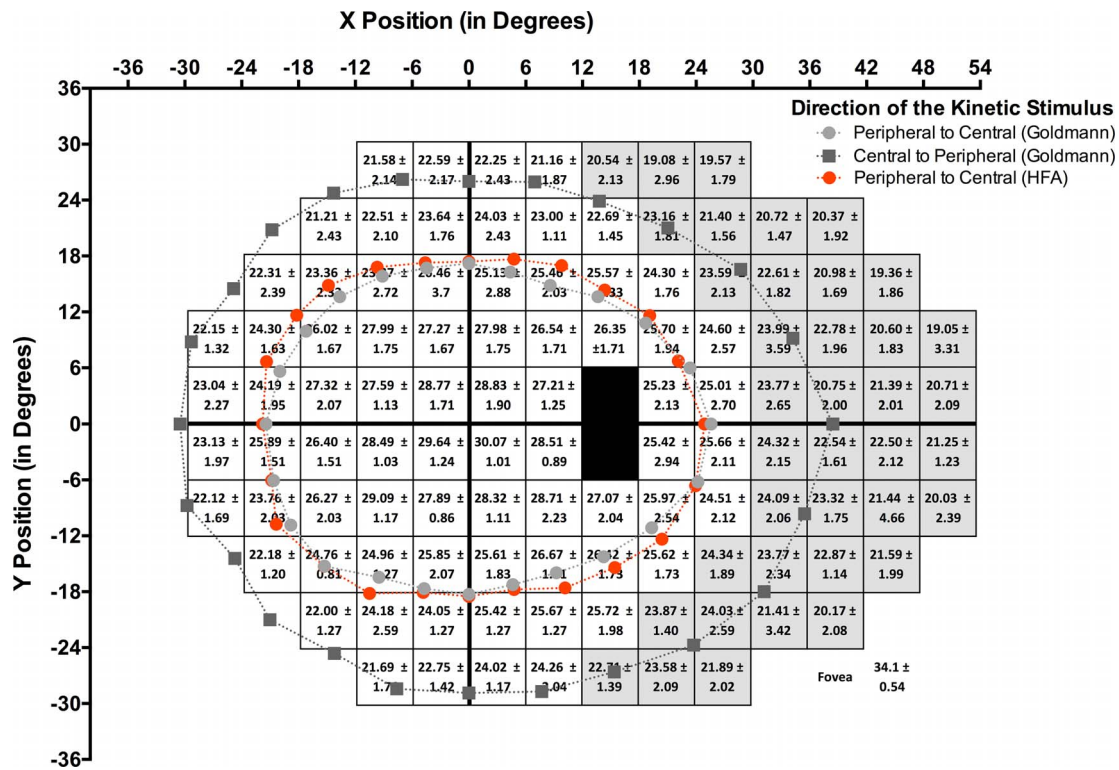


Figure 2. Average isopters superimposed upon the spatial map showing static contrast thresholds (geometrically averaged dB \pm 95% confidence limits) from seven observers for the 30-2 and custom test patterns. The gray symbols indicate isopters obtained using Goldmann manual kinetic perimetry (Goldmann size II, 24 dB) with squares representing the isopter from the outward direction of stimulus movement and circles representing the inward direction of movement. The red symbols indicate the isopter (inward) obtained from the HFA kinetic perimetry mode.

was calculated retrospectively through video recordings of the moving stimulus during testing. Kinetic testing was undertaken along 24 different spatial meridians (at 15° steps) and repeated twice for peripheral to central (inward) and central to peripheral (outward) directions of movement, obtaining an average location for each. The different meridians and directions of movement were presented in random order.

To further establish the reliability of manual operation when using the Goldmann perimeter, the manual measurements (for all seven observers) were compared with those obtained with the automatic kinetic perimetry procedure found on the HFA set to the same stimulus parameters. The concordance between manual and automatic procedures are shown in Figure 2 for one motion direction in which the stimulus was moved from a peripheral location to the center of the instrument.

Statistical analysis

Static thresholds were reported in a schematic displaying the 105 test locations of the combined 30-2 and custom test patterns. Kinetic isopter locations were

converted from polar coordinates to Cartesian coordinates and were superimposed upon the spatial map of static thresholds for comparison. For clarity, error bars were not shown in the superimposed figure, but the standard deviation was on average approximately 2°. Due to differences in instrument luminance parameters and testing grid arrangement, the static threshold locations and isopter locations could not be directly compared (see Experiment 2, which overcomes this limitation); instead, a global comparison is made based on the superimposed spatial arrangement. Within kinetic test results, the effects of stimulus size, meridian angle, motion direction, and technique were compared using ANOVA.

Results and discussion

Averaged observer data for kinetic isopters and static thresholds are shown in Figure 2. Although age has been shown to affect contrast sensitivity (Heijl et al., 1987), the age range of participants was too small for age to greatly impact the results and was not used to correct the thresholds.

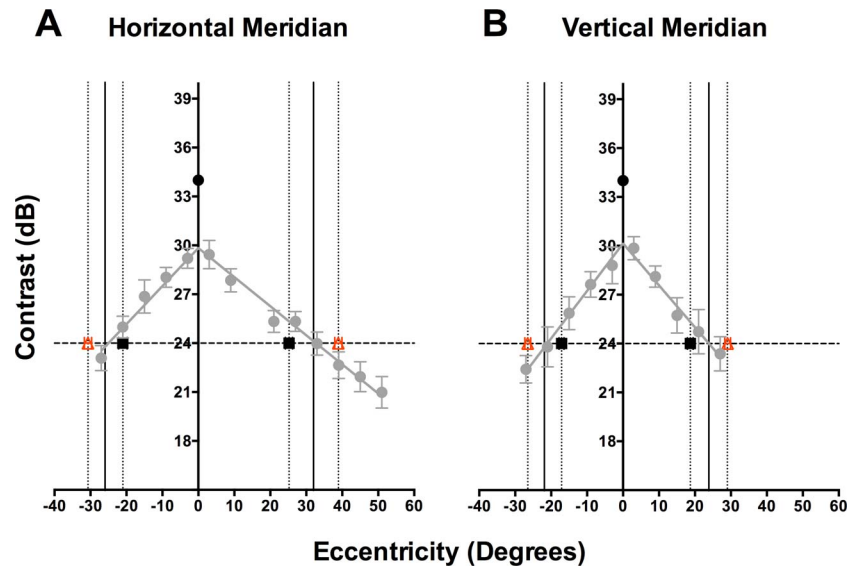


Figure 3. Geometrically averaged static contrast thresholds (gray circles) along the horizontal (A) and vertical (B) meridian are plotted as a function of the eccentric location of the target. The foveal value is represented by the black circle and is not continuous with the foveal point. Additionally, in these figures the spatial locations of the inner (black squares) and outer (red triangles) isopter locations for a particular meridian are shown. By inspection, it is apparent that the region bounded by these locations (vertical dashed lines) is approximately 8° – 12° . Error bars signify one *SEM*. The slopes of the best fit functions ($R^2 = 0.98$) were -0.255 , -0.171 , -0.277 , and -0.272 for nasal, temporal, superior, and inferior, respectively.

Isopter positions for both motion directions were dependent on the meridian. The three most horizontal axes (0° – 180° , 15° – 345° , 30° – 330°) revealed asymmetries in position such that the temporal location of the isopter was significantly displaced away (from central vision) compared with the nasal isopter location for both for both inner, $F(1, 36) = 17.29$, $p = 0.0002$, and outer, $F(1, 36) = 7.493$, $p = 0.010$, isopters (Figure 2). As expected, isopters produced with a target moving inward toward the center of the instrument are smaller than those produced when the target moves from the center outward to the periphery. The average separation between inner and outer isopters was approximately 8° – 12° although this showed a degree of variability depending on the meridian angle.

Two-way ANOVA showed that the kinetic inward isopters obtained manually with the Goldmann perimeter (gray circles) were not significantly different from the isopters obtained using the HFA (red circles), $F(1, 288) = 3.20$, $p = 0.078$. A main effect of meridian angle was observed, $F(23, 288) = 3.29$, $p < 0.0001$, indicating that the isopters were also asymmetric, extending farther in the temporal direction. No interaction between techniques was observed, $F(23, 288) = 0.963$, $p = 0.511$, which showed that isopter shape measured using manual and automatic techniques were the same. Hence, these findings show that manual measurements of inner isopter locations with the Goldmann perimeter were no different from controlled automatic procedures using the HFA, which

minimizes the possibility that experimenter error contributed to the manual estimation of isopters.

For static perimetry, contrast thresholds decreased with retinal eccentricity. To provide an indication of this effect, we report the contrast thresholds along the two cardinal vertical and horizontal axes (see Figure 3A, B). A one-way ANOVA demonstrated that contrast thresholds (converted to linear scale by logging dB values) significantly decreased with retinal eccentricity in both directions for both horizontal, $F(12, 161) = 19.62$, $p < 0.0001$, and vertical, $F(9, 130) = 22.86$, $p < 0.0001$, meridians. To provide an indication of the magnitude of change in static contrast sensitivity, a two-line segment was fitted to data (average $R^2 = 0.98$) and the best fit functions are shown as gray lines in Figure 3. There was asymmetry in the change in contrast sensitivity between nasal and temporal fields (as indicated by the best fit line slopes: nasal -0.255 ± 0.018 and temporal -0.171 ± 0.008) along the horizontal meridian but not along the vertical meridian (superior -0.277 ± 0.014 , inferior -0.272 ± 0.022), consistent with the work of Khuu and Kalloniatis (2015b) and Phu et al. (2016, ARVO E-Abstract 4744).

Figure 3A and B also show the inner and outer isopter locations (triangles and squares, respectively) that delineate the isocontrast area (demarcated by the vertical dotted lines) for both vertical and horizontal axes; the center of the isocontrast area along nasal and temporal locations is indicated by the solid vertical lines. A prediction is that the spatial location at which static thresholds are equal to 24 dB (the intensity of the

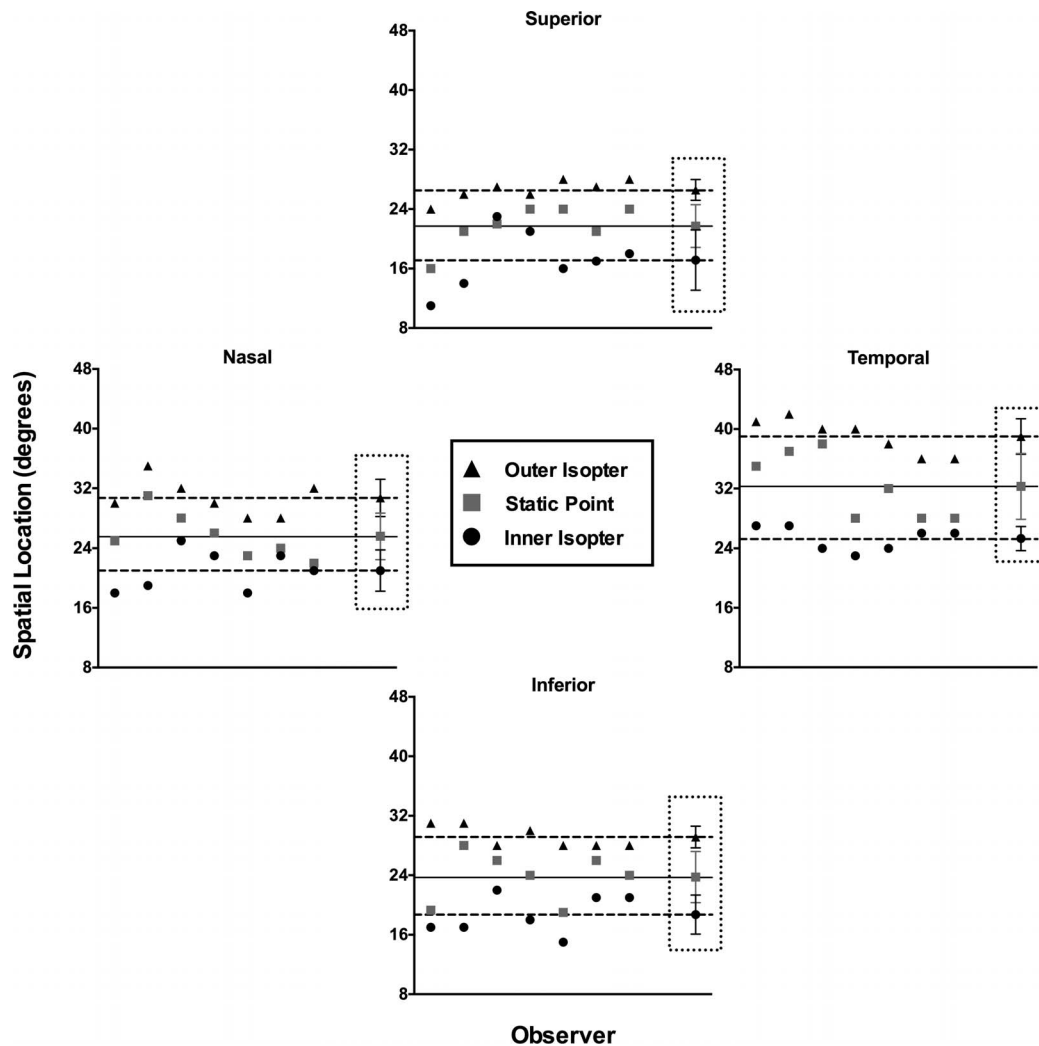


Figure 4. Spatial location of the inner (black triangles) and outer (black circles) isopters and the extrapolated location of the static spatial location at which the contrast threshold is the same (24 dB) are plotted for each individual observer at each meridian. Average observer data is shown on the far right of each graph enclosed in a dotted box. Error bars signify 1 *SD*. The upper and lower dashed lines indicate the average inner and outer isopter locations, and the solid line in between indicates the average static isocontrast spatial location.

stimulus used in the kinetic phase) might lie within the isocontrast region (horizontal dotted line). Note that the spatial location at which the static contrast threshold is equal to 24 dB is derived from the line of best fit as the coarse sampling of the 30-2 grid prevented us from deriving this point directly from the data. Figure 3A and B show that such a location intersects the interval of the isocontrast region at its approximate middle location, indicating that, on average, there is some degree of symmetry between inner and outer disparate isopter positions.

Consistent with the average data, the reported inner and outer isopter locations are equidistant about the static threshold point. However, the subjective nature of kinetic perimetry might result in differences within and between observers in the reported isopter locations at different meridians. Thus, the static threshold location

with the same contrast sensitivity (24 dB) was also extrapolated and compared with inner and outer isopter locations for each individual observer (Figure 4).

There was variability in the location of individual inner and outer isopter locations relative to the static threshold point (Figure 4). A two-way ANOVA showed main effects of meridian (superior, inferior, nasal, or temporal), $F(3, 72) = 51.37$, $p < 0.0001$, and method (inward, outward, or static presentation), $F(2, 72) = 99.55$, $p < 0.0001$, with no significant interaction effects, $F(6, 72) = 0.8373$, $p = 0.5452$. Tukey's post hoc analysis showed significant differences when comparing the methods (inner isopter, outer isopter, and static presentation) in a pair-wise fashion (all $ps < 0.05$) for the different locations; however, there was no evidence of a systematic bias in direction or evidence of intraobserver consistency across the different meridians

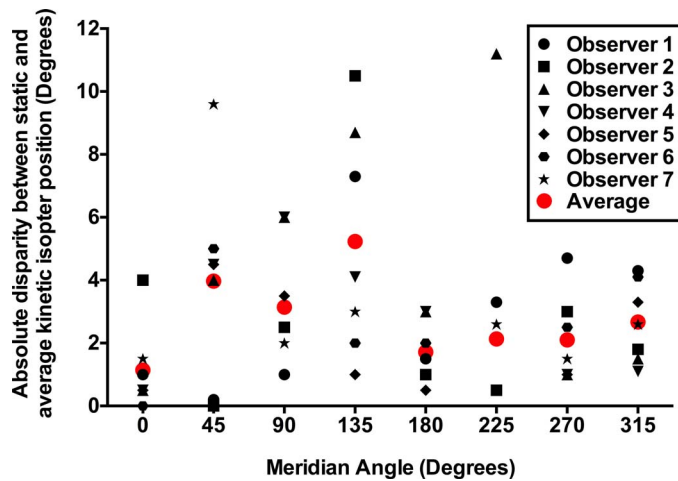


Figure 5. Absolute disparity in the position of average kinetic isopter and isocontrast static threshold locations, which were extrapolated using the same best fit method of adjacent static thresholds as described for Figure 4 (in degrees) plotted as a function of meridian angle (in degrees). Each observer's magnitude of disparity is shown in different black symbols, and the average of all observers ($n = 7$) is shown by the red circles. There were three observers for which the static position could not be reliably estimated for the 225° meridian.

(Figure 4). As inner and outer isopter limits are, in isolation, one-way MoL methods, we averaged the two to obtain an “average” isopter—the product of the two-way MoL methodology—and compared this with the isocontrast static threshold location with the difference being what we now define as *physiologic* SKD (Figure 5).

There was significant individual variation, both within the same observer and for each meridian (Figure 5). On average, there was a disparity of $2.8^\circ (\pm 1.3^\circ)$ across all meridians and all observers. All individual meridians had mean disparities significantly different from 0° (one-sample t test: $p < 0.05$), except at 0° and 225° , which had mean disparities of $1.1^\circ \pm 1.3^\circ$ and $4.4^\circ \pm 4.7^\circ$, respectively, that did not reach statistical significance in their difference from 0° ($p = 0.0656$ and $p = 0.1571$, respectively). The Kruskal-Wallis test showed no significant difference between the magnitudes of SKD between the meridians, $H(8) = 11.17$, $p = 0.0923$. Therefore, we argue that the variability associated with individual responses is perhaps borne by the subjectivity of kinetic perimetry and criterion bias. Significantly, the lack of consistency within observers highlights an obvious limitation with current kinetic perimetry procedures in estimating the boundaries of vision.

We reason that the isopter location does not coincide with the point at which the stimulus is just detectable (i.e., the threshold point at which uncertainty is still high), but represents a spatial point at which the

stimulus is supra- or subthreshold (thus, with relatively lower uncertainty) as depicted in Figure 1. In Experiment 1, we confirmed different locations for inner and outer isopter limits delineating the isocontrast region; however, they were not necessarily symmetrical about the isocontrast static threshold location. Instead, it was likely that their position was dependent upon individual criterion bias.

The results also confirm previously demonstrated asymmetries in contrast sensitivity and isopter locations around the HoV (Heijl et al., 1987; Katz & Sommer, 1986; Khuu & Kalloniatis, 2015b; Niederhauser & Mojon, 2002). Previous studies have suggested that automated kinetic perimetry may be more reliable, repeatable, and efficient in comparison to manual kinetic perimetry (Johnson, Keltner, & Lewis, 1987; Nowomiejska et al., 2005; Ramirez, Chaya, Gordon, & Giaconi, 2008; Schiller, Paetzold, Vonthein, & Schiefer, 2002). Interestingly, we found no significant difference between manual and automated methods of kinetic perimetry in our cohort.

Although on average the intersection of the static test location of equivalent contrast approximately bisected the isocontrast region, there was significant *individual* physiological SKD, which we defined as the disparity between average isopter and the isocontrast static threshold location not solely due to a methodological issue of a one-way MoL. Based on these results, there were no apparent clinically significant meridian-dependent effects, and it is therefore likely that the application of individual criterion bias leads to small differences between kinetic isopter location and isocontrast static threshold location, i.e., physiologic SKD.

Experiment 2: Objective measurement of static and kinetic contrast detection thresholds

In Experiment 2, we sought to determine the concordance of static and kinetic thresholds objectively instead of relying upon an observer's subjective response, using MoCS in conjunction with a 2IFC procedure. This equates static and kinetic procedures, allowing for comparisons between their resultant psychometric functions. Thus, it is possible to determine whether the psychometric curves obtained from static and kinetic stimuli are comparable or indeed if a SKD effect exists that cannot be accounted for by methodological differences. Using a computer-based system, the psychometric curve can be accurately derived by sampling more points within the isocontrast area rather than being limited to the 6° spacing interval

inherent to the HFA 30-2 paradigm. By adopting a 2IFC procedure, subjective bias is minimized (Geisheider, 1997) as the observer is not required to directly indicate the presence or absence of the stimulus but rather to qualify his or her judgment by indicating the interval in which the stimulus is present. The use of a fixed stimulus presentation (200 ms) prevents the observer from directly controlling the duration of the stimulus as with kinetic perimetry, thereby eliminating factors such as speed and reaction time.

We predicted that, if the visual system is indeed preferentially sensitive to moving stimuli, the psychometric curves for detecting a kinetic stimulus would be shifted in the motion direction relative to the static psychometric curve, confirming true physiologic SKD. However, if psychometric curves for both static and kinetic were identical, this would suggest that the originally reported SKD might stem from methodological differences in how they are measured.

Observers

Six healthy observers (three males and three females, age 20–57) participated in this experiment. Two (JP and MK) were authors on the study. The same inclusion and exclusion criteria as per Experiment 1 were utilized. Ethics approval was given by the relevant University of New South Wales Ethics committee, and the experiment followed the tenets of the Declaration of Helsinki.

Stimulus

Stimuli were white circular spots of light of constant size (Goldmann size II 0.23° in diameter) presented on a white-gray background (10 cd/m^{-2}) for 200 ms (Figure 3). The stimuli were presented at nasal and temporal meridians. The stimulus size and contrast were fixed; however, as contrast sensitivity differs with age and refractive state, the contrast levels used for each observer differed slightly. Weber contrast levels were determined using their individual HFA contrast thresholds (see Khuu & Kalloniatis, 2015b, equations 1 and 2). A black fixation mark ($0.28^\circ \times 0.28^\circ$, Weber contrast -0.2) was placed at the center of the screen upon which the observer was instructed to fixate during the trial. Fixation was monitored externally by the experimenter. Stimuli were generated and presented on a linearized 27-in. iMac computer (resolution 2560×1440 pixels) driven at a frame rate of 60 Hz using custom-written software in Matlab (Mathworks, version 7) and Psychtoolbox (version 3.0.11). A chin rest was used to ensure a constant viewing distance of 30 cm. To mitigate the optic effects of a trial lens, all

observers' refractive errors and presbyopia were corrected using contact lenses.

Procedure

Participants were instructed to maintain central fixation. After a period of 3 s, the presentations began. Three different testing paradigms were examined: static, kinetic inward, and kinetic outward. In the static trial, the stimulus was presented for 200 ms at one location. In the kinetic conditions, the stimuli were moved inward or outward at a constant speed (4° per second) for an interval of 200 ms, equal to the stimulus duration of the static presentation (hence, it travelled a distance of approximately 0.8°). This test speed was chosen due to the short stimulus duration. Note that this brief presentation does not prevent the observers from reliably detecting whether the stimulus is static or kinetic (see Results and discussion section and Supplementary Material). In each condition, a 2IFC procedure was used with the stimulus appearing in one of two intervals. The first interval was shown for 200 ms, after which the background was shown for 200 ms, followed by the second interval also shown for 200 ms. After the second interval, the background was shown while the program waited for the observer's response before starting again. The two intervals were each cued with a beep. The task of the observer was to indicate in which interval—first or second—the stimulus appeared by pressing one of two buttons on a computer keyboard (Figure 6).

MoCS was used to present the stimuli in random order, which could appear at nine possible positions, centered about 23° nasal and 37° temporal and offset nasally or temporally in 1.5° steps. Thus, the range of testing was essentially 17° – 29° nasally and 31° – 43° temporally: a 12° range that sampled the width of the isocontrast region. Within each block of trials, stimuli were presented 10 times at each of the nine possible eccentric locations. Each subject underwent testing with at least three blocks of trials (i.e., at least 30 presentations at each location for each paradigm) until the fit of the psychometric function could no longer be notably improved. The proportion of times the stimulus was seen was recorded and averaged. Each meridian and testing paradigm was tested separately.

Statistical analysis

The proportion seen was plotted as a function of stimulus eccentricity (degrees) for each meridian with the three testing paradigms plotted within the same figure. Psychometric curves were fitted using a sigmoidal nonlinear regression function with variable slope

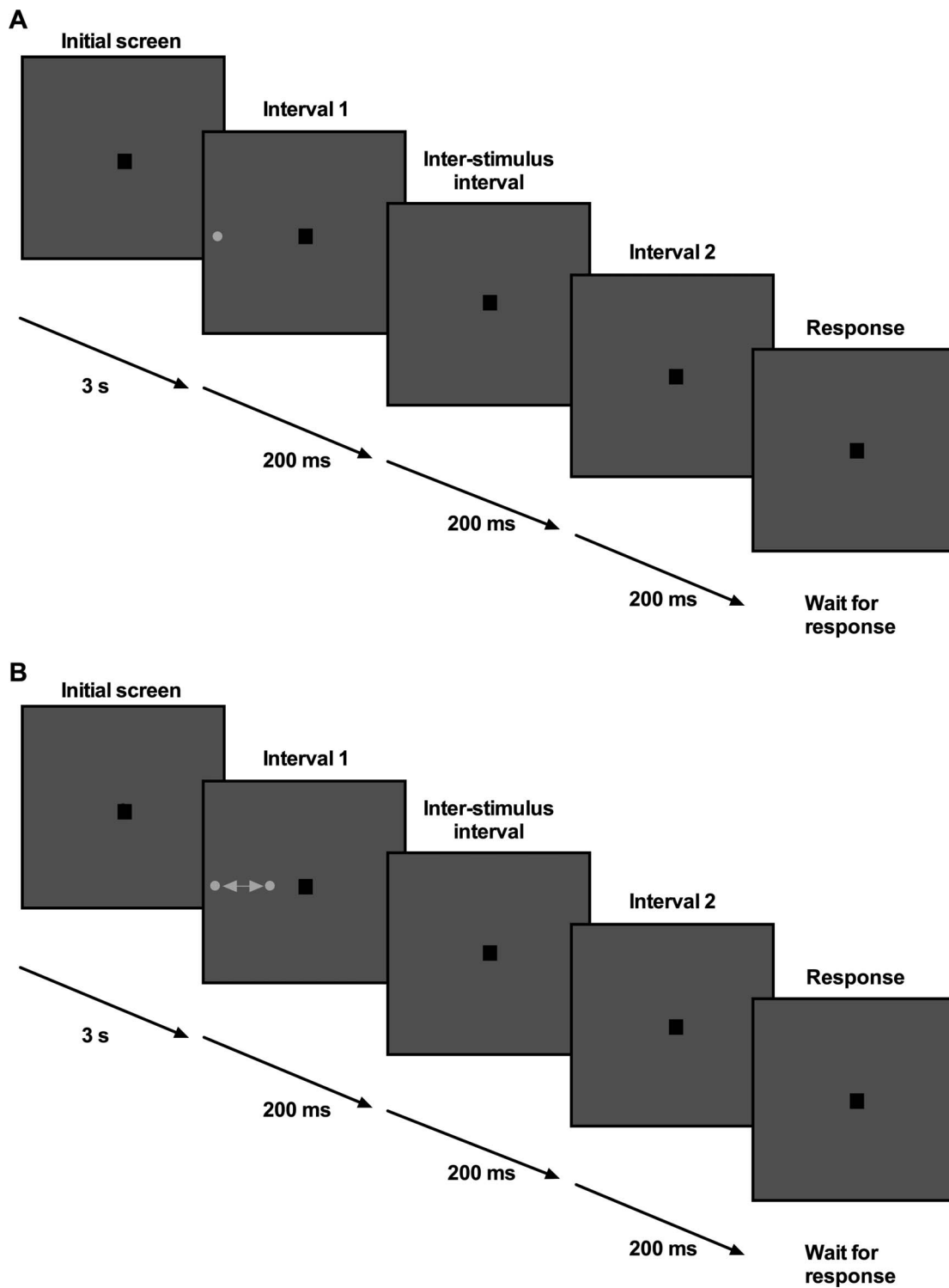


Figure 6. A schematic showing the experimental stimulus and procedure for static (A) and kinetic (B) presentations. In panel B, the arrowhead represents the possible directions of motion (inward or outward) although each condition was tested separately. At the presentation of the response screen, the observer indicated in which interval they thought the stimulus appeared while maintaining fixation upon the central black spot throughout the test.

(GraphPad Prism, version 6) with the bottom fixed at 0.5. To allow for a degree of false negatives (approximately 10%) at the higher end of the psychometric function, we allowed the top of the function to float

between 0.9 and 1.0 (Wichmann & Hill, 2001). We defined threshold (in the ensuing sections) as the 0.75 proportion-seen level and report the standard error of the residuals as a measure of deviance of points from

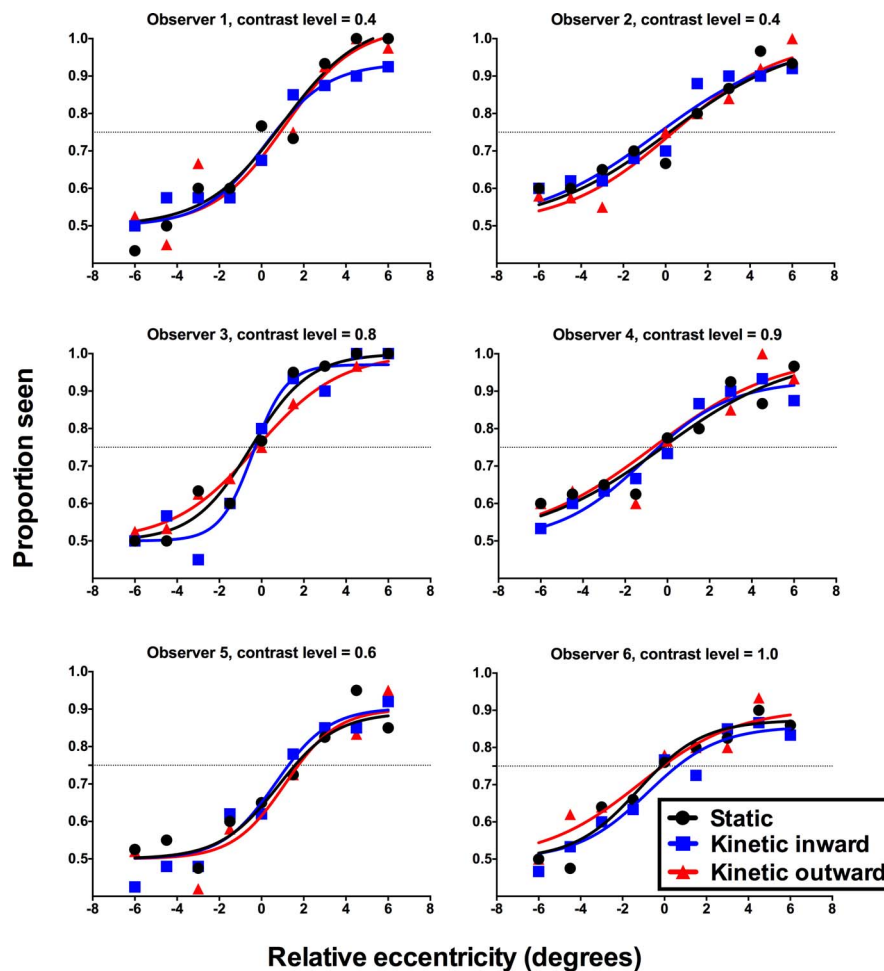


Figure 7. Psychometric functions (fitted with a sigmoid dose–response nonlinear regression) for each individual and the respective Weber contrast levels plotting proportion seen as a function of relative eccentricity (in degrees) for the nasal test meridian centered about 23° . Along the x-axis, a positive value indicates an eccentricity closer to fixation, and a negative value indicates an eccentricity farther away from fixation. The dotted line indicates the 0.75 proportion seen, which was taken as the threshold eccentricity. The different conditions are depicted by different colored symbols and lines.

the psychometric function (Wichmann & Hill, 2001). Using $n = 6$ and assuming a conservative SD of approximately 1.5° (Grobbel et al., 2016; Niederhauser & Mojon, 2002), this experiment could detect a magnitude of SKD of approximately 1.9° at $\alpha = 0.05$ and $\beta = 0.80$.

Results and discussion

Psychometric functions fitted to graphs depicting proportion seen as a function of eccentric location were plotted for each observer with the different colors indicating the test paradigm (static, kinetic inward, and kinetic outward) for nasal and temporal meridians, respectively (Figures 7 and 8). The dashed lines at $y = 0.75$ indicate the threshold frequency of seeing. The average standard error of residuals for the fits were

0.111 (± 0.019) for nasal and 0.103 (± 0.016) for temporal.

There were no significant differences in function midpoint found between conditions using pair-wise comparisons for each observer (nasal, all pairs $p > 0.9999$; temporal, all pairs $p > 0.9999$) or when averaging the group data: Kruskal-Wallis test, nasal, $H(2) = 0.8358$, $p = 0.6828$; temporal, $H(2) = 0.0819$, $p = 0.9721$ (Figure 9A, B). None of these conditions were found to have means that were significantly different from 0 (one sample t test, average p value for all conditions: 0.5196 ± 0.3111).

There was no significant difference found in slope value between all conditions using pair-wise comparisons for each observer (nasal, all pairs $p > 0.9999$ except inward vs. outward, $p = 0.9912$; temporal, all pairs $p > 0.9999$) or when averaging the group data: Kruskal-Wallis test, nasal, $H(2) = 1.088$, $p = 0.6001$; temporal, $H(2) = 0.9240$, $p = 0.6522$

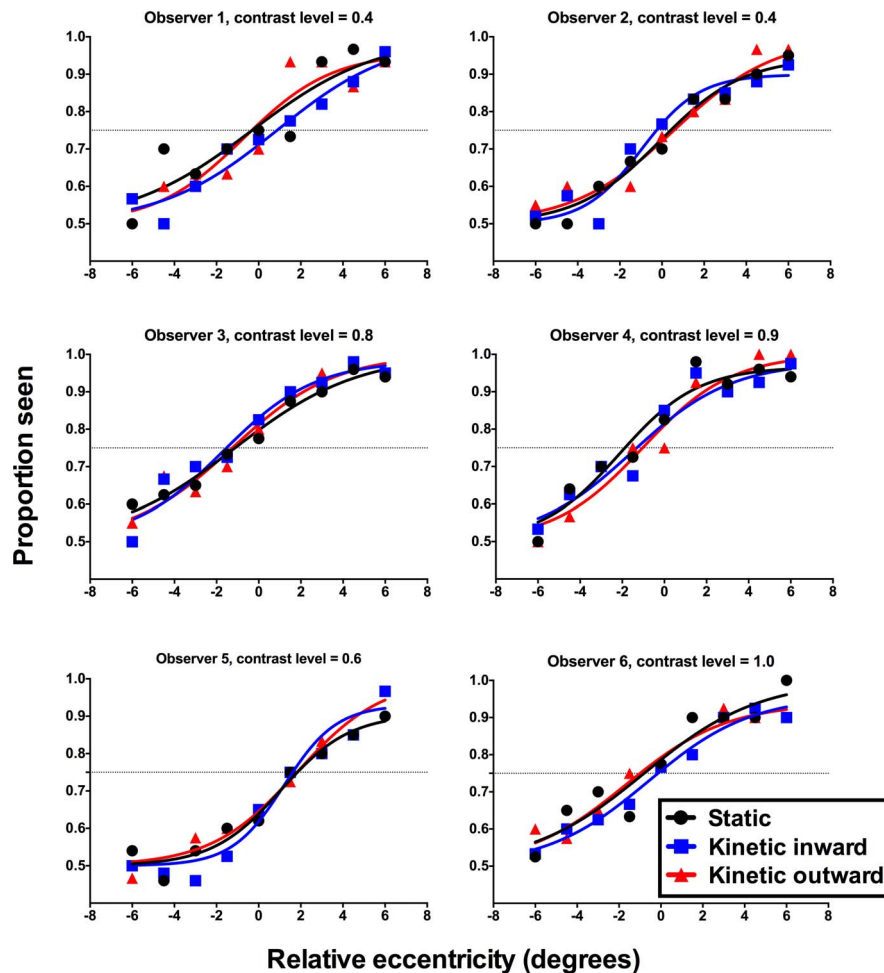


Figure 8. Psychometric functions for the temporal meridian with relative eccentricities centered about 37° as per Figure 7.

(Figure 9C, D). The spread of results was larger with static and inward movement conditions in comparison to outward.

By introducing a 2IFC procedure, we confirm not only that the static threshold lies within the isocontrast region, but also that a concordance of results obtained from both techniques can be achieved. There was no longer a systematic bias associated with inward or outward direction of movement of the stimulus as found when using MoL, such as in Experiment 1.

Although criterion bias has been removed using the 2IFC procedure, inward motion and static presentation of targets have no visible cue and may therefore introduce spatial uncertainty. In comparison, an outward-moving target may be cued by attention to its path of movement (Phu et al., 2016). There was no bias found in the present results. The lack of difference in slope values suggests that the level of uncertainty across all three conditions was similar, most likely due to the testing procedure wherein only one meridian was tested at a time. It is possible that if more meridians were tested at once and in random order that a cueing effect may be introduced, such that an

outward stimulus may display less uncertainty and hence a steeper slope.

One possible limitation of the paradigm used in Experiment 2 is that in equating the kinetic and static perimetry tasks, the stimuli may have also been inadvertently equated due to their brief presentation time. If that were the case, then the 2IFC procedure would not necessarily be testing whether or not static and kinetic perimetry tasks were the same. To address this issue, we conducted a supplementary experiment using the same observers in Experiment 2 to determine whether or not they were perceiving the stimulus as static or kinetic (see Supplementary Material).

In the supplementary experiment, a three-alternative forced choice (3AFC) procedure was utilized, and observers were required to indicate whether a 200-ms stimulus (of the same configuration as that used in Experiment 2) was static, moving inward, or moving outward. We presented targets at three eccentric locations—at the nasal eccentricity threshold (i.e., 23° from fixation), 3° more nasal to this location, and 6° more nasal to this location—to determine if discrimination also differed with the performance level found

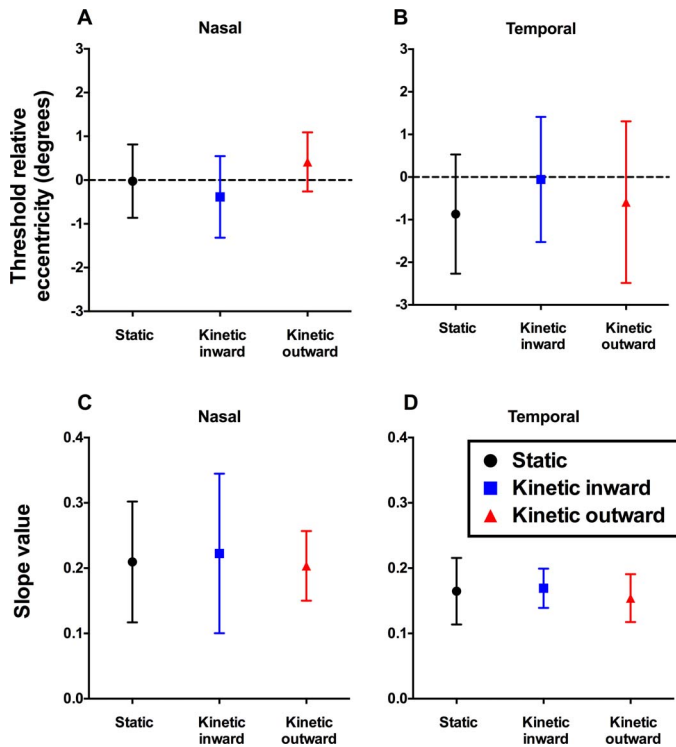


Figure 9. Average threshold relative eccentricity (panels A and B, in degrees, $\pm SD$) and average slope value (panels C and D, $\pm SD$) across all six observers plotted as a function of condition tested for nasal and temporal conditions. The dashed line in panels A and B at 0 means that the threshold eccentricity was centered at the midpoint of the MoCS set of tested eccentricities (23° for nasal and 37° for temporal).

in Experiment 2. Although performance declined closer to the threshold eccentric location, we found that observers correctly identified whether the stimulus was static, moving inward, or moving outward at a level well above chance performance (0.33 for a 3AFC) for all three stimulus configurations. Therefore, the testing paradigm in Experiment 2 facilitated comparisons between static and kinetic thresholds, and importantly, the results of Experiment 2 cannot be accounted for by the brief stimulus presentation as observers were able to discriminate between a static target and moving targets.

The shape of the functions showed that for the six observers the isocontrast region of 12° found in Experiment 1 was adequately tested with the majority of eccentricities falling within the region rather than being clustered at the plateaus. These plateaus do not necessarily represent the exact locations of inner and outer isopters, such as those found in Experiment 1, because the isopter position depends upon the individual's criterion bias, but conversely, the location of the isopters is likely to be within that region for each subject. Indeed, the upper asymptote of the function, at times, did not reach a proportion of 1.0 correct due to

false negative responses from the subject (Wichmann & Hill, 2001).

General discussion

In the present study, we first confirmed the presence of physiologic SKD in normal observers when utilizing conventional visual field assessment techniques, which is not only in agreement with previous studies utilizing one-way MoL techniques (Casson et al., 1991; Gandolfo, 1996; Hudson & Wild, 1992; Osako et al., 1997; Rowe et al., 2013; Safran & Glaser, 1980; Schiller et al., 2006; Wong & Sharpe, 2000), but also with utilizing an average isopter generated using a two-way MoL. In comparing kinetic and static measurements, previous studies have converted static thresholds to isopters and/or kinetic isopters to location-specific thresholds to facilitate comparisons and SKD. As mentioned by Hudson and Wild (1992), the differences in the strategy of obtaining thresholds or isopters may contribute to SKD. Specifically, they and other researchers (Schiller et al., 2006; Schiller et al., 2002) have suggested the need for adjusting for individual reaction time. However, alongside substantial interindividual differences in reaction time and hence the need to tailor the adjustment on a case-by-case basis, the assumed displacement of 0.8° is still significantly smaller than the width of the isocontrast region found in Experiment 1, suggesting little contribution of reaction time. Furthermore, although using the two-way MoL produced the isocontrast boundary containing within it the isocontrast static threshold, a small amount of physiologic SKD was still present, which was also subject to a large degree of individual variability.

Other explanations for SKD suggest that kinetic and static procedures selectively measure different visual pathways, namely, the magnocellular (M) and parvocellular (P) systems (Safran & Glaser, 1980). A moving target in kinetic perimetry is thought to engage transient selective M cells (sensitive to temporal frequency), and static perimetry might activate P mechanisms, which are relatively insensitive to motion (Lee, 1993). Other theories include lateral successive spatial summation (Greve, 1973) and different movement-dependent and movement-independent channels in human vision (Tolhurst, 1973), which are thought to account for a preferential bias for kinetic stimuli. However, although it is clear that M and P pathways exist, their functions display a substantial amount of overlap (Lennie, 1998), which questions the appropriateness of perimetric stimuli to selectively activate one but not the other pathway. To selectively measure M and P pathways, the spatial and temporal properties of the stimulus must be appropriately curtailed to activate

one but not the other (Kulikowski & Tolhurst, 1973; Pokorny & Smith, 1997). Both static and kinetic perimetric stimuli have not been designed with this in mind, and their spatial and temporal properties are likely to mutually activate both pathways (Hudson & Wild, 1992). Specifically, the square wave temporal profile (abrupt on- and offset) of the static perimetry stimuli stimulates M cells quite effectively (Swanson, Sun, Lee, & Cao, 2011). In conjunction with our results, further doubt is cast upon the explanation of selective M pathway activation in SKD.

Another suggested explanation of physiologic SKD is the role of spatial and temporal summation characteristics (Greve, 1973). Successive lateral spatial summation describes the process by which a series of detector units are successively stimulated by an infraluminal level of light. During the course of stimulus movement from periphery to center, its energy is summed even though it might not be immediately perceived—hence, the reason why it is thought a kinetic stimulus is seen more peripherally than a static stimulus (Greve, 1973). This has been suggested in the case of disease in which both the area of spatial summation is enlarged (Casson et al., 1991; Mulholland, Redmond, Garway-Heath, Zlatkova, & Anderson, 2015b; Redmond, Garway-Heath, Zlatkova, & Anderson, 2010; Sloan & Brown, 1962) and the duration of temporal summation is extended (Mulholland et al., 2015b). In addition, prolonged exposure of a kinetic stimulus lends itself to a greater extent of temporal summation in lieu of a fixed duration static stimulus (Casson et al., 1991). However, our present results are incompatible with a theory of summation properties affecting SKD. A size II target, used in the present study, has been shown to be within complete spatial summation in that region of the visual field (Khuu & Kalloniatis, 2015a, 2015b). Under a theory of successive lateral spatial summation, the summation of the stimulus traveling a greater distance and hence stimulating adjacent detector units should yield a higher rate of detection and thereby shift the eccentricity threshold toward a more outward location, but none was found in the present study. Temporal summation is unlikely to play a role here as a stimulus duration of 200 ms has been shown to be outside of total temporal summation (Mulholland, Redmond, Garway-Heath, Zlatkova, & Anderson, 2015a; Mulholland et al., 2015b).

As mentioned, one of the chief sources of error is individual subject criterion bias (Green & Swets, 1966). This occurs when an observer adopts a criterion, typically to minimize the total error rate. In the case of kinetic perimetry and the MoL, this manifests in the two distinct isopters generated from inward and outward movement. Although, at face value, the spatial uncertainty from an inward-moving isopter may result in a skewed inner isopter—as the observer needs to be

confident of the stimulus appearance—we found no evidence of a systematic bias toward a greater discordance of inner isopters from the isocontrast static position in comparison to the outer isopter. Further studies are required to determine the role of spatial uncertainty on isopter position.

The use of a more objective 2IFC procedure reduces subject criterion bias by forcing a choice upon them. The similar slope values in the results of Experiment 2 suggest that spatial uncertainty is relatively uniform across the test conditions in the present study as expected from testing only one meridian. The brief stimulus duration meant that the kinetic stimulus only traveled 0.8° . Coupled with the results showing that the border between seen and not seen was not distinct, the starting location of the kinetic stimulus was unlikely to contribute to attentional cueing. In spite of a small presentation window and travel distance, there was no significant difference in subjective perception of whether the stimulus was static or kinetic, indicating that comparisons could be made between static and kinetic perimetry tasks. The use of external monitoring in lieu of a direct gaze tracker for such a brief stimulus presentation is also a limitation in the present study.

Stimulus velocity has been shown to be an important factor in kinetic perimetry, and recommended velocities may vary from $2^\circ/s$ (Wabbels & Kolling, 2001) to $4^\circ/s$ (Johnson & Keltner, 1987). The rate of movement has implications for reaction time, perceptual smear, variability, and hence isopter limits (Burr, 1980; Hirasawa, Shoji, Okada, Takano, & Tomioka, 2014; Westheimer & Wehrhahn, 1994). For practical reasons, we chose a $4^\circ/s$ stimulus as we wished to equate the stimulus durations for each condition, which meant that the stimulus travelled approximately 0.8° , which was approximately equal to the magnitude of error due to reaction time cited by Hudson and Wild (1992) although still able to be discerned as a moving, rather than static, target (Westheimer & Wehrhahn, 1994; see Supplementary Material). Future studies could investigate the contribution of stimulus exposure duration and stimulus velocity on concordance when using a 2IFC procedure.

Overall, the results of the present study suggest that physiologic SKD is largely an artifact from inherent differences in the psychophysical procedures used in static and kinetic perimetry. Although the biases associated with inward- and outward-moving targets was removed by using a two-way MoL, average isopter and static threshold locations were still disparate, which we refer to as *physiologic* SKD. By equating the procedures, we found no evidence of physiologic SKD in a cohort of normal observers, suggesting that kinetic and static perimetry have the same underlying detection mechanism. This has implications in clinical ophthalmic practice in which static and kinetic perimetry

thresholds have traditionally been taught to be disparate entities. Subsequent studies could then test more parameters to determine the extent of their contribution to physiologic SKD or lack thereof. In particular, this task may be performed on patients with ocular disease to see if SKD (i.e., Riddoch's syndrome) is really present or if that too is product of criterion bias.

Keywords: perimetry, Goldmann, Humphrey visual field analyzer, method of constant stimuli, retinal eccentricity, statokinetic dissociation, criterion bias

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