




# Scotopic and Photopic Conventional Visual Acuity and Hyperacuity – Binocular Summation

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**Purpose:** The purpose of this study was to determine and compare binocular summation (BiS) of conventional visual acuity (cVA) versus hyperacuity (hVA) for photopic and scotopic luminance conditions as a potential biomarker to assess the outcome of interventions on binocular function.

**Methods:** Sixteen young adults (age range [years] = 21–31; 8 women; cVA logMAR < 0.0) participated in this study. The Freiburg Visual Acuity Test (FrACT) was used for VA testing and retested on another day. Both cVA and hVA were determined for dark grey optotypes on light grey background. Participants underwent 40 minutes of dark adaptation prior to scotopic VA testing. Binocular and monocular VA testing was performed. The eye with better VA over the 2 days of testing was selected, the BiS was quantified (binocular VA – better monocular VA) and repeated measures ANOVAs were performed.

**Results:** Binocular VA exceeded monocular VA for all luminance conditions, VA-types, and sessions. We report BiS estimates for photopic and scotopic cVA and hVA, (logMAR BiS ± SEM [decimal BiS]): photopic =  $-0.01 \pm 0.01$  [1.03] and  $-0.06 \pm 0.03$  [1.15]; and scotopic =  $-0.05 \pm 0.01$  [1.12] and  $-0.11 \pm 0.04$  [1.28], respectively. Improvement for binocular vision estimates ranged from 0.01 to 0.11 logMAR. A repeated-measures ANOVA (RM ANOVA) did not reveal significant effects of LUMINANCE or VA TYPE on BiS, albeit a trend for strongest BiS for scotopic hVA (15% vs. 28%, photopic versus scotopic, respectively) and weakest for photopic cVA (3% vs. 12%, photopic versus scotopic conditions, respectively).

**Conclusions:** Our results indicate that BiS of VA is relevant to scotopic and photopic hVA and cVA. It appears therefore a plausible candidate biomarker to assess the outcome of retinal therapies restoring rod or cone function on binocular vision.

**Translational Relevance:** Binocular summation of visual acuity might serve as a clinical biomarker to monitor therapy outcome on binocular rod and cone-mediated vision.

## Introduction

Vision ranks top among sensory modalities in humans and its loss has a fundamental impact on

the quality of life.<sup>1,2</sup> This motivates extensive research on this modality as well as innovative restoration therapies for its loss, for example, the recently approved voretigene neparvovec (Luxturna)<sup>3,4</sup> or the current initiatives for a gene therapy in patients with

CNGA-3 related achromatopia.<sup>5,6</sup> With the advent of such vision restoration, there is an increasing need for sensitive and efficient biomarkers of monocular as well as binocular visual function. Beyond state-of-the-art visual acuity (VA) measures might be of assistance to meet this need.

The photopic spatial resolution limit that is normally referred to as VA, is only one of a number of possible VA measures that can be obtained.<sup>7</sup> This assessment of the limit to discriminate spatially separated targets<sup>8</sup> is here termed conventional visual acuity (cVA). In comparison, hyperacuity (hVA) describes the limit to discriminate the relative position of targets.<sup>9–12</sup> The cVA is limited by the optics of the eyes and the retinal sampling of the receptor lattice, and usually markedly lower than hVA.<sup>13</sup> The latter draws more strongly on post-retinal resources and is therefore more closely related than cVA to the availability of cortical processing resources.<sup>14–16</sup> Decimal photopic VAs (cVA and hVA) exceed their scotopic counterparts by a factor of around 10<sup>13,17–19</sup> due to the difference in retinal photoreceptor sampling and signal convergence by cone and rod systems,<sup>20,21</sup> which mediate photopic and scotopic vision, respectively. This distinction of VA types bears great potential to differentiate between the functional consequences of retinal and cortical abnormalities and for a separate assessment of the effect of rod and cone pathologies on visual function.

Testing binocular VA might offer deeper insights into the performance of individuals during daily activities and disease related complaints. Indeed, studies of patients with central visual loss demonstrated that binocular summation of visual acuity, that is, the superiority of binocular over monocular vision, affects the maximum reading speed, whereas VA alone was not a good predictor of maximum reading speed.<sup>22</sup> The realistic binocular function used in everyday life in the elderly is not sufficiently estimated by testing only the best-corrected visual acuity (BCVA) of the better eye.<sup>23</sup> Further, for binocular summation in visual field, testing was reported to correlate well with the estimation of activity limitations, as reported in patients with glaucoma.<sup>24</sup> A recent investigation of binocular contrast summation, underlined the sensitivity of this measure to visual dysfunction, as binocular processing deficits were evident even in the absence of detectable visual field (VF) defects.<sup>25</sup> Determining the effect of binocular viewing, that is, binocular summation (BiS), on the different VA-types, might therefore provide a detailed account of visual function and dysfunction.

BiS can be explained on the one hand by probability summation, first described by Pirenne.<sup>26</sup> The study

by Pirenne concluded that if both eyes see equally well, binocular performance improves by  $\sqrt{2}$ . Since then, other studies reported BiS values to be above  $\sqrt{2}$ , especially for contrast sensitivity,<sup>27</sup> additional neural summation processes in the central nervous system may underlie BiS.<sup>28</sup> The extent of this binocular summation depends on test configurations and the visual tasks, as well as on participant specific conditions.<sup>29</sup> In addition, the test location, fovea versus eccentric retinal position, showed differences in binocular recognition summation.<sup>30</sup> Furthermore, there were differences in contrast summation between stimuli on corresponding retinal areas, which showed higher summation than the tested non-corresponding areas.<sup>31</sup> Age<sup>32–34</sup> and visual system diseases<sup>35–39</sup> influence BiS. As a consequence, there are different, partly contradictory accounts on BiS in the literature. Even though smaller summation values are known for resolution tasks than for detection tasks, summation has also been demonstrated for VA.<sup>40,41</sup> BiS has been demonstrated for both cVA and hVA.<sup>40,42–48</sup> The binocular advantage for cVA and hVA disappears at high luminance contrasts,<sup>43,48</sup> whereas at lower contrast levels, BiS increases for both VA<sup>49,50</sup> and hyperacuity.<sup>51</sup> Binocular summation has been reported to be evident for scotopic conditions.<sup>52,53</sup>

Here, we established an approach for a combined measurement of binocular summation for photopic and scotopic visual acuity and hyperacuity (cVA and hVA) in participants with healthy vision and for the assessment of their reproducibility. Importantly, as the acuity/hyperacuity test used for our measurements of binocular summation is freely available, our approach is readily accessible for use by laboratories worldwide. In this work, we hypothesize that BiS for scotopic conditions is higher than for photopic conditions, and BiS of cVA and hVA is comparable to the previously reported BiS-contrast summation, that is,  $\geq \sqrt{2}$  approximating a 40% of improvement.

## Methods

### Participants

Sixteen young adults (age range [years] = 21–31; 8 women) with cVA  $\geq 1.0$  (decimal), without self-reported neurological or ocular conditions were included after providing written informed consent. BCVA was checked with Freiburg Visual Acuity Test (FrACT) and Early Treatment Diabetic Retinopathy Study (ETDRS) charts to ensure proper refraction and stereopsis with the Lang test. The inclusion crite-

tion for the study was a successfully completed Lang Stereotest I. The procedures followed the tenets of the Declaration of Helsinki and the study was approved by the ethical committee of the Otto von Guericke University Magdeburg, Germany.

## Visual Acuity Measurement

### Stimuli and Setup

Freiburg Visual Acuity and Contrast Test (FrACT version 3.10.5), a computer based automated VA platform using an adaptive algorithm (BestPEST), was used for testing cVA and hVA under photopic and scotopic conditions.<sup>54</sup> (i) Photopic setup: The FrACT test was conducted in a dimly lit room (room luminance, maximum [screen], and minimum [optotype] luminance, measured with a photometer [CS-100A photometer; Konica Minolta Holdings, Inc.; Japan]: 3.5, 67, and 39 cd/m<sup>2</sup>, respectively) at 4 m viewing distance on an LCD monitor. Whereas under (ii) scotopic conditions, both VAs were measured in a completely dark room (maximum [screen] and minimum [optotype] luminance = 52.1 and 20.8 cd/m<sup>2</sup>, respectively) at 0.75 m viewing distance to an LCD monitor and viewed through a neutral density filter (Haida, Neutral Density ND, Optical Glass, 150 Series; transmission factor: 1/32,000). This filter was mounted in front of the participant allowing light from the monitor only to be perceived through the filter. From this, a luminance of 0.0017 cd/m<sup>2</sup> is calculated using the formula:  $\text{Luminance} = \text{Luminance}_{\text{screen}} \times \text{transmission factor}_{\text{filter}}$ . For both setups, the same LCD-monitor model with 60 Hz refresh rate (resolution = 3840 × 2160 pixels and screen size = 59.8 × 33.6 cm) was used. Both cVA and hVA were tested under photopic and scotopic (after 40 minutes of dark adaption) conditions, for 42% Weber contrast under photopic and 60% Weber contrast under scotopic conditions, that is, dark grey optotype on light grey background (positive). Monitors were calibrated using a Data SpyderX Pro (Datacolor, Lawrenceville, NJ, USA).

### Stimulus Types

The FrACT test of cVA consists of single Landolt-ring optotypes presented 18 times and tested in an 8 alternative-forced-choice design (8-AFC; 8 possible gap orientations). For hVA, FrACT uses the Livingstone and Hubel<sup>9,13</sup> paradigm by presenting a “three-bar-stimulus” where a central bar is displaced to the left or right (2-AFC design with 42 trials) of 2 vertically aligned bars, subtending 0.8 degrees × 0.03 degrees and 12.8 degrees × 0.4 degrees, under

photopic and scotopic luminance conditions, respectively.

## Testing Procedure

To calculate binocular summation, cVA and hVA was tested for each eye (right eye = oculus dexter = OD, left eye = oculus sinister = OS) separately and binocularly (oculus uterque = OU) for photopic and scotopic luminance conditions. We tested monocular VAs by occluding the unstimulated eye using a frosted foil (8 cm × 8 cm), as suggested by Baker et al.<sup>27</sup> The testing procedures are detailed in Freundlieb et al.<sup>13</sup> Sequences were counter-balanced for ocularity (OD/OS/OU, each determined twice) and VA type (cVA/hVA). Tests were conducted on 2 different days, each session lasted about 3 hours.

## Analysis

Monocular and binocular cVA and hVA were determined as logMAR and the subsequent analysis of the data was performed in IGOR Pro 8.04 (WaveMetrics Inc., Lake Oswego, OR, USA) and SPSS 28 (Statistical Package for the Social Sciences; IBM, Armonk, NY, USA). We have used logMAR values for averaging and calculations of VA.<sup>55</sup> Inspired by previous investigations, BiS was identified by selecting the monocular VA following three different approaches:

Approach A: *The better eye for each day*<sup>22,39,42,46</sup>

Approach B: *The better eye over both days*<sup>22,39,42,46</sup>

Approach C: *The mean of the monocular measurements*.<sup>25,27</sup>

It should be noted that under- and overestimations of VA can occur for approaches A and C, respectively, whereas approach B is less prone to these misestimations. Consequently, our analyses focus on approach B; for transparency and comparability, results A and C are also reported. Binocular summation was calculated as binocular improvement in the logMAR range by subtracting monocular from binocular VA as follows:  $\text{BiS} = \log\text{MAR}_{\text{OU}} - \log\text{MAR}_{\text{Monocular}}$ .<sup>34,42</sup> As typical for logMAR, negative values indicate improvement, 0 = no summation, and positive values indicate inhibition. The BiS calculation reads for the approaches A to C (see Supplementary Table S1 for different approaches):

Calculation A:  $\text{BiS} = \text{OU} - \text{BE}(\text{better eye for each session and VA test})$

Calculation B:  $BiS = OU - BE(\text{better eye over both sessions for each VA test})$

Calculation C:  $BiS = OU - \frac{OD+OS}{2}$

As indicated above, we focus on calculation B in the present study. The binocular summation ratio (BSR) VA, was determined as delogarithmized BiS ( $\log MAR_{BiS}$ ) values.

## Statistics

We applied a repeated-measures (RM) ANOVA with four factors to determine the effects of OCULARITY, VA-TYPE, LUMINANCE, and SESSION on the monocular/binocular VAs. Subsequently, the latter 3 factors were tested further for binocular summation using a 3-way RM ANOVA. Post hoc tests were applied where significant main or relevant interaction effects were reported and  $P$  values were corrected for multiple comparison using the Bonferroni-Holm correction<sup>56</sup> and reported as  $p_{\alpha}$ , that is, the uncorrected  $P$  values are given and the alpha-adjusted significance threshold is given as the subscript to the “p” (i.e., “ $\alpha$ ”).

Further, the BiS was tested using the one sample  $t$ -test to estimate the significant of summation factor from the zero, that is, no summation. In addition, we assessed the correlation of the BiS under different luminance levels, photopic versus scotopic BiS for

each type of VA. We have also added a Bland-Altman analysis for VA estimates for each session under the respective luminance levels, see Supplementary Figure S1.

## Results

### Visual Acuities

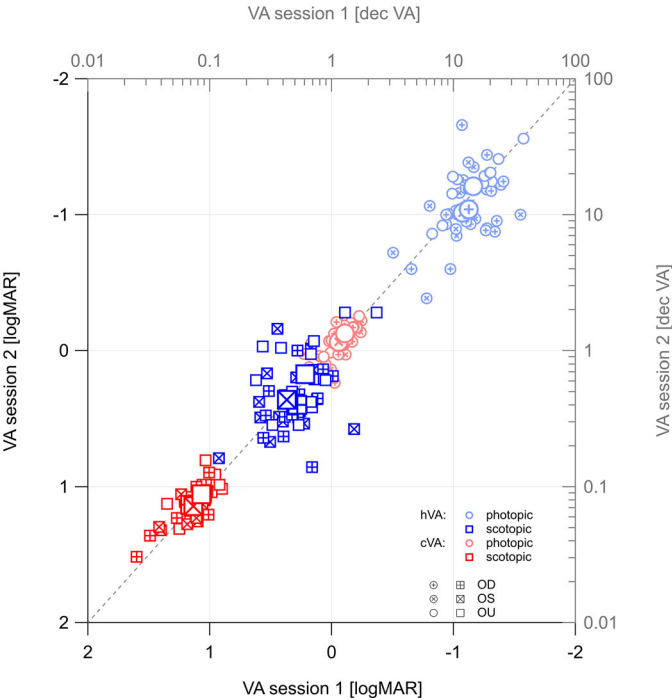
Average binocular performances for cVA and hVA were better than monocular performances in both sessions (first/second) and under both luminance conditions (photopic/scotopic; see Table 1). This was further validated in a four-factor repeated measures ANOVA (factor 1: LUMINANCE [photopic/scotopic]; factor 2: VA-TYPE [cVA/hVA]; factor 3: OCULARITY [OD/OS/OU]; factor 4: SESSION [first/second]). We found a main effect of LUMINANCE ( $F(1, 15) = 923.25, P < 0.001$ ), VA TYPE ( $F(1, 15) = 1220.45, P < 0.001$ ) and OCULARITY ( $F(2, 30) = 24.52, P < 0.001$ ), and a significant interaction of VA TYPE  $\times$  OCULARITY ( $F(2, 30) = 4.14, P = 0.026$ ). Post hoc  $t$ -tests showed the same trend for both acuity types, that is, no significant difference between OD and OS, whereas OU was significantly better than each eye separately ( $P \leq 0.016$ ). The main effect of SESSION, that is, an indication of learning effects, was also investigated (see Fig. 1) and we

**Table 1.** A Summary of Visual Acuities Tested Under Different Conditions in Two Different Days

Acuity Type	Ocularity	Session 1	Session 2	Mean
		Visual Acuity	Visual Acuity	Visual Acuity
		Decimal • logMAR ± SEM	Decimal • logMAR ± SEM	Decimal • logMAR ± SEM
Photopic				
cVA	OD	1.15 • −0.06 ± 0.03	1.15 • −0.06 ± 0.03	1.15 • −0.06 ± 0.02
	OS	1.15 • −0.06 ± 0.04	1.15 • −0.06 ± 0.03	1.15 • −0.06 ± 0.02
	OU	1.29 • −0.11 ± 0.02	1.35 • −0.13 ± 0.03	1.31 • −0.12 ± 0.02
hVA	OD	13.49 • −1.13 ± 0.05	10.96 • −1.04 ± 0.07	12.09 • −1.08 ± 0.04
	OS	12.02 • −1.08 ± 0.06	10.23 • −1.01 ± 0.06	11.09 • −1.04 ± 0.04
	OU	14.45 • −1.16 ± 0.05	16.22 • −1.21 ± 0.05	15.34 • −1.19 ± 0.03
Scotopic				
cVA	OD	0.07 • 1.16 ± 0.04	0.07 • 1.13 ± 0.04	0.07 • 1.15 ± 0.03
	OS	0.07 • 1.14 ± 0.03	0.07 • 1.14 ± 0.02	0.07 • 1.14 ± 0.02
	OU	0.09 • 1.07 ± 0.03	0.09 • 1.06 ± 0.03	0.09 • 1.06 ± 0.02
hVA	OD	0.52 • 0.28 ± 0.04	0.40 • 0.40 ± 0.05	0.46 • 0.34 ± 0.04
	OS	0.43 • 0.37 ± 0.06	0.44 • 0.36 ± 0.06	0.43 • 0.36 ± 0.04
	OU	0.60 • 0.22 ± 0.06	0.68 • 0.17 ± 0.06	0.64 • 0.19 ± 0.04

cVA, conventional visual acuity; hVA, hyperacuity; LogMAR, Logarithm of the Minimum Angle of Resolution; OD, oculus dexter (right eye); OS, oculus sinister (left eye); OU, oculus uterque (both eyes); SEM, standard error of the mean.





**Figure 1. Acuity comparison between sessions.** For each of the four visual acuity conditions (scotopic versus photopic), individual cVA and hVA values (*small symbols*) for OD, OS, and OU, are shown along with group averages (*large symbols*;  $n = 16$ ; SEMs are smaller than symbol size). No significant effects on visual acuity were observed across sessions. Note the inverted axes for logMAR values (this measure describes visual loss), such that poor visual acuity is in the *bottom left quadrant* and good visual acuity is in the *top right quadrant*; the identity line is dashed.

found neither an effect for SESSION ( $F(1, 15) = 0.19$ ,  $P = 0.67$ ), nor its interactions.

### Binocular Summation

BiS values for photopic versus scotopic cVA and hVA were [ $\log\text{MAR}_{\text{BiS}} \pm \text{sem}$  (decimal BiS)]:  $-0.01 \pm 0.01$  (1.03);  $-0.06 \pm 0.03$  (1.15) vs.  $-0.05 \pm 0.01$  (1.12);  $-0.11 \pm 0.04$  (1.28), respectively (see Table 2, Table 3, Fig. 2). We performed a three-factor RM-ANOVA (factor 1: LUMINANCE [photopic /scotopic]; factor 2: VA-TYPE [cVA/hVA]; and factor 3: SESSION

[first/second]). The RM ANOVA did not reveal a main effect of LUMINANCE ( $F(1, 15) = 3.51$ ,  $P = 0.080$ ) or VA TYPE ( $F(1, 15) = 2.46$ ,  $P = 0.137$ ), whereas a weakly significant effect of SESSION ( $F(1, 15) = 5.47$ ,  $P = 0.034$ ) was reported. There was a significant interaction of SESSION  $\times$  VA TYPE ( $F(1, 15) = 5.90$ ,  $P = 0.028$ ). Post hoc tests did not corroborate this finding. There was a trend of better performance for hVA in session 2, but it did not reach significance after correction for multiple comparisons (photopic hVA session 1 vs. 2:  $t(15) = 2.5$ ,  $P \leq 0.013 = 0.048$ ), as also depicted in Figure 1. We further tested the potential learning effect independent of luminance level and found a trend of better hVA in session 2 (see Fig. 3, of all 3 calculations and Supplementary Figure S2, Supplementary Figure S1 Bland-Altman), but, again, this was not statistically significant after correction for multiple testing (hVA session 1 vs. 2:  $t(15) = 2.5$ ,  $P \leq 0.025 = 0.026$ ).

Taken together, in controls with healthy vision, an improvement by binocular vision was demonstrated in the range of  $-0.01$  to  $-0.11$  logMAR. BiS did not differ significantly between luminance levels and acuity types, although there is a nonsignificant trend for higher BiS for scotopic conditions as well as for hVA. Best BiS (average over both days) was measured for hVA (15% vs. 28%, photopic versus scotopic conditions, respectively) in scotopic conditions, and worst for in cVA (3% vs. 12%, photopic versus scotopic conditions, respectively) in photopic conditions.

We tested for a correlation with the BiS for the standard condition, that is, photopic cVA versus hVA-BiS, scotopic cVA-BiS, and scotopic hVA-BiS. No significant correlations were evident,  $r^2$  values ( $P$  values) were 0.042 ( $P > 0.44$ ), 0.048 ( $P > 0.41$ ), and 0.07 ( $P > 0.32$ ), respectively. Neither were there any correlations for photopic versus scotopic VA-BiS of cVA and hVA ( $r^2 = 0.048$ ,  $P = 0.41$ ;  $r^2 = 0.038$ ,  $P = 0.47$ , respectively), nor for cVA versus hVA VA-BiS of photopic and scotopic conditions ( $r^2 = 0.04$ ,  $P = 0.44$ ;  $r^2 = 0.15$ ,  $P = 0.15$ ). We also investigated BiS associations with monocular VA where neither cVA nor hVA

**Table 2. BiS Data for Approach B (See Methods)**

Acuity Type		Session 1	Session 2	Average
		BSR $\cdot \log\text{MAR}_{\text{BiS}} \pm \text{SEM}$	BSR $\cdot \log\text{MAR}_{\text{BiS}} \pm \text{SEM}$	BSR $\cdot \log\text{MAR}_{\text{BiS}} \pm \text{SEM}$
Photopic	cVA	$1.03 \cdot -0.01 \pm 0.01$	$1.03 \cdot -0.01 \pm 0.01$	$1.03 \cdot -0.01 \pm 0.01$
	hVA	$0.96 \cdot 0.02 \pm 0.04$	$1.38 \cdot -0.14 \pm 0.06$	$1.15 \cdot -0.06 \pm 0.03$
Scotopic	cVA	$1.15 \cdot -0.06 \pm 0.01$	$1.10 \cdot -0.04 \pm 0.02$	$1.12 \cdot -0.05 \pm 0.01$
	hVA	$1.07 \cdot -0.03 \pm 0.07$	$1.53 \cdot -0.18 \pm 0.04$	$1.28 \cdot -0.11 \pm 0.04$

BSR, binocular summation ratio; cVA, conventional visual acuity; hVA, hyperacuity;  $\log\text{MAR}_{\text{BiS}} = \log\text{MAR}_{\text{OU}} - \log\text{MAR}_{\text{BE}}$ ; SEM, standard error of the mean.

**Table 3.** Mean BiS Data for All Three Calculations

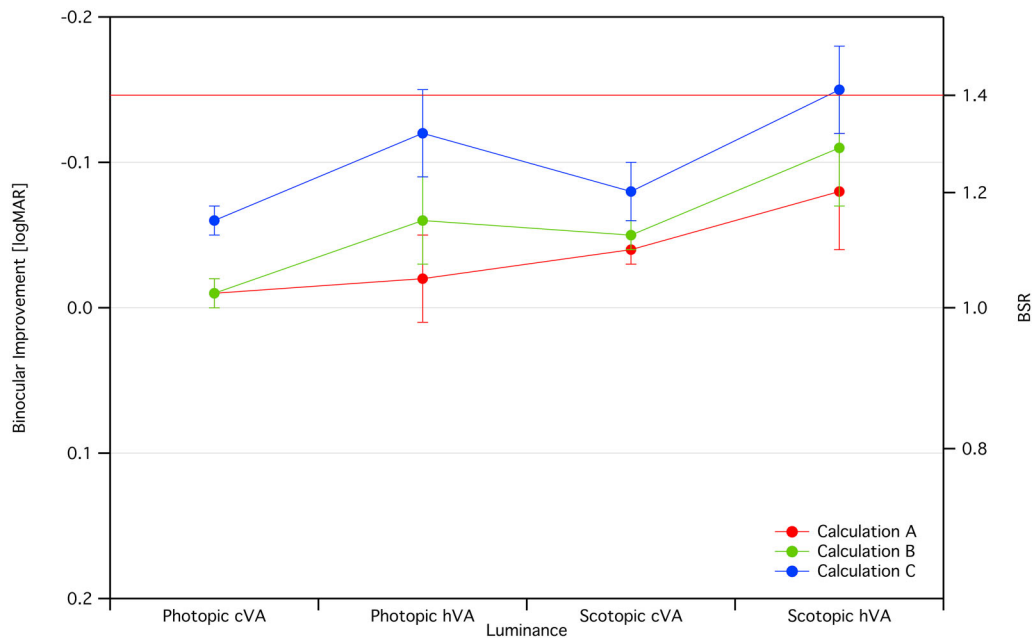
Acuity Type	Approach A		Approach B		Approach C	
	Mean BSR • logMAR <sub>BiS</sub> ± SEM	P Value	Mean BSR • logMAR <sub>BiS</sub> ± SEM	P Value	Mean BSR • logMAR <sub>BiS</sub> ± SEM	P Value
Photopic						
cVA	1.03 • -0.01 ± 0.01	0.250	1.03 • -0.01 ± 0.01	0.22	1.14 • -0.06 ± 0.01	<b>0.000</b>
hVA	1.07 • -0.02 ± 0.03	0.431	1.15 • -0.06 ± 0.03	0.099	1.32 • -0.12 ± 0.03	<b>0.001</b>
Scotopic						
cVA	1.11 • -0.04 ± 0.01	<b>0.006</b>	1.12 • -0.05 ± 0.01	<b>0.002</b>	1.21 • -0.08 ± 0.02	<b>0.000</b>
hVA	1.20 • -0.08 ± 0.04	0.088	1.28 • -0.11 ± 0.04	<b>0.017</b>	1.43 • -0.15 ± 0.03	<b>0.000</b>

BSR, binocular summation ratio; cVA, conventional visual acuity; hVA, hyper visual acuity; SEM, standard error of the mean.

Approach A and B:  $\log\text{MAR}_{\text{BiS}} = \log\text{MAR}_{\text{OU}} - \log\text{MAR}_{\text{BE}}$ .

Approach C:  $\log\text{MAR}_{\text{BiS}} = \log\text{MAR}_{\text{OU}} - (\log\text{MAR}_{\text{OD}} + \log\text{MAR}_{\text{OS}})/2$ .

P value – significance threshold < 0.05 (bold).

**Figure 2.** Mean binocular summation across different luminance and VA conditions determined with three different approaches.

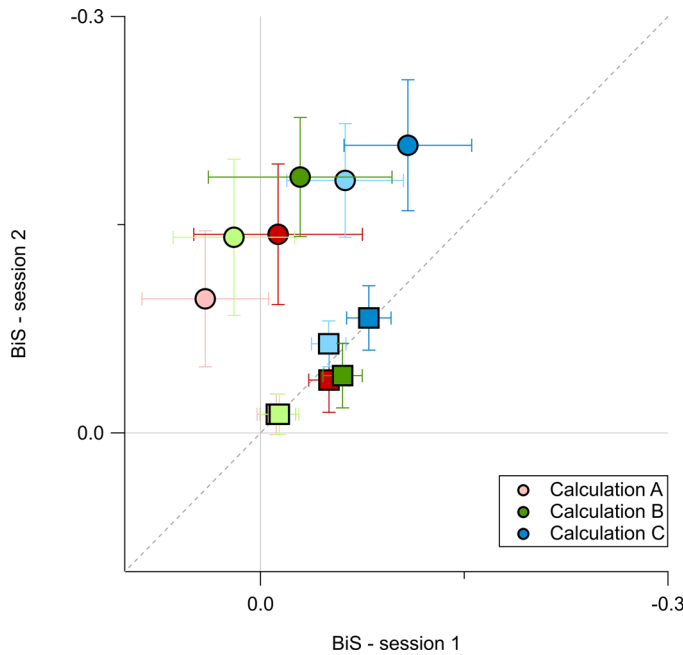
Mean values and SEM of mean BiS for both luminance conditions (photopic and scotopic) and both VA types (cVA and hVA) [logMAR] are given for each group of calculations. BiS are calculated as the difference of binocular LogMAR and monocular LogMAR (A) For the better eye of each day; (B) for the better eye of both days; (C) for the mean across both days; approach B is less prone to misestimations (see text). Binocular improvement is given in logMAR, *left*, and as the corresponding binocular summation ratio (BSR), *right*. Note the inverted axis for the logMAR values so that binocular inhibition is shown at the *bottom* and good summation is at the *top*. There were no significant main effects of VA type and of luminance on BiS. The *horizontal line* indicates the established binocular improvement in literature, 40%.

BiS were correlated with monocular VA of either eyes, that is, OD or OS.

## Discussion

Binocular visual acuity measures were, on average, significantly better than monocular for cVA and

hVA under both luminance levels. Upon calculation of binocular summation, improvement of VA reached [3% photopic|12% scotopic] for cVA and [15% photopic|28% scotopic] for hVA. However, these trends of binocular-summation differences did not reach significance, that is, binocular summation did not differ significantly between cVA and hVA and for photopic and scotopic conditions.



**Figure 3. BiS comparison between sessions.** For each of the four VA conditions, the average BiS  $\pm$  SEM indicate the binocular VA improvement (cVA = squares; hVA = circles; photopic = light fill; and scotopic = dark fill; colors indicate BiS calculation method, see Methods). Although there is a trend for hVA improvement in session 2, no significant session effect was evident as detailed in Results and Figure 1. Note the inverted axes for logMAR values resulting in weaker BiS in the bottom left and stronger BiS in the top right. The identity line is dashed, the two solid zero lines indicate the transition from BiS to binocular inhibition for sessions 1 and 2.

## Comparison to Previous Studies

For photopic BiS, others reported a BiS between 7% and 17% of binocular cVA compared to monocular cVA.<sup>40,42,57,58</sup> These estimates were slightly higher than the cVA BiS in the present study, that is, 3%, for photopic conditions. This could be due to different test settings, calculation approaches, and individual conditions of the test subjects. In the previous studies, letter recognition tasks<sup>42,58</sup> and Landoldt rings<sup>40,48,57</sup> were also used to measure cVA BiS. For hVA, previous studies reported a BiS from 60% to 0 (binocular equivalence),<sup>43,44,59</sup> that is, a range that covered our finding of 15%.

For scotopic BiS, we found no comprehensive investigations of hVA under scotopic conditions. Under comparable contrast conditions, Home found a summation between 20% and 25% for cVA.<sup>48</sup> Furthermore, a higher BiS for cVA was shown in a darker environment.<sup>48</sup> This aligned with our results, whereby we were able to extend this finding to hVA. We filled this gap and found 28% BiS for hVA under scotopic conditions. For other visual tasks, scotopic BiS ranged from 80% to 0%, that is, binocular equivalence.<sup>52,53,60</sup>

Most studies addressing BiS under scotopic conditions were of small sample size, dated back to the first half of 20th century, and varied in visual tasks, which might explain the discrepancies of the findings. Thylefors et al. recently investigated retinal sensitivities using dark adaptometry and found a BiS of  $> 40\%$  in healthy individuals in comparison to monocular recordings.<sup>52</sup>

Several factors might influence VA BiS, such as attention and test complexity.<sup>29,40</sup> Further, the greater interindividual variability reported in BiS might be due to different numbers of binocularly gated neurons in the cortex.<sup>40</sup> We report similar BiS for both VA types, that is, cVA and hVA, and for scotopic and photopic conditions. This indicates that similar binocular summation mechanisms might be in operation for both luminance levels independent of acuity type. In this study, we used Landoldt rings, possibly relying on orientation recognition, to investigate BiS and we believe this would apply to other forms of VA, namely letter recognition VA tests. Pardhan, for example, reported independence of target from either orientation or contrast levels.<sup>30</sup> Zlatkova et al. also demonstrated comparable BiS for both recognition, letters A to Z, and resolution acuity, gratings in 45 degrees and 135 degrees, at the fovea.<sup>61</sup> More sensitive paradigms would be needed to probe for potential differences in binocular processing for the different acuity conditions/luminance levels used. This might be achieved by increasing the sample size.

## Dependence on Session

To assess test reproducibility, we tested intersession differences for each type of VA BiS. Here, we found for hVA borderline learning effects, which, however, failed to reach significance. To the best of our knowledge, a learning effect in BiS has not been reported before. Consequently, this issue deserves revisiting in a dedicated study. With respect to monocular VA testing, we did not find any effects, which is in accordance to our previously demonstrated absence of learning effects for VA.<sup>13,62</sup> In fact, monocular learning effects were reported after hundreds of trials between sessions.<sup>62</sup> FrACT is, thus, a reliable and reproducible VA test and can, due to the lack of a significant learning effect, be used without previous training sessions.

## Binocular Summation Correlations Across Different Conditions

Inference of one visual task on another, for example, photopic and scotopic, might spare efforts and time to test each one separately. In addition, it might elucidate common or separate mechanisms of binocular

summation for the different VA types. In line with other studies, we did not observe any correlations, neither between photopic versus scotopic measures<sup>13</sup> nor between cVA versus hVA tests. It should be noted, though, that the correlation analysis in our study was limited by the small range of the VA data, which warrants further investigations in future studies.

## Practical Considerations and Potential Applications

The findings of this study promise potential in clinical practice. BiS was evident for both cVA and hVA under scotopic and photopic conditions. The obtained BiS values for the different conditions could serve as a reference in future studies. The freely accessible test FrACT allows the assessment of VA over an extremely wide range and is thus ideally suited to extend our findings to other age groups and distinctive disease entities, for example, rod dystrophy and achromatopsia. Consequently, BiS might serve as a diagnostic biomarker in these diseases with a potential to monitor the effect of novel therapeutics on binocular function. Here, for the BiS to change, the relationship between monocular and binocular testing must change. This can be caused by a change in the VA of the individual eyes. However, the BiS takes place in the visual cortex and thus provides more information about neuronal processing than individual VA measurements per se. The testing paradigm used in this study warrants further optimizations in future studies, for example, shortening of scotopic adaption duration, 40 minutes, or shortening hyperacuity trials.

## Limitations

The following limitations need to be acknowledged in this study. (1) Only young healthy participants were included, and it would be interesting to replicate these findings across different age ranges as well as in diseases affecting both scotopic and photopic VA. (2) The currently long measurement duration of scotopic VA, that is, a 40-minute time of dark adaptation, limits the application of such testing in VA in clinical practice. This might be addressed by investigating the best adaptation duration and VA trade-off; for example, routine mesopic contrast testing for certain German traffic licenses requires only 5 minutes of dark adaptation. (3) No compelling significant session effect was evident, although there was a nonsignificant trend for higher hVA in the second session. Whereas this hints at a binocular learning effect that might be specific to hVA, its significance remains unresolved and would

need to be addressed in future research. (4) Weber contrast was not identical for the two luminance conditions (scotopic < photopic contrast), which might account for the, albeit nonsignificant trend, of higher BiS under scotopic conditions.

## Conclusions

This study represents the first evaluating BiS for both cVA and hVA under different luminance conditions. Here, we demonstrated that BiS is readily determined for various VA conditions, using a freely accessible online VA test, that is, FrACT, and can thus be applied by other laboratories for follow-up studies. Our results indicate that binocular summation of VA is equally relevant for hVA and cVA as well as scotopic and photopic conditions.

All in all, we, here, introduce a readily reproducible approach to determine BiS measures, that are of promise as a specific biomarker to monitor therapy outcome on binocular rod and cone-mediated vision.

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