The relationship between visual resolution and cone spacing in the human fovea

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Abstract

Visual resolution decreases rapidly outside the foveal center. The anatomical and physiological basis for this reduction is unclear. We used simultaneous adaptive optics imaging and psychophysical testing to measure cone spacing and resolution across the fovea, and show resolution is limited by cone spacing only at the foveal center. Immediately outside the center, resolution is worse than cone spacing predicts and better matches the sampling limit of midget retinal ganglion cells.

Neural sampling of the retinal image plays an important role in limiting human visual resolution at all locations in the visual field except the fovea, where optical aberrations usually impose a fundamental limit1–5. When aberrations are minimized, the instantaneous postreceptoral information is believed to be limited by the spatial sampling of the cone photoreceptor mosaic in the fovea and possibly beyond1–5. To the first order, this limit can be considered to be the Nyquist sampling limit of the cone mosaic (Nc). Foveal cones each connect via a cone bipolar cell to at least two retinal ganglion cells (RGCs) and since the majority of the RGCs in the central retina are of the midget class, it is presumed that each cone in the central fovea connects to both an ON-and OFF-center midget retinal ganglion cell (mRGC)6–7. This is the so-called “private line” hypothesis8 which forms the basis of the argument that cone spacing should limit resolution wherever this retinal circuitry is in place. At some point outside the fovea, signals from multiple cones converge onto single mRGCs, compromising resolution, and thus at some point visual resolution no longer matches Nc but instead matches the Nyquist limit of mRGCs6–7.

The eccentricity where convergence in the mRGC network begins is not clear, with anatomical evidence suggesting between 3.5 degrees6 to 6 degrees7 from the foveal center. Psychophysical studies which sought to compare Nc to visual resolution vary considerably, with estimates of the match between Nc and resolution persisting to anywhere from 2
degrees to 10 degrees from the foveal center. Consequently, the relationship between visual resolution and \( N_c \) remains unknown (see Supplementary Information). The large variability in psychophysical investigations stems in part from the difficulty in directly measuring both \( N_c \) and optically optimal visual resolution in the same individuals, forcing comparisons of their resolution measurements with sampling limits derived from different eyes, primarily from histological reports. It is now well established that cone spacing, especially in the central fovea, is highly variable between individuals, making these comparisons susceptible to error. The adaptive optics scanning laser ophthalmoscope (AOSLO) overcomes these limitations, allowing simultaneous measurement of the minimum angle of resolution (MAR), the cone spacing, and the precise location and motion of the stimulus across the retina.

An AOSLO was used to project an adaptive optics corrected tumbling E stimulus onto the retina at several locations within the central fovea (0–2.5° from the foveal center) of five observers. Adaptive optics minimizes blur by measuring ocular aberrations and compensating for them with an adaptive element, improving optical quality for imaging and high resolution stimulus delivery. Adaptive optics significantly improves vision and has been shown to reduce the MAR at the preferred retinal locus of fixation (PRLF) by ~33% in normal observers. In a four alternative forced choice task, observers reported the orientation while fixating the stimulus or a peripheral target. Each observer was tested at retinal locations temporal to the PRLF; one (S4) was also tested at superior, inferior and nasal locations. A video of the retina was acquired on each trial, encoding the exact location of retinal stimulation (see Supplementary Videos 1 & 2).

Retinal imagery is overlaid with a topographic map of stimulated cones in Fig. 1 for observer S3. A map was generated for each observer by precisely determining each cone that interacted with the stimulus over the course of each trial (see Supplementary Methods and Supplementary Video 3). The expected falloff in MAR with increased distance from the PRLF was observed (Fig. 2a). Fixational variability caused some test locations to deviate slightly from the horizontal meridian (Fig. 1), so actual distances from the PRLF are shown in Fig. 2. The magnitude and rate of reduction in MAR matched the performance reported in the literature from studies that measured resolution across the fovea using high contrast laser interference fringes (see Supplementary Information). An important value to note is the \( E_2 \) value (the eccentricity in degrees at which the threshold doubles); the mean \( E_2 \) of the MAR (\( E_{2m} \)) for all observers was ~1.275° (n = 5).

\( N_c \) along the horizontal temporal retina is plotted in Fig. 2b. Where cones were well resolved, center-to-center inter-cone distance (ICD) was measured directly from identified cone centers and used to calculate \( N_c \), where: \( N_c = \frac{\sqrt{3}}{2} \times ICD \). This conversion is required because the Nyquist limit for a triangularly packed cone photoreceptor mosaic is based upon the spacing between rows of cones. An assessment of mosaic regularity confirmed that this was an appropriate method for calculating \( N_c \) (see Supplementary Information). Cones were resolved at the PRLF for one observer (S3); cones became resolved for other observers between 0.14°–0.5° from the PRLF. \( N_c \) at the PRLF for these observers (and S2 at 0.4°) was therefore estimated from retinal imagery (see Supplementary Information). Similar to \( E_{2m} \),
we can compute $E_{2c}$, the value at which $N_c$ doubles; mean $E_{2c}$ was $-2.224^\circ$ ($n = 5$), nearly double $E_{2m}$.

MAR is plotted against $N_c$ at test locations in Fig. 2c. MAR agreed well with estimates of $N_c$ at the PRLF, in agreement with previous researchers\textsuperscript{1-5}. However, MAR decreased at a greater rate with increasing eccentricity than was predicted by $N_c$. If MAR exactly matched $N_c$, data points would be expected to fall on the dashed 1:1 line shown in Fig. 2c. The slope is the important factor in this comparison, as a slope of 1 demonstrates that MAR is governed by $N_c$. A linear regression line was fit to the data of each observer independently. The mean slope was 0.6355 (SD = 0.1058; $n = 5$). This value was significantly different from 1 (t-test; one sample; $p = 0.00153$), indicating that MAR was worse than predicted by $N_c$ at locations eccentric to the PRLF. Choosing a different threshold for acuity (i.e. 75% vs. 82.5%) would only have resulted in horizontal translations of the regression line fits. Choosing a different metric to represent $N_c$ would have changed the slope; for the most extreme case, of a square mosaic, the slope would still only have been $-0.73$. Bland-Altman analysis\textsuperscript{13} confirmed poor agreement between MAR and $N_c$ across test locations (see Supplementary Information). This discrepancy does not seem to be explainable by the nature of the stimulus (see Supplementary Information) or task, as the tumbling E task has been shown to be a sampling limited task\textsuperscript{14}.

The area where visual resolution most closely matched $N_c$ (0–0.5°) corresponded well with the anatomically distinct foveola, the nearly flat floor of the foveal pit\textsuperscript{8}. This retinal area has several features that are seemingly optimal for high spatial resolution, including: maximum cone density, elongated waveguides, the absence of rods and S-cones, and the lack of overlying vasculature and nerves\textsuperscript{8,9}. However, we believe the discord between resolution and $N_c$ seen outside the foveola was primarily due to differences in retinal circuitry across the fovea. Since the fibers of Henle displace RGCs from the photoreceptors of the central retina to which they form connections, foveal circuitry has historically been difficult to characterize\textsuperscript{6,8,15}. Careful study of these fibers leads to new predictions of mRGC receptive field density across the visual field\textsuperscript{15}. Using a theoretical model of mRGC receptive field density\textsuperscript{15}, we estimated the Nyquist limit of the mRGC mosaic (the spacing between neighboring ON- or OFF-center mRGC receptive fields) at the resolution test locations along the horizontal meridian (see Supplementary Information) and compare it to MAR in Fig. 2d. An individual regression line was fit for each observer; the mean slope was 1.0111 (SD = 0.1105; $n = 5$), this value does not differ significantly from 1 (t-test; one sample; $p = 0.8333$), indicating that MAR for this task is governed by the Nyquist limit of the mRGC mosaic across the fovea. Cortical mechanisms ultimately utilize the information provided by the earliest stages of visual processing in the retina to make a decision in a visual resolution task; that those decisions so closely match the theoretical sampling limits imposed by the first stages of retinal processing is remarkable.

**Supplementary Material**

Refer to Web version on PubMed Central for supplementary material.
Acknowledgments

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Figure 1. Cone stimulation map for subject S3
Cones appear as bright circles arranged in a triangular lattice pattern. Stimulated cones are shown as topographic maps overlaid in color. Color bar shows normalized level of cone stimulation.
Figure 2. Visual resolution matches the Nyquist limit of the mRGC mosaic, not the cone Nyquist limit

a, Visual acuity as a function of eccentricity. Symbol legend is inset in (d). For observer S4, t, n, s, and i denote temporal, nasal, superior and inferior locations. Error bars are ± s.e.m. and omitted when smaller than symbol. 
b, Cone Nyquist limit across the horizontal temporal retina. Lines colored by subject in the same way as symbols (see legend inset). Solid lines are measurements; dashed lines are predictions.
c, Cone Nyquist limit and MAR for temporal test locations. Cone Nyquist limit is mean of cones within an elliptical area subtending ± 2SD of mean stimulated location. Error bars are ± s.e.m. and omitted when smaller than symbol. Dashed black line is the 1:1 line.
d, Nyquist limit of mRGC and MAR. Only results along horizontal meridian are shown for S4. Dashed black line is the 1:1 line.