

Frequency-Doubling Technology and Parasol Cells

Swanson et al.¹ have reported an excellent study of the responses of macaque retinal ganglion cells (RGCs) to Goldmann size III stimuli and contrast-modulated grating stimuli. They estimated the contrast gain of the initial rising phase of the contrast response function of the cells. From the physiology shown, the extracellular recorded RGCs are parasol and midget RGCs and are referred to in terms of their lateral geniculate nucleus (LGN) targets as M- and P-cells, respectively. The ratios of the gains for the two RGC types indicated that size III stimuli have higher relative gain for M-cells than the grating stimuli. Given that the gratings are described as displaying the frequency-doubling (FD) illusion, this may be taken to mean that the stimuli of the FDT perimeter do not preferentially stimulate a pathway that is useful for glaucoma diagnosis.

The original idea of FD stimuli was that they might stimulate nonlinear Y-cells.² Such cells had been reported from extracellular recordings of the M-layers of the primate LGN and so were dubbed M_Y -cells. No anatomic substrate was known. The concept was that if humans were like all other mammals, Y-like cells should be larger and less densely overlapping than their X-like (parasol cell) partners. Cell losses could be more easily detected if the lower densities meant few of these Y-cells saw each point in visual space.²⁻³ Recently, anatomic substrates for primate Y-cells have been reported: the smooth monostratified cells.^{4,5} These cells match the proposed requirements for cell density but otherwise receive the same inputs as the smaller, denser parasol cells and are anatomically similar to cat α -cells, the original Y-cells. Thus, whether parasol cells prefer size III stimuli to gratings may say nothing about FDT perimetry. Parasol cells projecting to the superior colliculus have also been reported to have Y-like responses.⁶ Swanson et al.¹ do not cite these recent papers on primate Y-cells.

Another caveat is that the grating stimuli used would probably not display the FD illusion. A recent examination of the probability of humans reporting FD at 8 parts of the visual field indicates that subjects would have only a 50% chance of reporting an FD percept for the grating stimuli used.⁷ That study also indicated two possible independent sources of the FD illusion at every point in the visual field. So perhaps FD has multiple causes, some of which are useful for visual field assessment. By contrast, small size II stimuli may promote test-retest variability.⁸

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Author Response: Frequency-Doubling Technology and Parasol Cells

The authors thank Dr. Maddess for his letter. As previously,¹ he suggests that nonlinear Y-like retinal ganglion cells are responsible for the frequency-doubling (FD) illusion, an argument that we challenged in White et al.,² on three grounds: (1) No evidence was obvious at that time of a separate nonlinear Y-like MC cell class in primate retina ganglion cells; (2) even if there were such nonlinear ganglion cells, the responses of linear MC cells to FD stimuli are robust, and there is no reason they should be ignored; (3) no spatially modulated signals (which might underlie the FD illusion) could be expected from the nonlinear responses of such ganglion cells; their response is nonlinear in time but not in space. We suggested that the FD illusion is due to a psychophysical loss of phase sensitivity at a central site. Dr. Maddess only addresses item (1), the existence of nonlinear cells, referring to new anatomic and physiological studies that demonstrate the presence of a rare Y-like class of primate retinal ganglion cells. However, items (2) and (3) still refute his suggestion: The linear MC cells respond robustly to the FD stimuli, and the FD illusion cannot be explained by nonlinear responses of Y-like ganglion cells.²

The purpose of our recent study³ was to compare MC and PC cell responses to stimuli used in conventional perimetry and FD perimetry. We did not make assumptions as to whether FD perimetry is related to the FD illusion, or whether M_Y cells mediate the FD illusion. FD perimetry is a flicker-detection task, and there is very good evidence that the "regular" MC pathway mediates sensitivity to luminance flicker.⁴ We chose our FD stimulus parameters on the basis of stimuli used in clinical FD perimetry, which measures flicker sensitivity and not the FD illusion. In a prior clinical study⁵ we used the 12-Hz, 0.5-cyc/deg stimulus for FD perimetry and generated predictions that we tested with the present study, using a 13-Hz, 0.5-cyc/deg stimulus; 13 Hz was the closest approximation we could make to 12 Hz with this monitor, and any effect caused by such a small change in temporal frequency should be insignificant.

At the end of his letter, Dr. Maddess suggested that conventional size III stimuli may "promote" test-retest variability. We

addressed this before⁵ and in the present study³: For both FD and size III stimuli, as contrast increases above normal contrast threshold, the ganglion cell responses begin to saturate, and this effect will increase test-retest variability. Much of the reported high test-retest variability for size III can be accounted for by the large range of high stimulus contrasts. Perimetry with the size III stimulus uses a much greater range of contrasts than does perimetry with FD stimuli, because FD stimuli cannot exceed 100% contrast. Ganglion cell saturation means that contrasts greater than 100% produce little additional visual response, so that the use of these high contrasts increases variability. Figure 1 illustrates this with unpublished size III and FD variability data from five patients with advanced field loss, with variability for the size III stimulus computed using both the entire 3.5-log-unit range, as well as with a range comparable to that of FD (created by assigning all size III contrast thresholds greater than 100% contrast to be equal to 100% contrast). When the difference in range is accounted for, variability for size III and FD are comparable (solid and dashed horizontal lines show averaged SDs for FD and size III perimetry with comparable ranges).

There is very good evidence that the “regular” MC pathway can account for sensitivity to luminance flicker; it appears that MC cells can mediate contrast sensitivity for stimuli such as those used in FD perimetry: low spatial frequencies modulated at high temporal frequencies. These stimuli are in what Kelly⁴ called the “high-velocity corner” of the spatiotemporal contrast-sensitivity surface. Behavioral studies in macaques with lesions showed that damage to the M-pathway reduces contrast sensitivity for this high-velocity corner.⁶ Single-unit electrophysiology showed that M-cells have a signature characteristic of such psychophysical mechanisms.⁴

The origin of the FD percept is more difficult to pin down. We originally proposed it to be due to a loss of phase discrimination at a central site² and provided some other arguments against an origin in an M_v-based cell type. It is interesting to note that Y-like cells, although delivering a frequency-doubled response to counterphase-modulated gratings, also deliver a very strong first-harmonic response to such a stimulus at low spatial frequencies. Since the FD illusion is independent of spatial frequencies in the lower spatial frequency range (as shown in the recent paper by Maddess et al.,⁷), this would be in favor of the phase explanation rather than one involving Y-like cells. Another interesting point is that with the FD illusion, the transition areas between the flickering bars appear rather static (“null points”), yet this is the point at which the second harmonic (2F) response should be most obvious. In general, we have found it difficult to provide a strong link between the frequency-doubled response and the FD illusion.

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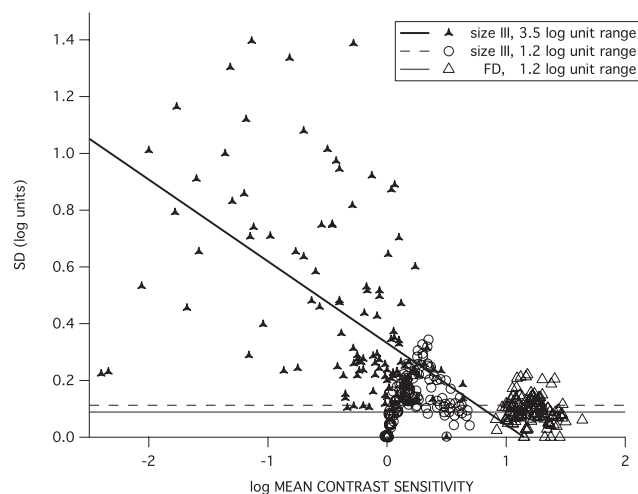


FIGURE 1. Test-retest variability versus contrast sensitivity for FD perimetry (*open triangles*) with a 1.2-log-unit range of contrast sensitivities, and conventional (size III) perimetry with both 1.2-log-unit (*open circles*) and 3.5-log-unit (*solid triangles*) ranges. For size III with the 3.5-log-unit range, SD increased as mean decreased ($P < 0.001$), but this was not the case for FD or size III with a 1.2-log-unit range ($P > 0.12$).

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