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Retinal Electrophysiology

A multiple-frequency, multiple-region pattern electroretinogram investigation of non-linear retinal signals

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ABSTRACT

It has been proposed that the spatial frequency doubled (FD) illusion may originate from Y-like non-linear retinal ganglion cells. If the contrast of multi-frequency stimuli is increased, Y cells show a phase advance in the self-sum frequencies but not in other output frequencies. We looked for these effects with a multi-region pattern electroretlnogram (PERG) displaying the sum of two temporal frequencies in each visual field location Regional variation was found in the recorded sum and difference frequencies. The results indicate that PERG signals become dominated by responses from Y-like cells when the FD illusion is seen.

Key words: magnocellular; multi-region non-linear, pattern electroretlnogram, rectifying, sandwich model, spatial frequency doubled illusion sum of sinusoids, Y cells.

Retinal ganglion cells projecting to the magnocellular layers of the primate dorsal lateral geniculate nucleus (dLGN) are divisible into the quasilinear M_x cells and the non-linearly responding M_y cells. The retinal gain control described by Shapley and Victor[1,2] for cat X and Y cells is strongly expressed in primate M cells[3]. There is an increasing body of evidence suggesting that the frequency doubled (FD) illusion of Kelly[4,5] corresponds to M_y cell gain control-mediated activity[6,7]. The FD effect is that low spatial frequency gratings modulated at high temporal frequencies (where the gain control is strongest[2,8,9]) are seen with twice their original spatial frequency[4,5,7,10].

The Y cell non-linear pathway has been described as a contrast-dependent linear-non-linear-linear sandwich model[2]. The model includes an initial linear filter (L1) at the receptive field subunit level, a subsequent non-linear transduction (rectification) followed by a second linear filter (L2) at the level of summation of the subunit outputs.[8] The non-linearity is well-modelled by squaring and thus produces intermodulation frequencies ($f_i + f_j$) in response to multiple input frequencies. For Y cells, the phases of responses at self-sum frequencies ($f_i + f_i$) advance with increasing contrast but the phases of the other output frequencies ($f_i \pm f_j$, $i \neq j$) advance less,[2] suggesting that contrast primarily modifies L1 For example, the two output frequencies 7 and 7.1 Hz may be produced by inputs such as 37.1-30 and 3+4 Hz. If the phases of these similar outputs change together, this means L2 changes. This is not observed,2 instead, frequencies whose inputs are similar change together, suggesting changes to L1 by contrast. The present study examines whether contrast-dependent phase shifts characteristic of retinal gain control acting on Y type cells are observed in pattern electroretinograms (PERG) obtained using FD stimuli.

METHODS

The visual stimulus had nine regions (Fig. 1) and the outer eight were used. Each region contained an achromatic sinusoidal grating (45 cd/m^2). Two spatial frequency sets were examined: a coarse set, SF_{co} = (0.2 c.p.d. inner, 0.1 c.p.d. outer regions), and a very coarse set, SF_{vc} =(0.1 c.p.d. inner, 0.05 c.p.d. outer regions). Each trial lasted 40.35s , providing a frequency resolution (dF) of 0.0248 Hz. Two sets of temporal modulations were used, one combining low frequencies with high, $TF_{low} = F_{low} + F_{hi}$, and one combining medium frequencies with high, $TF_{low} = F_{med} + F_{hi}$ where F_{low} = dF* (108 111 115 120 128 138 152 173), F_{med} = dF* (188 242 275 309 438 573 629 676) and F_{hi} = dF*(676 715 908 1048 1073 1165 1256 1362). The frequencies were incommensurate and orthogonal so that discrete output fre-

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quencies could be obtained for all inputs (except dF*676). If only the high frequencies were used, the FD illusion would be seen well for SF_{VC}, and quite well for SF_{CO}[11]. The two modulation amplitudes tested had maximal contrasts of 0.48 and 0.96. Details of the electroretinogram methods are given elsewhere.[7] Subjects' right eyes were used and informed consent was obtained (ANU protocol M881).

Multiple regression analysis with an iterative stepdown model pruning procedure (SPSS, SPSS Inc., Chicago, IL, USA) produced the most parsimonious models explaining changes in phase and amplitude with increasing contrast. The fitting procedure was given the option of fitting a constant effect for phase, separate slopes for the self-sum ($f_i + f_j$ i=j), different sums ($f_i + f_j$, $i \neq j$) and differences ($f_i - f_j$, $i \neq j$). Variation due to different visual field regions was also examined but is not described here.

RESULTS

Subtracting small independent effects of spatial frequency and regional variation revealed a complex relationship between the phase differences of the responses and output temporal frequency (Fig. 2). For SF_{vc} (Fig. 2b,d) phase differences for the self-sum frequencies increase with increasing temporal frequencies. Different sums and difference frequencies showed little phase advance. In particular, self-sum and intermodulations ($f_i \pm f_j$, $i \neq j$) with similar output frequencies behave differently, reminiscent of changes by contrast gain control to the leading filter (L1) in sandwich models of Y cell responses.

For the less coarse patterns, SF_{co} as temporal frequencies increase phase differences for all frequencies decrease (Fig. 2a,c). However, self-sums still advance relatively more than intermodulations, suggesting that phase lags from some other cells create the net decrease in phase. It is worth noting that the iterative stepdown regression analysis consistently rejected the option of fitting the phase advances for different sums and difference frequencies in Fig. 2a,c with a single line. This was reflected in fits to the amplitude data (not shown), suggesting the effects observed for phase difference were real. Moreover, the multivariate regressions on amplitude were superior (F = 9.92 and 19.53 for contrasts 0.48 and 0.96) to those obtained for phase difference (F=6.05; all 14, 247 d.f.).

From Table 1 it can be seen that the FD illusion was seen mainly in response to the higher TF set While decreasing the contrast did reduce the probability of seemg the illusion, decreasing the spatial frequency did not have a major effect on the visibility of the illusion. At the low TF set, the illusion was seen only where the highest input frequency fell between 16 and 26 Hz (i.e. when gain control would act most strongly).

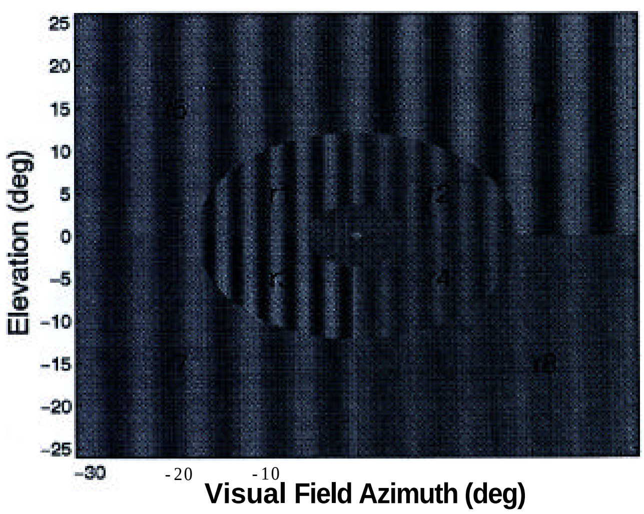

Figure 1. Illustration of the visual stimuli employed for both the PERG and psychophysical experiments. The picture is as if the stimulus sequence had been stopped midway through the experiment. As the pairs of temporal modulations in each region are asynchronous the contrasts of the individual regions differ in the stopped frame.

DISCUSSION

For the conditions TF_{med} and SF_{vc} it can be said that the phase differences observed for recordings obtained at contrasts 0.48 and 0.96 behave as Y cell physiology would predict. That is, the self-sum frequencies showed strong phase advances with increasing contrasts while the intermodulation frequencies did not. In particular, self-sum and intermodulation frequencies with similar output frequencies show different behaviour, consistent with little or no effect of contrast upon the second filter (L2) in sandwich models of Y cells.[2]

Table 1. Regions shown in Fig. 1 where the illusion is seen for the multi-frequency stimulus at contrast 0.96.

Subject	Stimulus conditions	Nasal regions	Temporal regions
	TF_{low}, SF_{vc}	5,* 7*	2,* 8*
2			None
3		None	None
	TF_{low}, SF_{co}	5,* 7	6,* 8*
2			None
3		1,5	6
	TF_{med} SF_{vc}	I, 3,* 5, 7*	2,* 4,* 6,* 8*
2		1, 3, 5, 7	2,* 4,* 6, 8
3		1, 3, 5, 7	2,* 2,* 6,* 8*
	TF_{med} SF_{co}	1,* 3,* 5,* 7*	2,* 4,* 6,* 8*
2		1, 3, 5, 7	2,* 4,* 8*
3		1,* 5*	2,* 4*

Results at contrast 0.48 were very similar. All subjects were experienced in judging the presence of the illusion.[11] * The illusion was seen very reliably in that region.

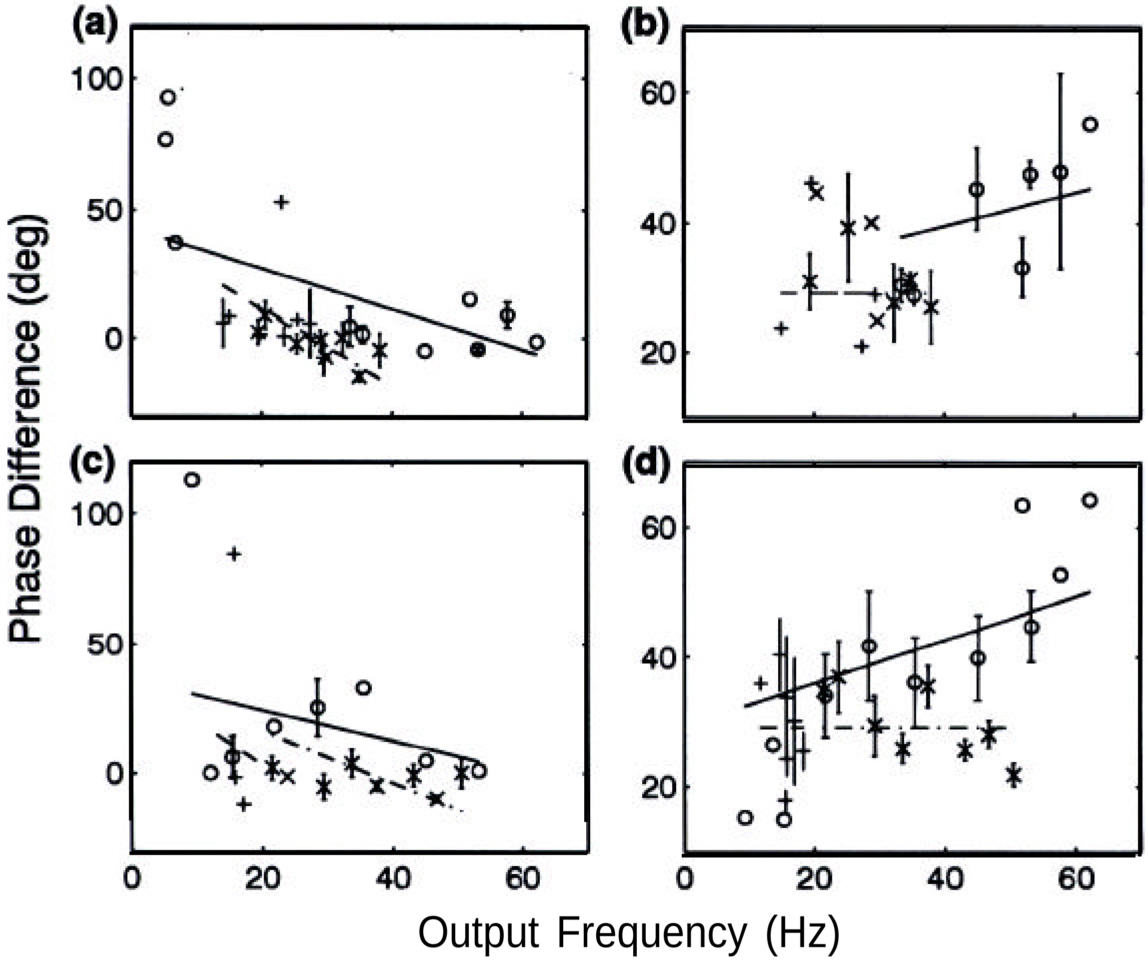

Figure 2. Independent effects of output temporal frequency upon phase difference for experiments at contrasts 0.48 and 0.96. (a,c) The data were obtamed with the higher spatial frequency condition SF_{co}, and (b,d) for SF_{vc} The rows correspond to the TF_{low} condition (a,b) and TF_{med} conditions (c,d). (o) Self-sums, (x) different sum, (+) difference, frequencies.

For the two SF_{co} conditions the behaviour of the intermodulation frequencies was more complex: different sum and difference frequencies having different slopes and all frequenτιεσ showing decreasing phases with increasing contrast. The overall phase decrease could be due to the contribution of other cell types. The more complex behaviour of the intermodulation frequencies could be modelled by a sandwich system in which L2 showed some change with contrast, again possibly reflecting the activity of other cell types being added to the PERC response. Nevertheless, a relative increase of the phases of self-sum frequencies occurred indicating some Y-like activity. The strong visibility of the illusion for conditions in Fig. lc, where evidence for Y-like activity is weaker, could indicate that there are two generators of the FD illusion, one operating at lower spatial frequencies and moderate temporal frequencies and another operating at higher spatial and temporal frequencies. This is also suggested by the psychometric functions describing the visibility of the FD illusion.[11]

The FD illusion was not seen well for either TF_{low} case. We interpret this as the activity of linear cells responding to the low frequencies with a strong response at the fundmental: swamping the FD component. The Y-like activity in Fig. 1b may be due to X-like M cells, which are similarly affected by gain control but which have a weak quadratic response.

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