A re-evaluation of the mechanisms underlying simple cell orientation selectivity

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Following from evidence supporting GABA as a putative inhibitory transmitter in the visual cortex, we have iontophoretically applied the GABA antagonist N-methyl bicuculline (Nmb) to simple cells in order to block the inhibitory inputs acting on them. We found that under these conditions previously sharply-tuned simple cells responded equally to all orientations. Moreover receptive field dimensions, judged by the response to stimuli at the optimal and orthogonal orientations, equated best with that expected from a single dLGN cell input. It seems thus, that asymmetries in the excitatory input are not a significant factor in the generation of simple cell orientation selectivity. The asymmetry underlying orientation selectivity rather originates from the operation of an intracortical inhibitory mechanism.

Orientation selectivity is one of the principal properties characterizing visual cortical neurones, and yet we know very little about the mechanisms that establish it. In their by now classical study of visual cortical organization, Hubel and Wiesel proposed that the orientation selectivity of visual cortical cells was established by the organization of the excitatory input to simple cells in layer IV. They suggested that each simple cell received convergent excitatory input from several dorsal lateral geniculate (dLGN) cells, with receptive fields displaced so as to form a row, the direction of which established the orientation of the field. Although this model only refers to the contribution of excitatory connections Hubel and Wiesel noted the possibility that inhibitory connections may be involved. Indeed there is good evidence supporting the view that inhibitory processes are a very important factor in the generation of orientation selectivity. Sillito reported that simple cell orientation selectivity was reduced but not eliminated during the iontophoretic application of the GABA antagonist bicuculline. This experiment followed from evidence suggesting that GABA is an inhibitory transmitter in the visual cortex and was based on the assumption that iontophoretically applied bicuculline would effectively block the action of the inhibitory synapses acting on the cell under study. The results were consistent with the view that simple cell orientation selectivity is basically set up by an excitatory mechanism, although enhanced by intracortical inhibitory processes. However, recently Tsumoto et al. claimed that simultaneous iontophoretic application of
bicuculline and an inhibitor of GABA synthesis, 3-mercaptopropionic acid, eliminated simple cell orientation selectivity in 2 out of 4 cells tested.

This introduced the possibility that the limited effect of bicuculline on simple cell orientation selectivity seen by Sillito\textsuperscript{10}, reflected only a partial block of inhibitory inputs rather than a limited involvement of these in generating the cell's orientation selectivity. We have reinvestigated this matter using the more potent GABA antagonist N-methyl bicuculline (Nmb).

The experiments were carried out on cats paralyzed with gallamine triethiodide and artificially ventilated with a mixture of 70\% N\textsubscript{2}O/30\% O\textsubscript{2} supplemented as necessary with 0.1–0.5\% halothane. Five barrel micropipettes were used for recording unit activity and drug application. Full details of procedures are given elsewhere\textsuperscript{12}. All simple cell responses were documented on line by constructing peristimulus time histograms (PSTHs) for each testing orientation. Stimulus contrast was adjusted to control for the possibility that saturation of the excitatory response mechanisms was contributing to loss of stimulus specificity\textsuperscript{10–12}.

The present data are based on cells recorded in area 17 and defined as simple both with respect to conventional criteria\textsuperscript{3,4}, and the response to moving light or dark edges\textsuperscript{7,8}. A total of 13 cells was studied for periods of 3 h or more and response properties compared before, during and after the iontophoretic application of Nmb. All showed a reversible and reproducible loss of orientation selectivity during Nmb application. This is illustrated in Fig. 1. Normally this cell responded to only one direction

![Figure 1](image-url)

Fig. 1. Action of N-methyl bicuculline (Nmb) on simple cell orientation selectivity. Testing orientation and direction of stimulus motion is indicated above each set of PSTHs. Dotted line subdivides records into zones corresponding to the two directions of motion. Optimal orientation is arbitrarily referred to as zero, –, indicates anti-clockwise rotation from optima, +, clockwise rotation. Each PSTH constructed from 25 trials. Bin size 50 msecs. Vertical calibration indicates number of counts per bin.
of motion at the optimal orientation and exhibited no response to testing orientations 45° either side of the optimal, or 90° to it. During Nmb application the cell responded to both directions of motion at all testing orientations. Further examples of the effect of Nmb on simple cell orientation selectivity are given in Fig. 2. If simple cell excitatory fields are elongated in the plane of the optimal orientation \(^4\) one would expect that the excitatory discharge zone revealed to stimuli moving at the orthogonal orientation (90°) during Nmb application would be more extended than that seen to stimuli moving at the optimal. Further to this, one would expect that the simultaneous activation of an elongated field by an optimally oriented slit passing over it, would still produce a larger response than that seen to the motion of a slit at the orthogonal orientation, which would successively rather than simultaneously activate the convergent dLGN inputs to the cell. Neither of these predictions are supported by our data. In fact during Nmb application the responses of 9 out of 13 of the cells examined, as exemplified by the records in Fig. 2, were compatible with an input derived from a single dLGN cell. The remaining cells (4 out of 13) exhibited responses in the presence of Nmb application of the type seen in Fig. 1, where their broader response to all testing orientations indicated the presence of some additional excitatory influences, but there was still no variation in response amplitude or discharge zone size consistent with the excitatory model \(^4\).

Considering the present results in the context of those of Tsumoto et al.\(^{13}\) and
other evidence favouring the view that simple cell excitatory fields are basically round rather than elongated\textsuperscript{2,6,7} there seems to be more than adequate grounds for totally revising the model for simple cell orientation selectivity. A revised model should take note of the fact that the responses to non-optimal stimuli are reduced because of the selective actions of an intracortical inhibitory mechanism, not a reduced summation of the excitatory mechanisms converging on the cell. The ‘spatial summation’ seen in some simple cell fields with increasing stimulus length\textsuperscript{3,4,7} may reflect either increasing disinhibition evoked by the change in stimulus length, or the bringing in of subliminal facilitatory influences present at all orientations but normally blanked by the inhibition at non-optimal orientations. Clearly this type of summation effect should no longer be considered to provide direct evidence for the nature of the spatial organization of the principal excitatory drive to simple cell fields.

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\textsuperscript{3} Gilbert, C. D., Laminar differences in receptive field properties of cells in cat primary visual cortex, \textit{J. Physiol. (Lond.)}, 268 (1977) 391–422.
\textsuperscript{5} Iversen, L. L., Mitchell, J. F. and Srinivasan, V., The release of \textgamma-aminobutyric acid during inhibition in the cat visual cortex, \textit{J. Physiol. (Lond.)}, 212 (1971) 519–534.
\textsuperscript{7} Schiller, P. H., Finlay, B. L. and Volman, S. F., Quantitative studies of single cell properties in monkey striate cortex. 1. Spatiotemporal organisation of receptive fields, \textit{J. Neurophysiol.}, 39 (1976) 1288–1319.
\textsuperscript{12} Sillito, A. M., Inhibitory mechanisms influencing complex cell orientation selectivity and their modification at high resting discharge levels, \textit{J. Physiol. (Lond.)}, 289 (1979) 33–53.