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# Quantitative Studies of Single-Cell Properties in Monkey Striate Cortex. V. Multivariate Statistical Analyses and Models

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## SUMMARY AND CONCLUSIONS

*1.* Several statistical analyses were performed on 205 S-type and CX-type cells which had been completely analyzed on 12 response variables: orientation tuning, end stopping, spontaneous activity, response variability, direction selectivity, contrast selectivity for flashed or moving stimuli, selectivity for interaction of contrast and direction of stimulus movement, spatial-frequency selectivity, spatial separation of subfields responding to light increment or light decrement, sustained/transient response to flash, receptive-field size, and ocular dominance.

*2.* Correlation of these variables showed that within any cell group, these response variables vary independently.

*3.* A multivariate discriminant analysis showed that orientation specificity, receptive-field size, interaction of direction and contrast specificity, ocular dominance, and spontaneous activity, taken together, can adequately assign cells into the S-type or CX-type subgroups.

*4.* Various models of visual cortex are examined in view of the findings reported here and in the previous papers of this series, which suggest that *a*) orientation and direction selectivities are produced by separate neural mechanisms, *b*) there may be a hierarchy among simple (S type) cells, and *c*) complex (CX type) cells appear to receive a prominent S-type cell input.

## INTRODUCTION

In the first paper of this series (19) we presented results on the properties of single cells in monkey striate cortex showing that reliable classification of cells into the simple (S type) and complex (CX type) classes can be achieved quantitatively on the basis of the spatial organization of the receptive field as determined with moving or flashing stimuli. S-type cells were defined as those orientation-selective cells which had one or more spatially separate subfields within which the cell responded selectively to either light increment or light decrement, but not to both. Orientation-selective cells which responded to both light increment and decrement throughout their receptive fields were classified as CX-type cells. We have also shown that these two classes of cells differed to some extent on a number of other measures. These included orientation selectivity, spontaneous activity, ocular dominance, receptive-field size, interaction between contrast and directionality, and the degree of temporal modulation to moving gratings. These may be thought to represent nondefining variables, since *a*) they were not part of the basic criteria in the classification of S-type and CX-type cells, and *b*) most of these measures lacked classificatory power in that they did not sufficiently discriminate the two classes. The question we set out to answer in the first part of this paper was whether or not multivariate statistical techniques could be used to significantly discriminate the S-type and CX-type classes employing the above-noted nondefining variables which, when taken singly, could not be so used.

In the second part of this paper we will consider models of visual cortex in light of the findings reported here and in the previous papers of this series (8, 19–21). Central to the question of models is how orientation and direction selectivities are achieved in striate cortex and to what extent the assumption of a hierarchy among cortical cells in general, and S-type cells in particular, is warranted.

## METHODS

Statistical analyses were done using the BMD biomedical statistical computer package (1, 4,

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17). Variables considered were those described in previous papers (8, 18–21): orientation tuning, end stopping, spontaneous activity, variability, direction selectivity, contrast preference with flashed or moving stimuli, interaction between contrast and direction of stimulus movement, spatial-frequency selectivity, spatial separation of subfields responding to light increment or light decrement, sustained/transient response to flash, receptive-field size, and ocular dominance. We were investigating the differences between S-type and CX-type cells, which are defined by two criteria (henceforth called defining variables), *1*) the spatial separation of subfields responding to light increment and light decrement, and *2*) the existence of a receptive field or subfield responding to only one sign of contrast change of a flashed or moving stimulus. The BMD-07D program was used to compute histograms of all variables stratified on the basis of an index variable, F statistics, and between-groups correlation analyses. The BMD-04M and -07M programs were used for within-group correlations and stepwise discriminant analyses.

Stepwise discriminant analysis involves the computation of a linear function of all variables entered in a stepwise manner measured for each individual of the two groups to be discriminated. A coefficient ($\lambda$) for each response measure is determined such that the differences between the means of the two groups (in this case S-type and CX-type cells) divided by a pooled standard deviation is maximized. The products of a cell's particular value on a response measure ($X$) and the coefficient for that response measure ($\lambda$) are summed to determine a scaler index ($Z$) for each striate cell:

$$(Z_{i\alpha} = \lambda_1 X_{i\alpha 1} + \lambda_2 X_{i\alpha 2} + \ldots \lambda_m X_{i\alpha m})$$

Variables are entered into this equation in the following stepwise manner. F statistics are computed on all the variables measured for the S-type and CX-type cell groups. The response variable with the largest F between the two groups is entered into the discriminant function. A coefficient for this response variable is determined such that the differences between the means of the S-type and CX-type groups is maximized. Then the variable with the second largest F is entered into the discriminant function and its coefficient is computed. Response variables are entered in this stepwise fashion until the discrimination of the S-type and CX-type groups is no longer improved by the addition of new variables. When the best discriminant function is obtained the "canonical variable," $Z$, representing the sum of each response variable times its coefficient, is the result. This canonical variable can be used to compute an index value for each unit, which can form the basis of an a posteriori classification of the units into S-type and CX-type classes. This a posteriori classification can be compared to the original classification to determine the power of the nondefining response variables to identify S-type and CX-type cells.

This discriminant analysis reflects differences between the means of the variables for the two groups; a very similar sort of procedure can be used to distinguish the relative variability of S-type and CX-type units on the response measures used. When a scattergram plot is shown in this paper, the abscissa represents the first discriminant function based on group means; the ordinate represents a discriminant of group variability.

## RESULTS AND DISCUSSION

### *Statistical analyses*

INDEPENDENCE OF RESPONSE VARIABLES. We have investigated the relationships between response variables in order to determine first which variables show consistent relationships with others. Second, we wished to determine if the relationships remained constant for the whole population and in the S-type and CX-type subgroups; 205 units were selected which had been completely analyzed on 11 variables of interest: orientation tuning, end stopping, spontaneous activity, variability, direction preference, interaction of direction and contrast preferences, contrast preference, sustained/transient response to flash, field width, ocular dominance, and flash contrast preference. Only S-type and CX-type cells were included in this sample. The methods of computing these variables have been described in previous papers (8, 18–21); in some cases, response measures were altered so that they described a monotonic change in some general quality. For example, the normal ocular-dominance range of 1 for contralateral, 7 for ipsilateral dominance was collapsed into 4 categories combining 1 and 7, 2 and 6, 3 and 5, and 4.

Correlations of all variables for these 205 units were computed. If one inspects the resulting correlation matrix for these variables (between-groups correlation matrix, Table 1) it is obvious numerous interrelations exist (an $r$ of 0.15 is significantly different from $\rho = 0$, at $P < 0.01$ for this sample size). Fully 67% of the correlations are significantly different from $\rho = 0$, the independence hypothesis; 15% have correlations greater than 0.40. However, these correlations may not necessarily be due to a functional relationship between the response variables, but rather to the effect of the S-type and CX-type

TABLE 1. *Between-groups correlation matrix*

| | RF Size | Sus/Trans | RF Homo | Inter | Contr | Direct | Var | Spont | Stop | Orient |
|---|---|---|---|---|---|---|---|---|---|---|
| RF size | 1.00 | | | | | | | | | |
| Sus/trans | 0.22* | 1.00 | | | | | | | | |
| RF homo | −0.51* | −0.01 | 1.00 | | | | | | | |
| Inter | 0.40* | 0.13 | −0.61* | 1.00 | | | | | | |
| Contr | 0.32* | 0.24* | −0.54* | 0.61* | 1.00 | | | | | |
| Direct | 0.00 | 0.07 | −0.19* | 0.22* | 0.29* | 1.00 | | | | |
| Var | −0.26* | −0.13 | 0.18* | −0.22* | −0.25* | −0.04 | 1.00 | | | |
| Spont | 0.49* | 0.27* | −0.45* | 0.35* | 0.31* | 0.03 | −0.19* | 1.00 | | |
| Stop | 0.02 | 0.27* | −0.09 | 0.07 | 0.18* | 0.07 | −0.10 | 0.11 | 1.00 | |
| Orient | 0.40* | 0.18* | −0.30* | 0.30* | 0.15* | 0.24* | −0.16* | 0.27* | −0.10 | 1.00 |

* $P < 0.01$.

subgroups. S-type cells are more tightly tuned for orientation and have small fields. CX-type cells are broadly tuned for orientation and have large fields. The correlation in the whole population of cells between field size and orientation tuning may be due solely to the effect of the S-type and CX-type subgroups; on the other hand, there may be a consistent relationship of field size and orientation tuning regardless of the effect of subgroup membership. If one wished to postulate a general functional relationship between two variables, this relationship should be of the same magnitude if one considers the whole-cell population, or considers any particular group, such as the S or CX type.

In order to discriminate between the two hypotheses: *1*) that the high correlations observed between variables are due to the S/CX subgroups, or *2*) that these correlations of response variables are unrelated to the S/CX distinction, a within-groups correlation analysis was done. This analysis (Table 2) shows that the S-type and CX-type subgroups did account for most of the high correlations observed in Table 1. In the within-groups correlation analysis, only a few significant correlations remain, and those are of small magnitude. For example, the correlation of receptive-field size and orientation tuning has now fallen to 0.06, indicating no relationship of these two variables within any cell group. Any theory which attempts to account for cortical response properties must be constrained by the independence of the response variables observed within these two major cell groups. Thus, one cannot postulate that the subfield separation of simple cells, for example, is responsible for both the spatial frequency and direction selectivity, since these two response properties are uncorrelated and thus statistically independent.

MULTIVARIATE DISCRIMINATION ANALYSIS. Since the response variables we have measured show little correlation of variables within the S-type or CX-type groups, but a great deal of difference between these groups, it is of interest to determine what variables are of importance to the S/CX distinction. One method by which a more complete description of these two populations may be obtained is by a discriminant analysis. The purpose of such a discriminant analysis is twofold. First, the variables which are of importance to the S/CX distinction will be identified, and the relative contribution of each variable to the S/CX distinction will be known. Sec-

TABLE 2. *Within-groups correlation matrix*

| | Orient | Stop | Spont | Var | Direct | Contr | Inter | RF Homo | Sus/Trans | Field Size | Oc Dom |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Orient | 1.00 | | | | | | | | | | |
| Stop | −0.10 | 1.00 | | | | | | | | | |
| Spont | 0.21* | 0.01 | 1.00 | | | | | | | | |
| Var | −0.11 | 0.00 | −0.10 | 1.00 | | | | | | | |
| Direct | 0.12 | 0.06 | 0.09 | −0.02 | 1.00 | | | | | | |
| Contr | −0.08 | 0.03 | 0.14 | −0.13 | 0.32* | 1.00 | | | | | |
| Inter | 0.10 | −0.01 | 0.22* | −0.19* | 0.14 | 0.51* | 1.00 | | | | |
| Rf homo | 0.08 | 0.04 | −0.32* | 0.09 | −0.12 | −0.23* | −0.28* | 1.00 | | | |
| Sus/trans | 0.06 | 0.24* | 0.18* | −0.15* | 0.03 | 0.07 | −0.02 | 0.08 | 1.00 | | |
| Field size | 0.06 | −0.05 | 0.31 | −0.17* | −0.16* | 0.06 | 0.13 | −0.27* | 0.05 | 1.00 | |
| Oc dom | 0.22* | −0.04 | 0.16* | −0.28* | 0.04 | −0.05 | 0.06 | −0.18* | 0.05 | 0.18* | 1.00 |

* $P < 0.01$.

ond, if the S/CX distinction is an artificial dichotomy placed on a cell population based on one bimodally distributed response measure, while other cell-response properties form a continuum, this fact will be apparent from the small degree of separation between the two groups on a multivariate discriminant measure and from the types of units which are identified as intermediate between the two groups.

We defined S-type and CX-type cells by two criteria: *1*) spatial separation of light- and dark-edge responses within their receptive fields, or *2*) the existence of a field that responds only to one sign of contrast. When these variables are used to define S-type and CX-type cells, how well do the other variables which we measured discriminate between the two cell types? That is, can one develop a composite, canonical variable not related to the variables used to define S-type and CX-type cells, that discriminates well the S and CX groups? A stepwise discrimination was used to accomplish this. In this sort of analysis, the nine variables measured can be used to place each cell at a point in nine-dimensional space. This nine-dimensional space is projected onto a one-dimensional space so that each cell is now represented as a point on a line. The projection is constructed so that to the maximum extent possible, all the S-type cells are on one side of some point on this line, and all CX-type cells are on the other. The number of S-type and CX-type cells which are intermingled in the middle of this line is a measure of the power of the discrimination made using the nondefining variables.

The same 205 units used for the previous correlation analysis were used for the stepwise discrimination analysis. The final classification matrix based on the discriminant function appears in Table 3. This represents a misclassification of 10%; seven cells originally classed as CX type are classed by this function as S type; eight cells originally classed as S type are misclassed as CX type. Variables that were useful in distinguishing S-type from CX-type cells were *1*) interaction of contrast and direction, *2*) receptive-field size, *3*) orientation tuning, *4*) ocular dominance, and *5*) spontaneous activity. The relative weights assigned to each of these variables appear in Table 4. Direction preference,

TABLE 3. *Final classification matrix*

| Original Classification | A Posteriori Classification | |
|---|---|---|
| | S | CX |
| S | 47 | 8 |
| CX | 7 | 64 |

TABLE 4. *Coefficients for response variables*

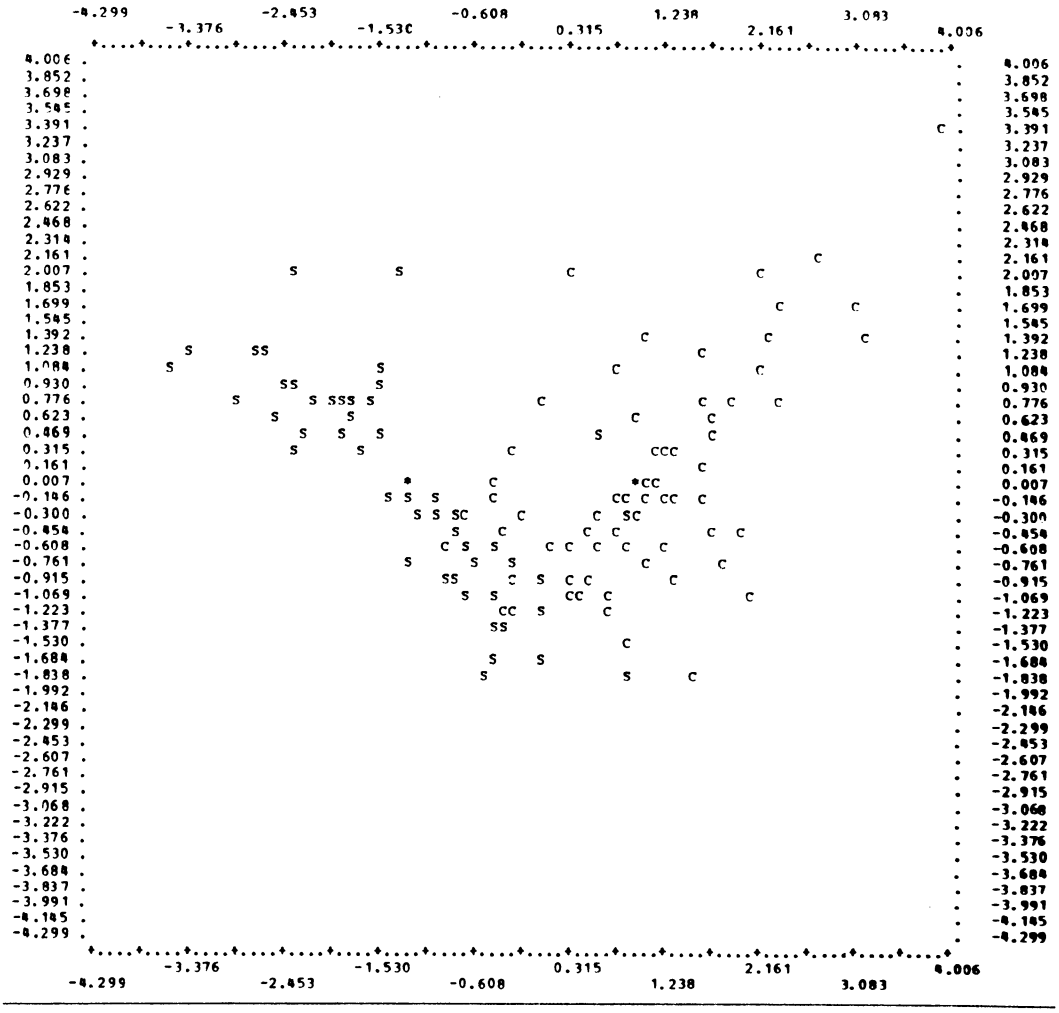
| | |
|---|---|
| Orientation | 0.00687 |
| Interaction | 0.05940 |
| Field size | 2.73809 |
| Ocular dominance | 0.16603 |
| Spontaneous | 0.00348 |

variability, end stopping, and sustained/transient flash response were not useful in distinguishing the cell groups. A scatterplot of the separation of the S and CX groups measured by this discriminant function, and a second discriminant function which sorts cells by differences in variability on the measures described, appears in Table 5. The abscissa is the canonical variable determined for differences between groups for each unit using the discriminant analyses based on all nine response variables. The ordinate reflects differences in the variability of S-type and CX-type cells on all the response variables measured. The scatter on the abscissa shows the discrimination of S and CX groups; the scatter on the ordinate shows CX-type cells are equal in variability to S-type cells on these response measures. Good discrimination of S-type and CX-type cells is possible using response variables unrelated to the defining variables suggesting S-type and CX-type cells reflect generally different principles of neuronal organization.

In a previous paper we showed that temporal response modulation to gratings is the best single measure that discriminates S and CX cell types (21). If the modulation of response to gratings is part of a multivariate discrimination, an even smaller misclassification ratio can be obtained. This analysis was carried out on a separate group of 76 cells on which modulation to gratings, orientation tuning, and ocular dominance had been assessed. The a posteriori classification matrix produced by this stepwise discriminant analysis appears in Table 6. All CX-type cells are correctly classed by this function. Six cells originally classed as S type are misclassed as CX type.

What types of units are misclassed by these discriminant functions? Are they units that are clearly members of the S-type and CX-type classes with anomalous values for one or more response variables, or are they unusual or truly intermediate cell types? The answer seems to be a little of each. In the group of S-type cells misclassed into the CX-type population by these functions are found two very unusual S-type cells with large receptive fields and high spontaneous activity, and two cells which were classified into the S-type population solely on the basis of subfield separation evaluated by moving

TABLE 5. *Scatter plot of separation of S and CX groups*




stimuli and could not be mapped adequately with flashes. Several others had unusually broad orientation tuning or were so variable that error in original classification was likely. These misclassed cells are examples of anomalous, not true intermediate cell types. The CX-type cells misclassified as S-type also include some units with clearly anomalous values for some variables, particularly interaction between contrast and directionality. There were CX-type cells with small receptive fields and low spontaneous activity, which may represent an intermediate cell type. These cells were "misclassed" as S type by the other measures (modulation tuning, etc.).

TABLE 6. *A posteriori classification matrix*

| Original Classification | A Posteriori Classification | |
|---|---|---|
| | S | CX |
| S | 25 | 6 |
| CX | 0 | 45 |

With this possibility in mind, we made a more general comparison of S-type cells with the CX-type cells which had small receptive fields to see if the other observed differences between S-type and CX-type cells were due primarily to the differences in receptive-field size. This choice of CX-type cells biases the sample toward upper cortical layer CX-type cells. For this analysis 267 cells were used, and all principal variables discussed in previous papers were analyzed (8,

18–21). Comparing S-type and small field CX-type cells, all but two differences on the variables mentioned remain significant, though in several cases the magnitude is reduced. Only the differences in orientation tuning and response variability become nonsignificant ($P = 0.05$, F). This change in the difference between groups in orientation tuning is puzzling since there is not significant correlation between receptive-field size and orientation within cell groups, but it may be linked to the somewhat sharper tuning of upper layer cortical units to which the small-field cell sample is biased. The degree of response variability is also related to depth of recording in cortex; this fact could contribute to the smaller difference between S-type and small-field CX-type cells on this variable. In summary, S-type and CX-type cells differ on most variables even when cells of the same receptive-field size are considered. We found little evidence for a population of cells intermediate between the S-type and CX-type populations.

The interest of the S/CX distinction is its power to delineate differences in many response variables. By contrast, it is interesting to note which variables fail to help make any distinction between these two major groups. Two such variables were end stopping (13) and the sustained versus transient nature of the response to a flashed bar. End stopping not only showed no difference between S-type and CX-type cells, but comparison of unstopped versus stopped units showed no relationship to any other variable but the sustained/transient measure. Several investigators have implicated the sustained or transient nature of the response to appropriately placed spots or bars of light in the cat (5) as useful in defining cell groups. The degree to which the response was sustained over a 1-s period to an appropriately oriented light bar was slightly negatively correlated with amount of end stopping; the more transient the more stopped a cell was likely to be. Likewise there was a small positive correlation between the degree of sustained response and spontaneous activity and a small trend for a more sustained response in cells with large fields. These trends, though statistically significant (at 0.05 level), are of small magnitude and no other variables are correlated with the sustained/transient response measure.

From these statistical analyses one can conclude the following: First, the response variables we analyzed were essentially independent within any cell class. No progressive change in any one response variable was accompanied by a progressive change in any other. These findings suggest theories accounting for cell response properties in cortex should produce such qualities as orientation selectivity, directionality, field size, and spontaneous activity by separate mechanisms. Second, these findings confirm that S-type and CX-type cells represent two different principles of neuronal organization. The S and CX groups differed in subfield separation and contrast preference, their defining variables. While orientation tuning, spontaneous activity, field size, ocular dominance, and interaction of direction and contrast preference were not, taken separately, the adequate criteria for the distinction of S-type and CX-type cells, taken as a group they distinguished S-type and CX-type cells very adequately. Modulation of response to gratings was the best nondefinitional discriminant between the S and CX populations. Finally, the S/CX distinction was the only distinction that separated whole classes of response variables. It is notable that other distinctions, such as the presence or absence of end stopping or the sustained or transient nature of a response to a flash do not correlate with differences in other response variables.

### *Models of visual cortex*

The first model of visual cortex based on data secured from single units was proposed by Hubel and Wiesel (11) when they made their initial discoveries. They hypothesized that simple cells in cat cortex receive direct input from a line of LGN cells so that the receptive field of the cortical cells is elongated. The regions flanking the central area were believed to be formed by surrounds of LGN cells and/or by centers of LGN cells of opposite contrast. The adjacent subfields of the receptive field of these cortical cells were thought to be mutually inhibitory when stimulated simultaneously. By virtue of this fact and the elongated nature of the field, these cells became orientation specific. Thus, stimulus edges or bars falling along the length of the field would excite the cell. When the stimulus was in the wrong orientation it fell on both regions at the same time and there was no response because of inhibition. The excitation and inhibition could be produced by direct inputs from the LGN.

Hubel and Wiesel (12) suggested that the direction preference of most simple cells could also be predicted from the spatial organization of the receptive field. Thus, when a light bar is moved from an off-area into an on-area, the cell discharges vigorously, because the response resulting from removal of the light bar from the off-area summates with the response produced by the entry of the bar into the on-region. Because of this arrangement, movement in the opposite direction is less effective. The model also predicts that the direction specificity of simple

cells with bipartite fields should reverse when contrast is reversed. This is certainly the case with one class of S-type cells in our sample ($S_3$ type) (19), but does not occur in several other S-type cells with similar spatial organization.

The main thrust of the Hubel-Wiesel model is their hierarchic principle. They proposed that the response properties of complex cells are brought about as a result of input to these cells from many simple cells. Subsequent elaboration of the model resulted from the discovery of hypercomplex cells (13) which were believed to be created as a result of input from several complex cells, some of which made excitatory and others inhibitory connections on the hypercomplex cell.

Hubel and Wiesel hypothesized that simple cells are stellate cells, and evidence has been presented suggesting that some of the stellate cells do have the properties of simple cells (16).

Subsequent work has raised questions about the hierarchic principle and about the way selectivity for direction and orientation were hypothesized to be produced in simple cells (11). We will consider the latter question first.

Our results suggest that one cannot reliably predict the direction preference of S-type cells in monkey striate cortex on the basis of the spatial arrangement of their receptive fields as determined by moving or stationary stimuli (19). Neither is it possible to derive the sharpness of orientation tuning and the optimal spatial frequency reponse on the basis of such maps. The problem appears to be that the inhibitory regions of S-type cells are often not synonymous with the regions mapped with stationary or moving stimuli (19, 20, 21).

Bishop, Coombs, and Henry (3) proposed another model of cortical connectivity based on several of the known features of the visual cortex. The hypotheses of this model are: that afferent visual connections to striate cortex are excitatory and all inhibition is intracortical, and that pyramidal and stellate cells both receive direct afferent input, with stellate cells mediating intracortical inhibition. These investigators proposed that the activity of geniculate afferents through stellate cells provides a tonic inhibition to pyramidal cells, some of which are the striate simple cells. Stellate cells are thus not orientation selective. Geniculate afferents also provide a direct excitatory link to pyramidal cells. The spatial arrangement of this geniculate input, together with the tonic inhibition through the stellate cells, supplies orientation and contrast sensitivity. In this model selectivity for both direction and orientation results from the same intracortical mechanism. Direction selectivity, however, is produced by the further elaboration of the disinhibition of the basic network in the preferred direction; the tonic inhibition limits responses in the null direction. The model does not deal with spatial frequency selectivity or with complex cells.

The basic feature of the model we will present is that orientation and direction specificities are achieved by two separate mechanisms. We propose that there are two layers of inhibitory interneurons in cortex that give rise to these specificities, and that the neural events elaborated at the basal dendrites of cortical pyramidal cells give rise to direction specificity, while orientation selectivity is the outcome of events occurring at the apical dendritic network.

In what follows we will first discuss direction selectivity in $S_1$-type cells which have one excitatory subfield and are sensitive to only one sign of contrast change. We will then consider orientation selectivity in these cells, the way other S-type cells may be constructed, and how CX-type cells might be formed. The last two subsections will deal with spatial-frequency selectivity and stimulus-length specificity.

DIRECTION SELECTIVITY IN SINGLE-CONTRAST, $S_1$ CELLS. We propose that the single-contrast, $S_1$ cells receive direct, excitatory input from the LGN and that direction selectivity is produced by inhibitory interneurons which receive the excitation from the LGN and make their inhibitory connections on the basal dendritic field of S-type pyramidal cells. The LGN is assumed to project onto visual cortex in an orderly, topographic fashion throughout. The characteristics of this model for directionality are shown in Fig. 1. Effective excitatory LGN inputs are represented as cone-shaped terminals in this figure (1,1). The inhibitory interneurons have T-shaped terminals (Fig. 1,2). The $S_1$-type pyramidal cell has only its effective basal dendritic field showing (Fig. 1, 3). Stimulus movement from left to right in this figure excites the cell; movement from right to left produces no response because of the inhibitory action of the interneurons. These interneurons must continue to discharge for a short time after having been activated and we believe that the T-type cells could serve this function (19). The manner in which this is accomplished is not specified in the figure. The time course of the T-cell firing pattern may be accomplished by the endogenous membrane characteristics of these cells, by virtue of the nature of the LGN input, or by a timing circuit of the sort described by Barlow and Levick (2) for the rabbit retina. The following are the features of this relatively simple model: *a*) It is the effective basal dendritic network receiving inhibitory input from T-type cells which defines direction specificity.

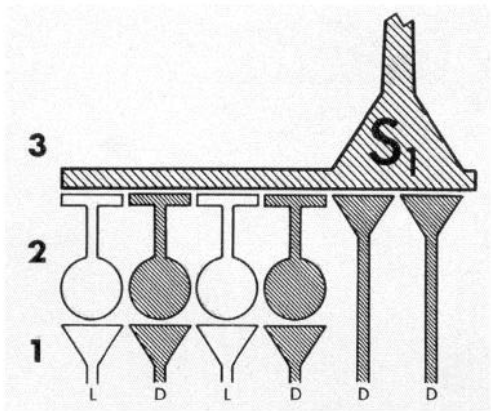



FIG. 1. Hypothetical scheme for direction selectivity in a dark-field $S_1$-type cell. 1: excitatory input from LGN to interneurons. Light cones are inputs from on-center LGN cells, dark ones from off-center LGN cells. 2: inhibitory interneurons. 3: $S_1$-type cell and its basal dendrite. Inhibitory interneurons make synaptic terminal on dendrite. Direct excitatory LGN input from off-center cells terminates near cell body of $S_1$-type cell. Cell responds to leftward movement of an edge and is unresponsive to opposite direction. In this and subsequent drawings, excitatory terminals are depicted as cones and inhibitory ones as T's.

This may be reflected either in the spatial organization of the basal dendritic field or in the geometry of the axons of the inhibitory interneurons. For sake of clarity, in this model effective connections are depicted in terms of the dendritic field of the pyramidal cell. *b*) Inhibition as depicted here is prominent at points distal to the cell body. *c*) Inhibition on the $S_1$-type cell need not be specific for contrast; interneurons can receive both on and off LGN inputs. *d*) The contrast response of the cell is determined by the direct excitatory LGN input which, in this figure, is only from off-center cells. *e*) Stationary flashes in the receptive field of the $S_1$-type cell will cause, as has been found, discharges (to light decrement in the cell depicted in Fig. 1) similar to those found in the LGN. By contrast, moving stimuli elicit only a transient burst and in the null direction elicit no response.

ORIENTATION SPECIFICITY. Our hypothesis is that orientation specificity is the outcome of neural activity involving the arborizations of the apical dendrites. A second layer of inhibitory interneurons with somewhat different properties from T-type cells is postulated to achieve this. The assumed bilobed shape of the effective apical dendritic field creates the orientation specificity, as already suggested in the second paper of this series (20). What configurations of neural events might give rise to this configuration will be considered below.

The arrangement depicted in Fig. 2 includes both the basal and apical fields, with two layers of interneurons, the lower for direction selectivity and the upper for orientation selectivity. Two direct excitatory terminals from the LGN are shown on the base of the apical dendrite of the pyramidal cell. The effective inhibitory neural connections are depicted by the shape of the dendritic fields of the pyramidal cell. Stimuli which activate those interneurons of the upper layer which innervate the apical dendritic field, inhibit the $S_1$-type cell. The cell should be excited by a bar or dark edge oriented parallel to the perspective line of the figure. Such a bar produces no inhibitory action on the pyramidal cell via the upper layer of interneurons.

Given this configuration of effective connections, what is the source of the input to the upper tier of interneurons? It is necessary that these interneurons, in contrast to those of the lower tier, respond only while the stimulus is in their receptive field. Persistent or slowly decaying activity in these neurons would render the $S_1$-type cell unresponsive to any moving stimulus.

Three possibilities may be considered for the input to the upper set of interneurons:

*Direct input from LGN.* It is now well known that the LGN projects to several layers of cortex, and seems to do so in a relatively selective manner (15). This fact makes the hypothesis of two layers of interneurons, each of which receives direct LGN input, feasible. The postulated difference in the poststimulus time course of upper- and lower-layer interneurons may be accomplished by assuming that they receive selective input from the LGN, perhaps from the different layers of this structure. The cells in the magnocellular and parvocellular layers of the LGN are anatomically different. The cells in the magnocellular layers are large, and presumably conduct at greater velocities than do the smaller cells in the parvocellular layers. Cells of the magnocellular layers tend to respond more phasically, which would seem to make them suitable for driving the upper tier of interneurons. This input is labeled *A* in Fig. 2. Another possibility is that there are two intermingled populations of phasic and tonic cells in the LGN which project in an orderly fashion to cortex. A division of phasic and tonic cells has been suggested for cat and monkey retinas and LGN (5, 9, 10), and this could conceivably be a source for these mechanisms in visual cortex.

*Direct LGN input coupled with reciprocal inhibition.* The phasic poststimulus discharge pattern of the upper tier of interneurons could be arrived at without a selective LGN input by assuming the existence of reciprocal inhibition among the interneurons. Such circuitry would

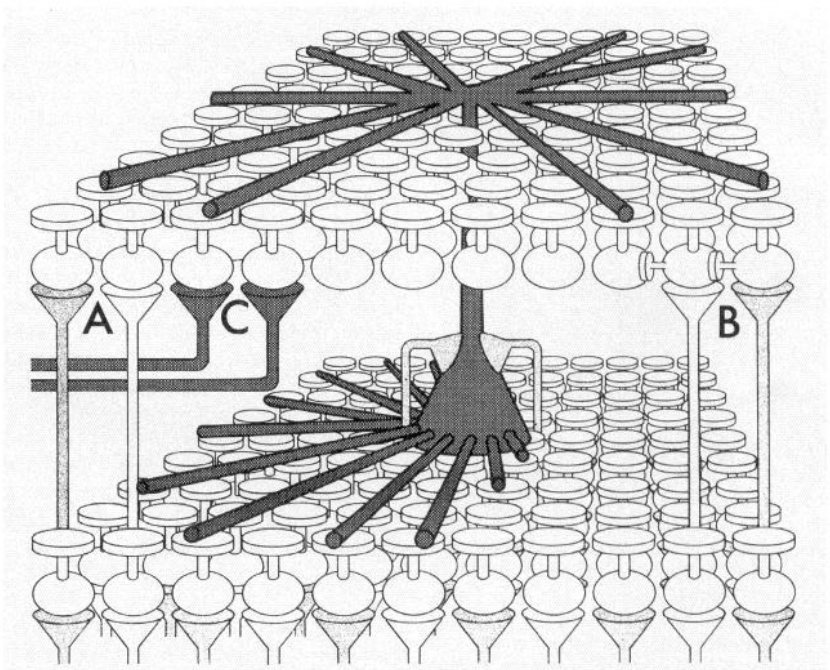



FIG. 2. Hypothetical scheme for an oriented, unidirectional, dark-field S-type cell. Two layers of inhibitory interneurons are shown. The lower layer makes contact with the basal dendrites of the S-type cell and provides direction selectivity. These interneurons are driven directly by LGN input. The excitatory terminals of two off-center LGN cells impinge on the cell body of the $S_1$-type cell. Orientation specificity is produced by virtue of upper layer of interneurons which inhibit the apical dendrites of the $S_1$-type cell. The effective dendritic arborization is bilobed. The axis of orientation is along the perspective line, where inhibition is ineffective on the cell. The upper layer of interneurons may be driven either by LGN cells directly (*A*), by LGN cells coupled with reciprocal inhibition (*B*), or by other pyramidal cells (*C*).

require that these interneurons have axonal termination on both the apical field of S-type cells and on neighboring interneurons. This is demonstrated in Fig. 2*B*.

*Input from pyramidal cells.* The third possibility is that the upper tier of interneurons receives its primary input from S-type cells. Since S-type cells are phasic in their response properties to moving stimuli, this property would be transmitted to the interneurons (Fig. 2*C*). This hypothesis predicts that interneurons in this region have receptive-field properties similar to the pyramidal cells innervating them. The stellate cells Kelly and VanEssen (16) identified could have the properties of simple cells for this reason.

The apparent problem with this hypothesis may be that a stationary, flashing bar in the receptive field of an S-type cell might be expected to elicit at least a few spikes even when it is in the worst orientation. This might be expected since the inhibition must arise as a result of the discharge of pyramidal cells. While in many cells it is true that flashing stimuli can elicit a weak response under such stimulus conditions, there are certainly quite a few which remain silent. Since in this circuitry a larger number of neurons are involved, they probably receive inputs from LGN fibers which have a range of latencies. Thus, those pyramidal cells which receive a short-latency input could silence, via the inhibitory interneuronal circuitry, those which have a long-latency input.

STRUCTURAL CONSIDERATIONS. The model of $S_1$-type cells is based on the assumption that two topographically ordered layers of interneurons give rise to orientation and direction selectivities whose effective connections on the basal and apical dendritic fields of $S_1$-type pyramidal cells determine the nature of these selectivities.

Several possibilities may be considered regarding the structural organization of these connections. First, the most straightforward possibility is that there is a physical isomorphism in the dendritic fields of these cells similar to what we depicted in the figures, where the basal dendrites of directional S-type cells are skewed relative to the cell body and the apical dendrites are bilobed. This would imply that the topographically highly ordered interneurons have short axons, and that the dendrites of the pyram-

idal cells "have to go to them" for their connection. This perhaps unlikely possibility is partially testable using the Golgi method by studying the dendritic fields of pyramidal cells in tangential sections.

The second possibility is that the structural aspects of orientation and direction are reflected in the distribution of inhibitory connections on the dendritic fields with dense connection to some regions and sparse ones to others. This possibility is less amenable for study, although the number of dendritic spines in Golgi-stained pyramidal cells may have a bearing on it even though such counts cannot discriminate the excitatory from the inhibitory terminals.

The third possibility is that it is the geometry of the interneuronal axons which determine the functional organization of the S-type cells. This would be even less open to structural analysis than the second possibility.

CONSTRUCTION OF VARIOUS S-TYPE CELLS. We would like to consider two alternate ways in which the various S-type cells may be constructed in visual cortex. The first is a hierarchic model and the second relies on parallel analysis of input.

*Hierarchic model.* Different kinds of S-type cells may be organized in a hierarchic fashion, as suggested in the first of this series of papers (19). The lowest member of the hierarchy is the unidirectional, oriented $S_1$-type cell which is excited by only one sign of contrast change. Other S-type cells could be constructed from them. Thus, for example, an $S_2$-type cell which has spatially separate light and dark regions, both of which respond to the same direction of stimulus movement, could receive input from one light-field and one dark-field $S_1$-type cell with the same orientation and direction specificities. An $S_3$-type cell, which has two subfields but with opposite direction selectivities for each, could be constructed in a similar fashion, with the two $S_1$-type cells being selective to opposite directions. An example of this is shown in Fig. 3.

More complicated S-type cells may be constructed in a variety of ways. Thus, an $S_4$-type cell, which is bidirectional for one contrast and unidirectional for the other, could be made up either with three $S_1$-type cells, or with one $S_2$-type cell and one $S_1$-type cell. A variety of combinations may be postulated in giving rise to the other S-type cells we described.

In favor of the hierarchic model is the observation that the size of the receptive field increases proportionately with increasingly complex S-type cells. Thus, the width of $S_2$-type cells is twice that of $S_1$-type cells (20). However, the fact that $S_1$-type cells are not neatly ordered

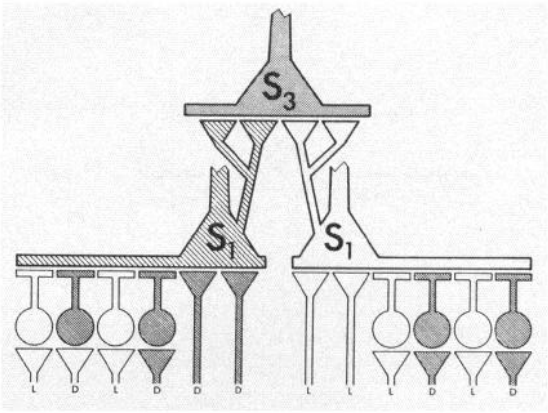



FIG. 3. Hypothetical scheme for the formation of an $S_3$-type cell which responds in one direction to a dark edge and in the opposite direction to a light edge. Two $S_2$-type cells of opposite contrast and direction selectivities terminate on the $S_3$-type cell to give rise to its characteristics.

in any one layer of cortex, may be considered to go against this hypothesis. It is possible, however, that the laminar segregation of different cell types in visual cortex may be greater than extracellular single cell recordings generally disclose. If spike activity were recorded not only near the cell body but also along part of the apical dendrite or along the axon, much less order would be apparent than actually exists. This possibility may seen unlikely to account for all the scatter we have seen because antidromic activation from the superior colliculus disclosed responses only in layers 5 and 6 (8). Thus, it appears that many of the cells in these two layers are not recorded from in other layers through which their apical dendrites extend.

*Parallel model.* This model proposes that each S-type cell can be made up of a direct input from the LGN. Similar principles to those used for the construction of $S_1$-type cells can be used to construct every S-type cell we have found. Examples of four different types of S cells constructed in this fashion appear in Fig. 4. An $S_2$-type cell, as shown in this figure, is created as a result of two spatially separate excitatory LGN inputs with an accompanying inhibitory network. The $S_3$-type cell, which has two subfields selective for opposite directions of movement with light and dark edges, is depicted to have contrast-specific inhibition on each leg of the basal dendrite and two excitatory inputs.

The last cell modeled in Fig. 4 is the $S_6$-type cell. This somewhat fanciful arrangement requires paired contrast-specific inhibitory and excitatory connections. Movement from left to right elicits a dark-edge excitation from the

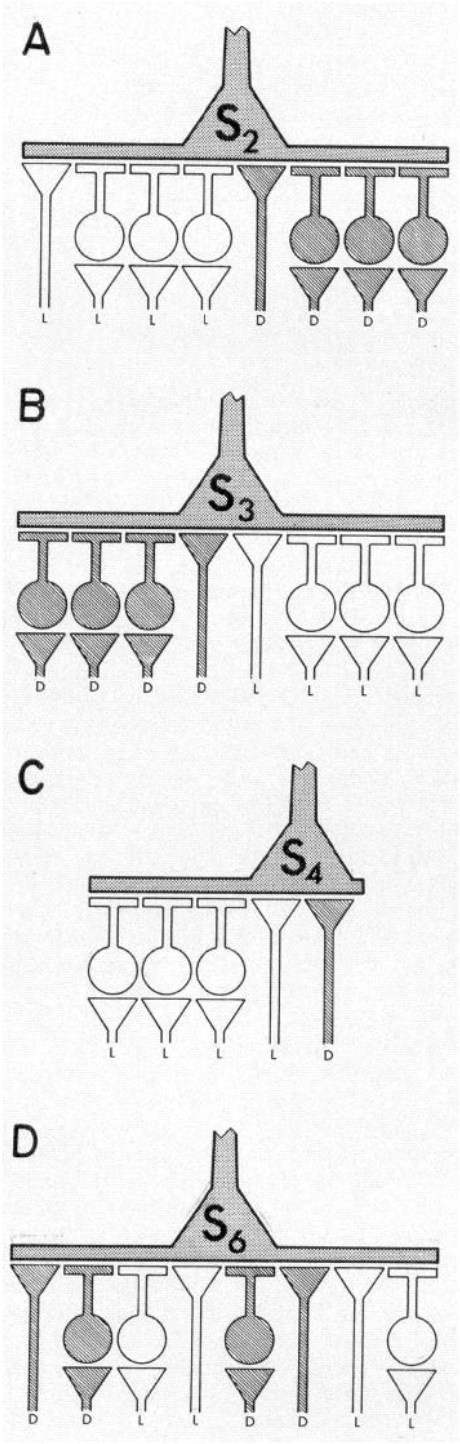



FIG. 4. Hypothetical scheme for the creation of four different S-type cells ($S_2$, $S_3$, $S_4$, $S_6$) from LGN and interneuron inputs.

leftmost off-input from the LGN and a light-edge response from the rightmost on-input. Movement in the opposite direction activates the off- and on-inputs closer to the cell body. Thus, the on- and off-regions are spatially disparate in the two directions of movement.

While the inputs at the basal dendrites may be rather cumbersome in these models, the apical network can remain the same as that proposed above. Thus, the orientation specificity of each cell can remain relatively independent of the nature of the input to the basal dendrites.

One of the difficulties with this model is that the increase in receptive-field width in more complex S-type cells is difficult to explain in view of the highly ordered nature of the LGN projections.

CX-TYPE CELLS. The pronounced difference between simple and complex cells as originally defined by Hubel and Wiesel (11) led to the idea that anatomically these cells might also be distinct. One position entertained was that simple cells are stellates while complex ones are pyramidal cells. Support for this view came from the work of Kelly and VanEssen (16). Their data, however, do not exclude the possibility that the principal S-type cells may be pyramidal cells (See ORIENTATION SPECIFICITY, Input from pyramidal cells). The fact that the amplitude of S-type cell signals is as large on the average as CX-type cells, that electrodes can be advanced without loss of the signal for comparable distances between S-type and CX-type cells, and that S-type cells can project out of cortex (14) would seem to be in agreement with the view that at least some pyramidal cells have the properties of S-type cells. If both the S-type and CX-type classes are comprised of pyramidal cells, anatomical distinctions may become more difficult. The fact that these cells tend to be intermingled in most layers of the monkey's cortex, compounds the problem.

A central tenet of the Hubel-Wiesel model, as already noted, is that there is a hierarchy among cortical cells. The properties of complex cells are an outcome of convergent excitatory input from S-type cells. Another view, the parallel model, has also been proposed. This model states that the properties of both simple and complex cells result from direct LGN inputs (22).

Our results lend partial support to the hierarchic model, although none of our evidence is direct. Orientation, direction, and spatial-frequency selectivities are believed to be brought about as a result of extensive inhibitory action. The study of the spatial organization of inhibition in cortical cells has shown, however,

that only S-type cells have demonstrable inhibitory sidebands (11, 23). The requirements for a parallel model would seem to necessitate such regions for CX-type cells as well. The hierarchic model is especially favored by our spatial-frequency data, which show a much enhanced selectivity for CX-type cells in comparison with LGN units. Since CX-type cells do not have a demonstrable inhibitory surround and since their optimal spatial frequency is often less than the half-cycle width of the receptive field, a direct LGN input cannot explain this selectivity. It is, therefore, likely that the S-type cell input is responsible for spatial-frequency selectivity in CX-type cells.

The direction-selectivity distribution of S-type cells is unimodal, with most of them strongly selective for direction of movement (19). CX-type cells, by contrast, have a bimodal distribution with approximately half the cells selective and half, nonselective for direction. These findings may also be interpreted to favor the hierarchy hypothesis, since a random convergent input from the predominantly unidirectional S-type cells would yield the kind of distribution we obtained for directionality in CX-type cells.

These considerations do not rule out the possibility that some CX-type cells receive an LGN input which is contributory to some of the receptive-field properties of CX-type cells. The presence of LGN terminals in layer 6, for example, makes this a likely possibility.

Finally, there is also the possibility that CX-type cells innervate S-type cells. Excitatory connections of this sort would seem rather unlikely since they could not give rise to the receptive-field properties of S-type cells.

If the assumptions that S-type cells innervate CX-type cells and that CX-type cells project out of area 17 are correct, a possible anatomical difference between these cell types might be expected; S-type cells should have profuse axonal arborizations within striate cortex while CX-type cells should not. In this respect it is interesting that our histological data show differences in the properties of CX-type cells in the various cortical layers without a comparable difference for S-type cells (19, 20). S-type cells are recorded in all layers, and their receptive-field size, number of subfields, sharpness of orientation tuning, ocular dominance, and spontaneous activity are not related to depth of recording. This kind of result would be expected if signals from S-type cells, in contrast to CX-type cells, were also to be recorded at places other than the cell body. The hypothesized profuse axonal terminations of these cells might provide these sites.

SPATIAL FREQUENCY. In the model we presented it was hypothesized that there are two distinct neural mechanisms in cortex giving rise to orientation and direction specificities. However, we and others (21) have discerned a third common property of visual cortex cells, spatial-frequency selectivity. Is this attribute created by yet a third neural mechanism, or is it possible that one of the two mechanisms we discussed could account for it? We have suggested that the circuitry giving rise to direction selectivity is not likely to be involved in spatial-frequency selectivity, since both direction-selective and nonselective cells have similar spatial-frequency properties (21). We proposed that the circuitry giving rise to orientation tuning may be the same one which is involved in spatial frequency tuning. Additional work is required to determine whether or not this is a viable hypothesis.

LENGTH SPECIFICITY. The pronounced inhibition along the axis of orientation of some cells renders them selective for stimulus length. Initial work on the cat has led to the hypothesis that this attribute reflects a third class of cells, termed hypercomplex, which in the Hubel-Wiesel model (13) is believed to form the most elaborate member of the hierarchy of cortical cells. They suggested that this attribute is brought about as a result of central excitatory and flanking inhibitory inputs from complex cells. Subsequent work on the cat suggested that some of the hypercomplex cells resemble simple cells in some of their attributes (6).

Our findings in the monkey show that the hypercomplex attribute in this species varies in a relatively continuous fashion among cortical cells, with it being more pronounced in the upper than in the deeper layers of cortex. We also found that clearly defined S-type cells also varied continuously in this attribute, in similar fashion to CX-type cells. The continuous and graded nature of the hypercomplex property among different cells makes it seem unnecessary to propose a separate mechanism of inhibition from CX-type cells to account for it. We would like to suggest that the same processes which give rise to orientation selectivity are responsible for end stopping. In cells which are strongly stopped, the inhibitory network giving rise to orientation extends into the region forming the axis of orientation, resulting in decreased responsiveness with increasing stimulus length.

An alternate possibility is that the hypercomplex attribute is the outcome of a sparse LGN input. This would give rise to pronounced inhibition with increased stimulus length, since this effect is already observable in the LGN. All other attributes in these cortical cells, such as orientation and direction selectivities, would be pronounced as already discussed.

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