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6. Because it is still possible for observers to shift their gaze just before they initiated a trial, we ran an auxiliary experiment to monitor their fixation patterns during figure-ground reversals. In this experiment, observers detected a pattern flashed at the region of the blind spot when they perceived faces in the Rubin picture and when they perceived a vase while fixating the fixation stimulus. On any trial, the pattern had a .5 probability of being presented. If observers' fixations deviated by more than 0.5° from the fixation point, detection of the blind-spot stimulus should be above chance level. Observers' accuracy in both conditions was $\leq .56$. Thus, observers did not significantly shift their gaze away from the fixation stimulus in the center of the Rubin picture by more than 0.5° when they perceived the faces. This control procedure monitors eye position with an accuracy of approximately 0.5° [E. Hering, *Spatial Sense and Movements of the Eye* (American Academy of Optometry, Baltimore, 1942)]. A further control for eye position was the presentation of targets randomly at each of three locations.
7. D. M. Green and J. A. Swets, *Signal Detection Theory and Psychophysics* (Wiley, New York, 1966). Data from discrimination tasks conducted according to a two-alternative forced-choice method can be analyzed in the same fashion as that from a yes-no detection task. Responding "left" when the target was tilted left constitutes a hit and responding "left" when the target was tilted right constitutes a false alarm. In our experiments, the estimated d' was based on the receiver operating characteristic (ROC) line drawn through the yes-no point. Data from two experienced psychophysical observers included confidence ratings on a six-point scale. These data best fitted ROC lines with unit slopes passing through the yes-no point, suggesting that the ROC curves did not vary as a function of d'.
8. Two preliminary experiments were run to estimate the luminance and the minimum tilt of the target required for 75 percent correct in discriminating whether the target was tilted left or right. The resulting display luminance ranged from 3.1 cd/m^2 to 3.9 cd/m^2 across five observers; for all observers, a tilt of 0.8° placed tilt discrimination at 70 percent correct. The parameter estimation by sequential testing (PEST) procedure [M. M. Taylor and C. D. Creelman, *J. Acoust. Soc. Am.* **41**, 782 (1977)] was used to determine the tilt threshold. Luminance thresholds were obtained for two tilt angles—0.8° and 1.6° from the vertical—by adjusting the luminance of the display until the accuracy was 75 percent correct.
9. Since the luminance threshold was more variable between individual observers than the tilt threshold, the luminance of the display was adjusted according to each observer's threshold in both conditions.
10. The randomizing of target location is perhaps the best argument against an eye movement explanation of our results. According to an eye movement account, observers would tend to move their eyes towards the flanking areas when these were perceived as faces. For example, if observers perceived faces, they might move their eyes to the left. Fixating the middle of the left face would improve discrimination if the target appeared there. But the target appeared there randomly only one-third of the time. The rest of the time it appeared at the center or at the right. In this case, looking at the left face would decrease discrimination because the target would be viewed off fixation. Overall performance would suffer if fixation were directed at any location other than the center. Hence, if observers moved their eyes to the flanking regions when these were perceived as figure, they should be less accurate than if they maintained fixation. But observers were more accurate when the flanking regions were perceived as figure than when they were perceived as ground. Therefore eye movements cannot explain these increases in accuracy.
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12. This implies that receptive field size and cortical magnification as one moves away from the fovea, as well as perceptual factors of figure and ground, contribute to discrimination performance.
13. Recent evidence shows that a figure in an Escher reversible picture is more likely to be seen to displace during an eye movement than a ground is (B. Bridgeman, *Acta Psychol.*, in press).
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Tetrodotoxin Blocks the Formation of Ocular Dominance Columns in Goldfish

Abstract. *Optic fibers from both eyes were made to regenerate simultaneously into one tectum in goldfish. Autoradiography at various times later revealed that regenerating left and right fibers overlapped extensively for up to 4 weeks and subsequently segregated into eye dominance columns by 8 weeks. Continuous tetrodotoxin treatment of both eyes prevented the formation of columns for up to 13 weeks and was equally effective if begun at 6 weeks. When tetrodotoxin treatment was stopped after 11 weeks, columns subsequently formed in the next 3 weeks. Blockade of only one eye did not prevent column formation at 8 weeks.*

Neurons are linked by highly ordered axonal connections that, in vertebrates, are typically topographical. This topography can be complex and discontinuous as in the alternating ocular dominance columns of visual cortex (*1, 2*). The formation of such diverse connections may be mainly attributed to a single mechanism such as chemoaffinity, spatiotemporal chronology, fiber guidance, or self-organization of fibers (*3*). Alternatively, there may be a number of different mechanisms, each with a specific and limited role. Impulse activity, for example, has been implicated in a number of developing systems, particularly the mammalian visual cortex (*1, 4–6*). Interpretation has been complicated by the multiplicity and sensitivity of developmental events. Because regeneration offers some simplification and a number of technical advantages, a model regenerating central nervous projection formally similar to the mammalian visual cortex was used to examine the effects of eliminating impulse activity.

In goldfish, optic fibers from both eyes can be surgically induced to regenerate into one tectum and eventually form eye-specific patches of innervation similar to cortical ocular dominance columns in mammals (*7, 8*). Tectal columns have also been demonstrated in developing three-eyed frogs (*9*). We studied goldfish, 5 to 7 cm in body length, because they are advantageous for a surgical technique by which the number, position, and time of ingrowth of optic fibers can be controlled (*7*). Specifically, optic fibers running near the medial edge of right dorsal "donor tectum" and innervating much of its dorsal posterior quadrant (10 to 15 percent of the tectum) were cut from the surrounding tectum by a three-sided incision that preserved the proximal segment of the fibers. The posterior end of this strip was lifted across the midline and inserted into a large mediolateral incision extending across the anterior end of the left ("host") dorsal tectum. The latter incision severed the optic fibers innervating this tectum and ensured that "donor" (ipsilaterally deflected) and host fibers regenerated from the same point.

Regeneration was studied autoradiographically from 13 to 90 days later by injecting 25 to 50 μCi of tritiated proline into one eye, donor or host, and fixing after 12 to 24 hours. Frontal paraffin serial sections at 20 to 30 μm were exposed to NTB-2 emulsion (Kodak) for 1 week. The normal chronology will be described first. At 13 to 14 days (four fish) regenerating host and donor (deflected) fibers coextended throughout the anterior half of dorsal host tectum and were largely absent from the posterior half. At the site of the insertion and incision, many fibers had been forced into the nonoptic laminae of the deep tectum. This depth error was quickly corrected by radially oriented growth toward the superficial main optic layer (stratum opticum and stratum fibrosum et griseum superficiale), and within 200 to 300 μm, label was largely normal in lamination. At 27 to 33 days (five fish)

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host fibers remained in the anterior half of the tectum and also had invaded the entire posterior half (Fig. 1a). Donor fibers grew beyond the anterior half, leaving only fasciculated and light label in that area, to terminate in the posterior dorsal half where they overlapped completely with host fibers without forming eye dominance columns. Beginning at 47 days (two fish) and definitively at 61 to 62 days (seven fish), label from host or donor fibers became discontinuous in the posterior dorsal tectum, that is, were segregated into eye dominance columns. These columns were always radial in orientation, spanning the entire depth of the main optic layer, but were variable in width, typically 200 to 500 μm (Fig. 1b). Some light intercolumnar label remained, but further diminished by 80 days (two fish).

Four groups of identically treated fish were injected intraocularly with tetrodotoxin (TTX), a highly specific inhibitor of the voltage-dependent sodium channel (*10*). For long-term blockade 0.1 μl of 0.3 m*M* TTX (ten times the minimum short-term blocking dose) was injected every 3.5 days by means of a 25-μm glass pipet inserted through the dorsal limbus. Extracellular recordings in the tectum or optic nerve showed that this dose blocked visually evoked action potentials and spontaneous activity (in nerve) in intact or regenerating nerves including those injected for 31 to 90 days and recorded at 3.5 to 4 days from the last TTX injection (32 different nerve recordings). In the largest fish ($N = 4$), weak recovery could be detected as early as 4 days, and in all fish, robust responses were found at 5 days.

For the first experimental group, both eyes were injected according to this dosage schedule beginning a few days after surgery. At 31 days (three fish), autoradiography was essentially identical to that of untreated fish at 27 to 33 days. Host and donor fibers had grown into the optic laminae from the insertion-incision site and had invaded posterior tectum in an overlapping fashion. Deflected fibers had withdrawn from the anterior half. At 59 days (three fish) and 90 days (two fish), host and donor fibers were similarly distributed (Fig. 1c); both remained dispersed throughout the dorsal posterior tectum without any indication of columns. However, in several ways the innervation was typical of 60 days regeneration. At 31 days label in the posterior tectum was highly fasciculated or stringlike in appearance, but at 60 days grains were homogeneous. The same sequence was observed in the fish without TTX and has been described for simple nerve crush (*11*). Also at 31 days, in fish with and without TTX, slight density variations were noticed in the posterior dorsal quadrant, with donor fibers typically favoring medial regions and host fibers lateral regions. By 60 to 90 days no regional differences could be detected in TTX fish. Finally, at 30 days a dramatic increase in labeling of regenerating fibers compared with unsevered fibers was seen throughout the tectum and optic pathway. Labeling subsequently declined to more normal levels by 60 days. These temporal changes, also seen in the group without TTX, can be attributed to altered axoplasmic transport in regenerating fibers (*8*).

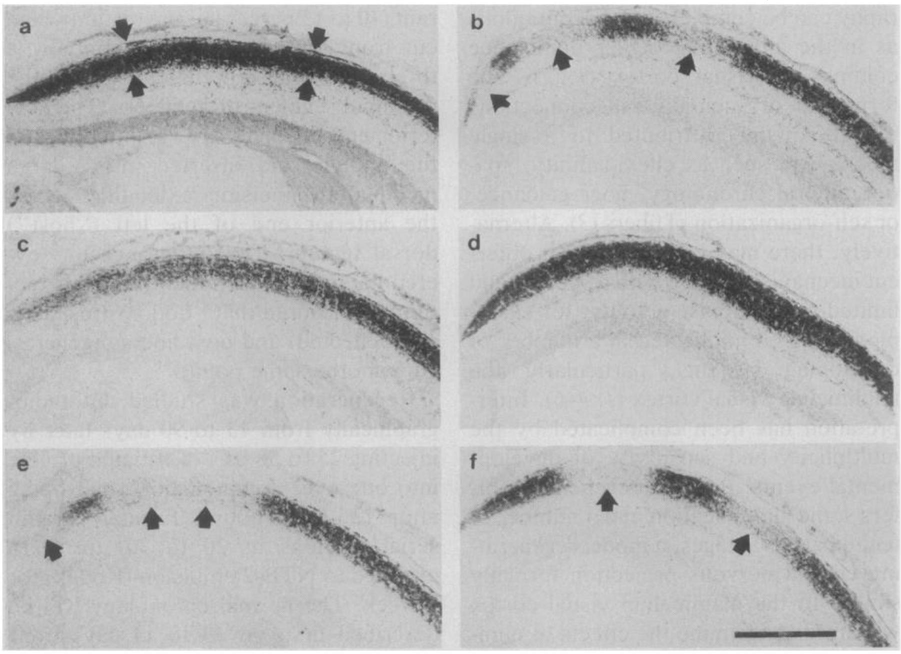

Fig. 1. Frontal autoradiograms through the dorsal posterior host tectum. Dorsal is at the top and the medial edge of the tectum is at the extreme left. Most of the lateral half of tectum is not shown. Host optic fibers were labeled in all cases. Calibration bar, 300 μm. (a) At 30 days postoperatively, no TTX. The innervation is essentially normal except for a slight increase in the thickness of the main optic innervation layer associated with this stage of regeneration. Arrows indicate this main optic layer, seen here as a continuous band of grains in the superficial tectum stretching from the medial edge at the left and into the lateral tectum on the right. (b) At 61 days, subthreshold TTX. Arrows indicate gaps in the main optic lamina. (c) At 90 days, long-term TTX blockade. Note the decreased density of medial label. Apparently the label which would have been confined to discrete columns of normal density is now spread over a greater area of the tectum in lower density. (d) At 59 days, TTX blockade begun 42 days after surgery. Label in regenerating fibers is still elevated relative to unsevered ones, as is normal at 2 months after surgery. This may have obscured any decrement in medial density as seen in (c). (e) At 105 days, TTX blockade given from 42 to 81 days after surgery and followed by 24 days without further TTX injections. Arrows point to gaps in the main optic layer. (f) At 60 days, TTX blockade only of deflected fibers. Host fibers were not blocked.

In four other groups, the timing or dose of TTX was varied. The first group (Fig. 1b) was injected with 0.1 μl of 0.01 m*M* TTX every 3.5 days, a dose which was just below threshold for impulse blockade. At 61 days (four fish), eye dominance columns identical to those of the group without TTX were found in the posterior dorsal quadrant. In the second group, the continuous blocking dose of TTX was begun 42 days after surgery (Fig. 1d). At 59 days (four fish) and at 80 days (two fish), columns were completely absent. For the third group (three fish), TTX blockade was also initiated at 42 days and a final TTX injection was given at 81 days. They were then allowed an additional 24 days without further TTX injections. Columns were found (Fig. 1e). Thus TTX did not irreversibly inhibit column formation but seems to indefinitely delay the time at which they form. In the fourth group (six fish), TTX was injected into only one eye, host (three fish) or donor (three fish), from 31 to 60 days. At 60 days normal columns showing no qualitative differences between host or donor fiber blockade were found (Fig. 1f). Thus, TTX-treated fibers could form columns, which would make a simple toxic effect of TTX very unlikely. A global effect of TTX on the tectum is also unlikely. Since donor fibers numbered only 10 to 15 percent of host fibers, the total number of blocked fibers in host tectum was not very different between the blockade of two eyes and that of the host eye only. Previous work on the neuromuscular and various other systems including the retinotectal projection also indicate no direct inhibitory effect of TTX on axoplasmic transport (*12*) nor on the capacity of fibers to grow, arborize, and form synapses (*13*). Histology on 12 representative retinas revealed no pathology.

The formation of gross retinotopography—as shown by the growth of donor fibers to the posterior dorsal quadrant and by previous work on developing urodeles—is insensitive to TTX (*15*) and is thus pharmacologically distinguishable from column formation. To some extent, then, the mechanisms producing gross topography must be different from those giving rise to columns. Column formation by regenerating fibers in the mature goldfish parallels the normal development of cortical columns in neonatal mammals. In both, there is an initial stage of extensive overlap between fibers designated to segregate (*2, 4*). In both, segregation is modulated by impulse activity; that is, it is inhibited by its elimination (*6*) or retarded by its decrement (*5*). For goldfish, and therefore by analogy for mammals, overlap is not a trivial consequence of developmental immaturity, that is, the role of activity is more than a nonspecific trophic factor for neural growth and differentiation.

Neighboring ganglion cells in goldfish retina are positively coupled, exhibiting positively correlated spontaneous activity (*15*). In this light, the present results can be taken to support the idea that columns are generated according to the rule that fibers that fire together, terminate together. This rule, together with correlated spontaneous activity, could explain why column formation in the goldfish (*16*) or the monkey (*2, 4*) is not prevented by continuous darkness. Studies in cats and monkeys showing that monocular deprivation reduces the size of cortical ocular dominance columns corresponding to the deprived eye (*4*) has led to the idea that some competition between fibers, perhaps linked to impulse activity, underlies the formation of these columns. However, the finding that TTX blockade of one eye did not prevent its fibers from forming columns shows that blocked fibers still retain a significant capacity to compete with unblocked fibers for tectal space.

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Atmospheric Trace Gases: Linear Relation Between Concentration and Time

Rasmussen *et al.* (*1*) have presented concentration data for a number of trace gases at the South Pole (SP) and the Pacific Northwest (PNW) and have interpreted these data in terms of a first-order growth rate equation,

$$\frac{1}{c}\frac{dc}{dt} = \beta$$

where c is the atmospheric concentration in parts per trillion (ppt) by volume, t is the elapsed time, and β is a constant. It is obvious, however, that this equation, which is identical in form to those of chemical kinetics, does not describe the behavior of atmospheric trace gases, since the growth curves do not in general have exponential forms.

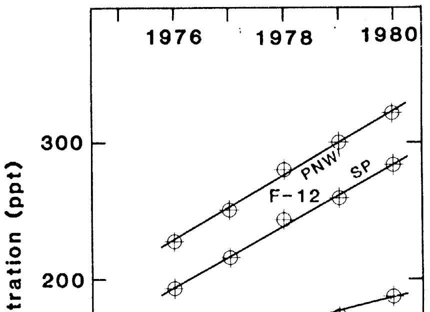

Fig. 1. Atmospheric concentration of three trace gases, F-11, F-12, and CH$_3$CCl$_3$, as a function of elapsed time at the Pacific Northwest (*PNW*) and South Pole (*SP*) locations. The curves are derived from tabulated data of Rasmussen *et al.* (*1*). The relations for F-12 are $c = 23.7t + 205$ (Pacific Northwest) and $c = 22.2t + 173$ (South Pole).

The growth of the concentrations of species CCl$_3$F (F-11), CCl$_2$F$_2$ (F-12), and CH$_3$CCl$_3$, based on the data of Rasmussen *et al.*, is shown for both localities in Fig. 1. Since uncertainties were not given for the tabulated values [table 1 in (*1*)], no error bars are given for the plotted points. However, the trends appear to be quite uniform, and in some cases appear to be linear, so that they may be approximated by the function

$$c = k_1t + k_2$$

where k_1 and k_2 are derived constants. For example, for F-12 (SP), $k_1 = 22.2$ ppt/year and $k_2 = 173$ ppt ($t = 0$ at 1975). This result is also consistent with the data and interpretation of Singh *et al.* (*2*).

Although Rasmussen *et al.* regarded β as a constant in the proposed rate equation, exponential behavior is approximated by the curve for only one species plotted in Fig. 1, CH$_3$CCl$_3$ (PNW), and even this interpretation depends on the positions of only two points. The data of Rasmussen *et al.* in general indicate that β does not remain constant but shows a marked decline with time, a finding that Rasmussen *et al.* suggest may be due to a leveling-off of emissions or global sinks. However, the observed decline in β is precisely what is to be expected on a purely mechanical basis, since the yearly increment dc (properly Δc) is added to steadily increasing values of c. Obviously also, dc/dt cannot be expected to be proportional to c but rather should approach a constant (k_1) if c undergoes steady buildup. However, it is possible that dc/dt contains a small term with a negative first-order rate constant, should the destruction of a given molecule fol-

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