

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  $\beta$  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.

The growth of the concentrations of species  $\text{CCl}_3\text{F}$  (F-11),  $\text{CCl}_2\text{F}_2$  (F-12), and  $\text{CH}_3\text{CCl}_3$ , 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

$$c = k_1 t + k_2$$

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  $\beta$  as a constant in the proposed rate equation, exponential behavior is approximated by the curve for only one species plotted in Fig. 1,  $\text{CH}_3\text{CCl}_3$  (PNW), and even this interpretation depends on the positions of only two points. The data of Rasmussen *et al.* in general indicate that  $\beta$  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  $\beta$  is precisely what is to be expected on a purely mechanical basis, since the yearly increment  $dc$  (properly  $\Delta c$ ) 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-

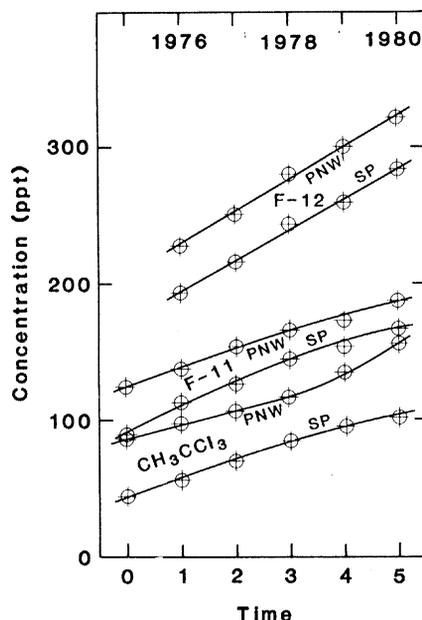


Fig. 1. Atmospheric concentration of three trace gases, F-11, F-12, and  $\text{CH}_3\text{CCl}_3$ , as a function of elapsed time at the Pacific Northwest (PNW) and South Pole (SP) locations. The curves are derived from tabulated data of Rasmussen *et al.* (1). The relations for F-12 are  $c = 23.7t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

low this law. In general, however, the first-order rate equation is inappropriate in this case.

It has been suggested (2) that, because of long residence times, the only major sink for F-11 and F-12 is the stratosphere and that  $\text{CH}_3\text{CCl}_3$  reacts with the HO radical. It is possible that details in the growth curves of Fig. 1 can be explained in this way.

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Whether one uses an exponential model or a linear model to describe the concentration data would matter only if these equations were to be used to predict concentrations of trace gases expected in the future. Such an extrapolation, however, is neither recommended nor was it even implied in (1). The rates of increase reported are designed to be used to test or establish the parameters of a global mass balance model and then to compute concentrations expected in the future based on probable scenarios of future global emissions. In general, such projections based on the mass balance of  $\text{CCl}_3\text{F}$  (F-11),  $\text{CCl}_2\text{F}_2$  (F-12), and  $\text{CH}_3\text{CCl}_3$  would not agree with either a simple linear or an exponential extrapolation of currently observed increases in these gases. For our data, the exponential model of increase is preferable as we will show here.

Since 1974 the global emissions of  $\text{CH}_3\text{CCl}_3$  have been rising at about 7 percent per year, and the emissions of F-11 and F-12 may have been falling at 3 to 4 percent per year, although some believe that the annual emissions of F-12 are still rising (2). For more than 20 years before 1974, the global emissions of F-11, F-12, and  $\text{CH}_3\text{CCl}_3$  had been rising exponentially at between 12 and 16 percent per year (3). Because of these year-to-year increases, decreases, or fluctuations in the global emissions and the finite lifetimes of these trace gases, matching the observed increase in atmospheric concentrations to a linear function [ $c \approx k_1t + k_2$ , where  $c$  is the atmospheric concentration in parts per trillion by volume (pptv),  $t$  is the elapsed time, and  $k_1$  and  $k_2$  are constants] is only an approximation, which at least over short time periods is no better than matching

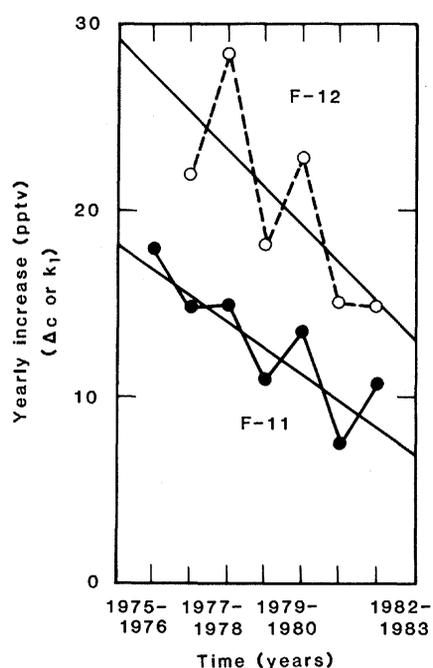


Fig. 1. Decline in the yearly increase in the atmospheric concentrations of F-11 and F-12 over 7 years (1975 to 1982). Linear least-squares calculations are shown by the solid lines.

the atmospheric concentrations to an exponential function ( $c \approx \alpha \exp \beta t \approx \alpha + \alpha\beta t$ ). The two functions are practically indistinguishable for many years of data; both can be justified as formal Taylor series expansions, and statistically for our data the linear expression is no better than the exponential one. The reason we chose  $\beta = (1/c)dc/dt$  is that it expresses a rate of increase that does not require knowledge of the absolute concentration of a trace gas. For gases such as F-11, F-12,  $\text{N}_2\text{O}$ ,  $\text{CH}_3\text{CCl}_3$ , and  $\text{CCl}_4$ , there is still some disagreement on absolute atmospheric concentrations (4). If two observers disagree on the absolute concentrations of a trace gas, they will also disagree on the linear rate of increase, but they will agree on the value of  $\beta$ .

The second point Mueller and Kretz

make is that the decline in  $\beta$  is due to adding the same increment ( $\Delta c$ ) every year to a rising atmospheric burden and not due to a slowdown in the rate of emissions. Thus, according to their linear model,  $dc/dt = k_1$  or a constant. We have plotted the measured value of  $\Delta c/\Delta t$  from 1975 to 1982 for F-11 and F-12 in Fig. 1. This plot shows that  $dc/dt$  is not a constant as Mueller and Kretz claim, and the accumulation rates are declining as we conjectured in (1). A linear least-squares analysis of  $dc/dt$  shows that  $dc/dt = a' + b't$ , where  $b' < 0$  ( $\alpha \leq 0.05$ ;  $t$ -test);  $b' = -1.4$  pptv/year<sup>2</sup> for F-11 and  $b' = -2$  pptv/year<sup>2</sup> for F-12. It does not matter whether one considers  $\beta$  or  $k_1$ ; both indicate that the accumulation rates of F-11 and F-12 are slowing down. The case for  $\text{CH}_3\text{CCl}_3$  is further complicated by cyclic variations in global emissions and its shorter lifetime (6 to 9 years). The case for  $\text{CH}_3\text{CCl}_3$  is treated in (5).

The data on F-11, F-12, and  $\text{CH}_3\text{CCl}_3$  (1) are in accord with current estimates of the global sources and sinks, including globally averaged first-order loss processes due to reactions with tropospheric OH radicals ( $\text{CH}_3\text{CCl}_3$ ) or photodissociation in the stratosphere (F-11 and F-12).

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## Naloxone and Ischemic Neurologic

### Deficits in the Gerbil: Is There an Effect?

Hosobuchi and colleagues recently reported in *Science* and elsewhere (1) that the opiate antagonist naloxone reversed the ischemic neurologic deficits induced by unilateral carotid ligation in gerbils. Using similar models, we have found that naloxone has no therapeutic effect in experimental stroke in the gerbil (2).

From the description given by Hosobuchi *et al.* of the procedures and statistical techniques used (1) it appears that the 15 control gerbils that received saline were studied separately from the 10 gerbils that received naloxone and that the raters were not blind as to drug treatments. The degree or lateralization of