will occur. The answers, assuming that all nations cease synthesis, depend on the relative sizes of S_A and S_N, on whether other sinks beside tropospheric OH radicals are significant, and on details of stratospheric chemistry that control the chain length of the cycle comprising reactions 6 through 8. The effectiveness of BrO clearly depends on ClO amounts, and with greatly reduced emissions of CFCs as a result of international agreements and industrial actions, ClO amounts will decrease but only slowly, requiring decades for complete purging.

By introducing biomass burning as a significant source, Manö and Andreae (*3*) have added more questions to the puzzle. For example, although most current biomass burning is probably human-controlled, amounts of material may be known only to within about 60% (*1*), and temporal trends are not known well. Further, the new data (*3*) raise other questions. For example, why is MeBr released both during the flaming phase (along with CO_2) and the smoldering phase of burning (along with CO), whereas CH_3Cl is released mostly during smoldering? How variable are the Br contents of plants, and how does one do a proper inventory of Br of the material burnt annually?

These new questions add to previous uncertainties about atmospheric MeBr amounts, sources, and sinks. To illustrate, in a first approximation, the total steady-state atmospheric inventory, B, is related to annual global sources, S, and the atmospheric residence time T by $B = S \times T$ [see (*6*) for a more general analysis]. At present, B is probably between 1.5 and 2.1×10^8 kg, although some published data suggest values 60% higher.

Individual components of S have been estimated, but only roughly in my opinion, so there is merit to estimating S as B/T. In turn, T is estimated from knowledge of elementary chemical and biological processes and atmospheric transport models; reaction with OH radicals limits T, to about 2 years. Other sinks discussed by Manö and Andreae (*3*) could lower T, but not to as little as 1 year, I believe. Further information can be deduced from two- or three-dimensional transport models that use the spatial distribution of atmospheric MeBr as input data, but our current knowledge of the distribution is also rough. Excesses are observed north of the equator, suggesting the dominance of anthropogenic (or at least continental) sources, but the north/south ratio is reported to be anywhere between 1.15 and 1.5, with seasonal variations of unknown origin (*6*). Altogether, $S = S_A + S_N$ is not known very well. Measured stratospheric concentrations of the key inorganic Br species, BrO, are generally consistent with BrO amounts predicted from halon and MeBr amounts (*7*), but these data cannot tell us how much of the BrO is from anthropogenic MeBr.

Unmentioned by Manö and Andreae (*3*) is another new proposal (*8*)—that the oceans may serve as a buffer in the global MeBr system. A decrease in anthropogenic emissions should induce a compensating flux from the ocean to the atmosphere, thus lessening the expected change in atmospheric amount (*8*); how much of a change depends on rates of chemical and biological consumption in oceanic surface waters. To my knowledge, there is very little research under way to address this idea quantitatively. Returning to anthropogenic MeBr, we have very little empirical evidence from which to estimate the fraction, F, that escapes to the atmosphere during and after agricultural soil fumigation, a principal target of the new regulations. The potential for fumigant MeBr to destroy stratospheric ozone has been calculated assuming that no MeBr is destroyed in the soil. Shouldn't we estimate F first and then calculate the effects of the MeBr that actually enters the atmosphere, as suggested by Ko *et al.* (*9*)?

The questions outlined here are intrinsically interesting to many atmospheric and oceanic scientists. We want to pursue them not only to understand how this system works, but also to provide a solid scientific basis for industrial decisions and governmental regulations concerning MeBr, and to be able to estimate how effective such actions can be.

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Precise Development from Imprecise Rules

Michael P. Stryker

Millions of neurons establish functional connections to one another each time the brain of an animal is formed. How this occurs seems almost incomprehensibly complex. At the moment we believe that the rules that refine the connections among neurons are stochastic. The strength and indeed the very preservation of nascent connections between neurons appear to depend on patterns of neural activity in the developing nervous system, and these patterns of activity vary among individuals—at best they are only statistically regular—so that the detailed wiring of each individual's brain is distinct. If this view is correct, a logical problem arises: How do we account for the close similarities among the brains of different individuals? A paper in this week's issue of *Science* (*1*) addresses a particularly clear example of this problem—the formation of layers in the primate lateral geniculate nucleus. The authors use a thermodynamic computer model to show that great regularity in the position of a subtle feature, a switch from six layers to four layers, can result from a slight discontinuity in the inputs to the lateral geniculate during development. To our present way of thinking it is astonishing that this small perturbation would so markedly affect the overall organization of such a large structure.

At least since D'Arcy Thompson's treatise on biological morphogenesis (*2*), it has been clear that simple rules of growth can give rise to precise and intricate forms. Just as crystals grow, with new molecules fitting precisely onto only certain specific points of the surface formed by their predecessors, so too may portions of the nervous system.

Formally simple rules of cell-cell adhesion and induction account well for the perfect assembly of cells in the eye of the fruit fly *Drosophila* (*3*), and the ingrowth of new axons on the surfaces of their earlier-growing neighbors can explain the crystalline regularity of the early stages of the visual projection in this species (*4*). Such systems, which grow in an orderly fashion by accretion, remain ordered throughout their length. In the fly, the bundle of nerve fibers that carries information from the eye is as precisely ordered as are its retinal cells of

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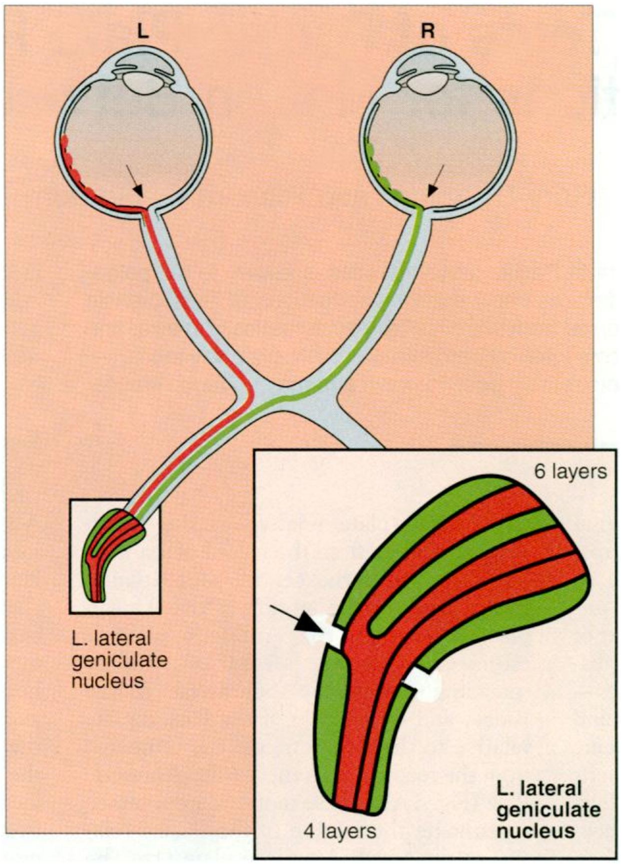
origin and their points of termination.

Things are different in the brains of vertebrates. In mammals, the nerve fibers from the eyes do not retain precise order between their origin in the retina and terminations in (among other structures) the lateral geniculate nucleus of the brain. Individual fibers may wander far and wide within the optic nerve and tract. How then do they terminate so precisely and reproducibly?

The early stages of vertebrate neuronal development proceed normally, or nearly so, even in the absence of neural activity: Neurons are generated in appropriate numbers at appropriate times; they migrate to appropriate positions; they send out axons that find appropriate paths to their target structures; and the axon terminals recognize the correct cell types and even the right general region in target structures. The specificity in such early stages of neuronal development appears to be due to chemical recognition events (*5*). But these mechanisms are not nearly precise enough to establish the final form of the mammalian nervous system, in which connections are defined at the level of individual neurons (*6*). For establishing precise order, these systems take advantage of a quite local correlation between the electrical activities of immediately neighboring retinal ganglion cells that is present even prenatally (*7*). Adjacent cells in the retina "know" to terminate in adjacent regions of the lateral geniculate because they have similar patterns of activity. That activity-dependent mechanisms are critical is illustrated by the experiment in which neuronal signaling by action potentials is blocked during development, and, as a result, the segregation of inputs from the two eyes into separate layers fails to take place (*8*).



Monkey see. The arrangement of inputs from the left eye (red) and the right eye (green) to the lateral geniculate nucleus of the macaque monkey. Optic disk (small arrows) representation in the lateral geniculate is indicated by the large arrow and the cellular discontinuity.

Lee and Malpeli (*1*) modeled the formation of geniculate layers by starting with overlapping and fairly disorganized inputs from the two eyes and making the termination of each model nerve fiber from the eye subject to several influences, some depending on its neighbors and some on its position. These influences changed gradually so as to favor a four-layered structure at one end of the nucleus and a six-layered structure at the other, as occurs in the real lateral geniculate. If the gradient of these influences was uniform, the transition from six to four layers occurred at any point in the middle half of the nucleus. But then they introduced a small discontinuity in one eye, modeling the "blind spot" or optic disk of the retina, where there are no retinal ganglion cells because of the exit of the optic nerve from the back of the eye. This discontinuity locally changed the influences that depended on neighboring terminations, and consequently the point of transition from four to six layers was nearly always trapped so that it took place at the discontinuity. In the real lateral geniculate nucleus, as in the model, the transition from four to six layers almost always takes place at the discontinuity of the optic disk representation (*9*).

These findings may not surprise many physicists. Singularities and edge effects clearly impose structure in many self-organizing physical systems. But in biology it is often assumed that causes must be similar in magnitude to their effects, so that a constant border should be the product of a regular and sharp difference between conditions on the two sides at an earlier stage of development. What is new in the paper by Lee and Malpeli is the demonstration that there may be a regular border with no significant gradient across it at most points, and only a slight singularity at some points.

There are numerous regular features in the brain (and elsewhere) that develop in all individuals of a species during morphogenesis. For example, the major gyri and sulci of the brain are found in similar locations in normal monkeys, while in animals in which early neural inputs have been manipulated, a highly regular but abnormal pattern of sulcation appears (*10*). What other features may be specified similarly to the geniculate lamination by small singularities? Is there a hallmark by which we can recognize features like this one?

As we search for the factors responsible for regularities in morphogenesis, we must not ignore the possibility that prominent and precise features may result from quite limited and apparently minor singularities.

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