The shuttle thus seems to be an established political reality. It will eventually open participation in space science to a wider group of scientists and may generate applications as yet undreamed of. Nonetheless, opponents of the shuttle—and most space scientists would be opponents if the issue came down to the shuttle versus science—argue that the volume of space traffic in the 1980's is unlikely to be large enough to justify the shuttle's cost, even including the military applications that now appear to be its main raison d'etre. It is widely acknowledged in military circles, moreover, that the shuttle will not reduce defense space costs substantially. The shuttle is vulnerable to attack, because the five orbiting vehicles and two landing sites could be quickly destroyed, so that the Defense Department will continue to stockpile enough rockets to launch spy satellites and other hardware without it.

With or without the shuttle, space scientists see a paradox in the fact that their field faces more uncertain prospects than ever before just when it is beginning to produce substantive results. There is a real threat, some believe, that the research groups built up in past years will be dispersed for lack of money. Some scientists in advisory positions are girding for an all-out fight to preserve the space science program, even to the extent of suggesting that a $1 billion cut in the NASA budget would be better for science than a $100 million cut, since the former would entail canceling the shuttle, in theory releasing lots of money for space science. Others are advocating that planetary scientists should seek to convince NASA to fund enough research to keep groups together, even if no new missions or spacecraft are approved. Thus, pessimism and optimism seem to coexist in the opinions of many of those associated with the space science program. This mixed view of the future was neatly summed up by one scientist who predicted that the space program will either phase out shortly or enter a very imaginative, and more scientifically-oriented era as the money now being used to build the space shuttle is poured into "doing" science in space.

It may be that such concerns are overdrawn, since, as one congressional aide pointed out, the modest cutback in the present NASA budget would seem to be inconsistent with a serious cut for next year. On a longer time scale, however, there is no doubt that space scientists will increasingly have to justify this expensive kind of research. There is good reason, as has been outlined in other articles in this series, to think that justification can be found, that exploration of the solar system and beyond is, as one scientist described it, "our obvious new frontier."—ALLEN L. HAMMOND

Developmental Neurobiology: Specificity in the Visual System

One of the major open questions in neurobiology is how nerve fibers make specific connections with other cells during the course of development. Some investigators believe that each nerve fiber must have a unique biochemical label. Others propose that the apparent accuracy with which nerves form connections can be explained by a well-defined temporal sequence of nerve growth and development. Results from studies of the visual systems of various species provide evidence that either explanation may be correct, depending on the organism. Since cells from the visual systems of certain species are thought to contain biochemical labels that mediate recognition, investigators are now developing ways to identify such labels.

The problem of explaining specificity in the visual system was popularized 11 years ago by Roger Sperry of the California Institute of Technology, in Pasadena. Sperry, studying regeneration of optic nerve fibers in amphibians, was impressed with the uncanny accuracy with which severed optic nerve fibers found their way through a maze of other neurons to their targets on the optic tectum of the brain. He advanced a hypothesis that this regeneration must be mediated by chemical labels on the cells.

In the decade since Sperry proposed his hypothesis, numerous investigators have searched for a simpler explanation of specificity that would not require so many chemical labels. One simple explanation is that specificity arises from a temporal sequence of growth and development of nerves. A nerve fiber would grow toward its target cells, contact those cells, and then the target in turn would differentiate so that it was receptive to the nerve fiber. Although it now seems unlikely that this hypothesis alone is sufficient to explain the visual systems of vertebrates, it can be used to explain specificity in the small crustacean *Daphnia*, according to Cyrus Levinthal of Columbia University in New York. Levinthal's results are of interest to neurobiologists because it is believed that phenomena observed in *Daphnia* may also be present in vertebrates, although vertebrates may have additional, more complicated, signals for cell recognition.

Is Cellular Communication Involved?

Levinthal and his colleagues find that nerve fibers grow outward from the eye of *Daphnia* in a certain temporal sequence while, concurrently, the target cells in the visual center of the organism's brain develop in a complementary sequence. Moreover, a group of target cells does not fully differentiate until it is touched by one of a bundle of eight optic nerve fibers. When such a nerve fiber contacts its target (which consists of five cells), each target cell in the group, in turn, wraps around the fiber. When a target cell is wrapped around an optic nerve fiber, small holes are formed between the membranes of the two cells (gap junctions); these junctions are large enough for molecules having a molecular weight of 300 to pass through. After a short period, the passageway between the two cells closes again. This process, Levinthal speculates, may be a way for the target cell and optic nerve fiber to communicate and may thus trigger the differentiation of the target cell. Levinthal points out that optic nerve fibers of vertebrates may also communicate with their targets to trigger differentiation of target cells.

It has become increasingly clear that specificity in the visual systems of vertebrates is not simply a result of temporal sequences of development. From data they accumulated while working with frogs, Marcus Jacobson and his colleagues at the University of Miami have ruled out such an explanation as have W. Maxwell Cowan and his colleagues at Washington University Medical School, in St. Louis, who worked with chicks.

Jacobson's group devised several experiments in which the time at which developing optic nerve fibers in the frog contacted their targets was later

than normal. For example, they transplanted an eye from one embryo onto the body of another embryo or grew it in a tissue culture. They let the eye grow for 2 weeks, and then transplanted it back to its original host. At this time, all of the normal connections between the optic nerve fibers and the tectum were made although the arrival of fibers in the tectum had been delayed by the experimental procedure.

Additional evidence against such a temporal hypothesis was obtained by Cowan and his associates when they used two types of experiments with chick embryos to show that optic nerve fibers grow across the surface of the tectum in search of their targets rather than making connections with the first part of the tectum they encounter. In their first group of experiments, Cowan and his colleagues removed part of a developing chick's retina before the nerve fibers left the eye to grow toward the brain. They observed that the nerve fibers that grow from the remaining retinal cells make connections in appropriate regions of the tectum although this means that they have to pass over empty regions that would ordinarily have been occupied by fibers from the ganglion cells in the excised portion of the retina.

Cowan's group next studied the penetration of optic nerve fibers from the surface layer of the tectum into the layer in which synaptic connections are made. They discovered that nerve fibers from the retina may grow over a fairly large area of the tectum before they begin to penetrate it. Moreover, the sequence in which they penetrate these layers does not parallel the pattern of the spread of optic nerve fibers over the surface or the sequence of development of tectal cells. The optic nerve fibers first contact the front end of the tectum about day 6 of development and grow across the tectum from front to back until eventually, by day 12, the whole surface is covered by optic nerves. The tectum itself develops similarly in that the cells near its front end develop first. However, penetration begins at the center of the tectum on day 9 of development and continues so that the region of penetrated tectum spreads concentrically.

The evidence that targets in the tectum most likely are recognized by particular optic nerve cells has been an invitation to research workers to seek the size and orientation of these targets. Jacobson and his colleagues have determined that, in the frog, a target consists of no more than five cells (50 micrometers) that are arranged in a straight line. They obtained this result by excising parts of the optic tectum of adult frogs and grafting these parts onto different parts of or in different orientations on the tectum. They then observed the regeneration of optic nerve fibers onto their transplanted targets. Jacobson and his associates obtain the same result in all parts of the tectum. This, they believe, indicates that every piece of the tectum may have a unique positional marker that is retained when that piece is transplanted.

Thus far, most research on neural specificity in the visual system has been phenomenological. While investigators agree that such research is essential to the definition of the problem, they are nonetheless anxious to know the molecular basis of neural specificity. Thus the few attempts to study this aspect of the problem have aroused considerable interest.

Molecular Basis of Specificity

Luis Glaser and his associates at the Medical School of Washington University, in St. Louis, have found that cell membranes from the retina of a chick will bind to its tectum, but not to other structures in the brain. However, as Glaser points out, this is too unrefined an assay to study precise recognition of targets on the tectum by nerve fibers from the retina. At best, he believes, it relates to the problem of how retinal fibers find the tectum in the brain.

A slightly more precise assay for recognition of the tectum was devised by Stephen Roth and his colleagues at Johns Hopkins University, in Baltimore. They found that retinal cells from the top (dorsal) half of a pigeon's eye will bind to the bottom (ventral) half of its tectum but not the top half, and that retinal cells from the bottom half of the eye will behave conversely. This effect is consistent with the fact that nerve fibers from the top half of the eye will connect with the bottom half of the tectum and vice versa.

In order to determine the basis of the specificity of the binding of retinal cells to tectum, Roth and his associates exposed the tectal cells to various enzymes. Thus far, they find that two sugar-degrading enzymes—a galactosidase and a glucosaminidase—will affect binding of retinal cells from the bottom half of the eye to cells from the top half of the tectum but will not affect binding by retinal cells from the bottom half of the eye. Roth suggests that these sugar molecules in the cell membranes may play a key role in recognition.

A third approach to studying the molecular basis of neural specificity is being taken by John Freeman and his colleagues at Vanderbilt University, in Nashville. These investigators noticed that cell recognition is affected by the receptors for neural transmitters on the surface of target cells. First, they ascertained that the neural transmitter in the visual systems of amphibians is acetylcholine. It had been shown previously that acetylcholine receptors in muscle cells are located in bundles in the cell membranes. These receptors can be blocked by a snake neurotoxin—α-bungarotoxin—that binds to them irreversibly.

Freeman and his colleagues severed optic nerves in amphibians, applied α-bungarotoxin to their targets on the tectum, and allowed the severed nerves to regenerate. The optic nerves, they found, regenerated to the wrong targets if the acetylcholine receptors on their proper targets were blocked. Roth and Freeman used their results to devise models that could be used to explain neural specificity in vertebrate visual systems. However, there are as yet too few results for these models to be evaluated. Little is known about membrane structure and cellular adhesion. Neural transmitters have been extensively studied in other systems, such as the nerve-muscle system, but not much is known about neural transmission in the visual system. Moreover, it is difficult to assess the universality of such models. As Jacobson stresses, a great deal of confusion in neurobiology is due to a lack of recognition or appreciation of species differences. Nonetheless, the results of Glaser, Roth, and Freeman are of interest because they provide a glimpse of what molecular features may be involved in neural specificity.

Because of the complexity of the problem of explaining neural specificity, progress in this field has proceeded by small steps rather than by dramatic breakthroughs. However, many believe that new explanations of specificity will be forthcoming, heralded by recent results that pin down the nature of the problem.

—GINA BARI KOLATA