Fish out of phase

from Marian Dawkins

ANIMALS often need to distinguish between stimuli which arise from their environment (which includes other animals) and those which are caused by some action of the animal itself. An apparent movement of an object or a sound, for example, may require a completely different response depending on whether or not the animal has produced that movement or that sound by its own behaviour, even though the pattern of stimulation reaching the animal's sense organs may be extremely similar in the two cases.

Although the ways in which animals make this distinction are many and varied, a recently described example in a species of electric fish by Scheich (*Science*, **185**, 365; 1974) is of particular interest as it illustrates how the distinction can be made even in a situation where the animal must distinguish between two similar and simultaneous wave forms.

Scheich studied a species of fish, *Eigenmannia*, in which the electric organ has a regular wave-like discharge, enabling the fish to locate objects by detecting disturbances in the resulting field. When two *Eigenmannia* which are discharging their electric organs at similar frequencies come close enough together, they both unerringly adjust their frequencies in opposite directions so that their frequencies are no longer similar and the danger of interference to their object-detecting systems is avoided.

Conveniently for experimental study, a fish will also alter its frequency if stimulated through an electrical dipole in its tank at a frequency near its own. Within wide limits of absolute frequency, the fish will correctly alter the frequency difference between its own discharge and that of the applied stimulus to maintain a difference. In order to do this the fish must be able to detect how near its own frequency is to that of the applied stimulus and to have information on whether it is lower or higher.

A possible, although cumbersome way of doing this would be to have an array of frequency-tuned filters and for the fish to respond whenever two filters near enough in frequency were active together, provided it had some way of telling which frequency filter was responding to its own discharge. In fact, as Scheich demonstrates, the fish's solution is much simpler and his theory accounts more satisfactorily for the fish's ability to recognise the sign of the frequency difference whatever the fish's own frequency within that range.

The analysis is done by sensitivity to the beating of the two signals in the electric field—that is, the coming into and out of phase of the two waves of slightly different frequency. The frequency with which the two waves come into phase with one another (like the frequency of beat notes with two sound waves) is the difference between the two frequencies and will be independent of absolute frequency.

If the electric organs discharged sinusoidally there would be ambiguity as to which signal belonged to which fish, but the discharge is not sinusoidal: the wave shape is rich in harmonics and is clipped in one polarity. By being sensitive to the peculiarities of beat patterns produced by the interaction of two such oddly shaped waves, the fish can tell whether the interference is above or below it in frequency as well as how near in frequency. By ingenious experiments in which the fish's own output was converted artificially into a sine wave, Scheich found that under these circumstances, the fish was completely unable to distinguish the sign of the frequency difference between its own output and a sinusoidal applied stimulus. Only when its own output was allowed to resemble more closely the normal discharge was its normal behaviour restored. Scheich also found neurones in the fish's midbrain which responded to differences in frequency in such a way that they could directly provide the input into the electric organ.

Thus the fish is able to obtain information about how near its own frequency another fish is discharging and whether the other is above it or below it in frequency, not by analysing constituent frequencies, but rather by beat analysis in the time domain. It is interesting that a similar mechanism is postulated by some theories of hearing.

RNA molecules in initiation of protein biosynthesis

from Alan E. Smith

TEN years ago the main interest in protein biosynthesis was the establishment of the genetic code by translating synthetic polynucleotides of known composition or sequence in bacterial cell-free systems. Then it seemed reasonable to suppose that any ribosome can attach to almost any RNA molecule and translate it into polypeptide. This view is now known to be totally naive. The initiation of protein synthesis is a highly complex interaction between a ribosome, the initiator tRNA, and the specific ribosome-binding site on the mRNA. Several protein factors which also play a part in this process have various enzymatic functions: dissociating the ribosome into subunits, binding the initiator tRNA and binding the appropriate mRNA molecule. It now seems that in addition to the protein initiation factors, there are RNA molecules involved.

For some time, Heywood and his colleagues have been studying the specificity of mRNA translation in heterologous cell-free systems and have concluded that a specific mRNA can only be translated in a heterologous ribosome if a specific homologous initiation factor (designated IF_3) is present. Thus the synthesis of myosin on, say, erythroblast ribosomes requires initiation factors obtained from muscle ribosomes (*Biochemistry*, **11**, 2061–2066; 1972). When they further fractionated red muscle initiation factors required for the synthesis of myoglobin and myosin in a reticulocyte cell-free system, Heywood, Kennedy and Bester (*Proc. natn. Acad. Sci. U.S.A.*, **71**, 2428–2431; 1974) found that two activities are present: one specifically stimulates myoglobin synthesis and the other stimulates myosin synthesis. In addition to these two proteins, an RNA molecule was isolated from the IF_3 preparation and this seems to inhibit the initiation and translation of heterologous mRNA molecules. Bogdanovsky, Herman and Schapira (*Biochem. biophys. Res. Commun.*, **54**, 25–32; 1973) have previously shown that a similar RNA molecule of molecular weight 11,000 is present in preparations of initiation factors from rabbit reticulocytes and that the RNA is required for the synthesis of globin *in vitro*.

The presence of a small RNA initiation factor may corroborate the observations of Reichmann and Penman. They found that the base analogue 5-azacytidine inhibits protein synthesis in HeLa cells with a half life of 90 minutes (*Biochim. biophys. Acta*, **324**, 282–289; 1973). The inhibition seemed to occur at the initiation of protein synthesis and was suppressed by actinomycin D. Earlier studies had established that the half life of mammalian mRNA is very long compared with the response to aza-cytidine, and this suggested that an RNA molecule other than mRNA or rRNA, which is rapidly metabolised *in vivo*, is involved in the initiation of protein synthesis. The authors then showed (*Proc. natn. Acad. Sci. U.S.A.*, **70**, 2678–2682; 1973) that the putative RNA species accumulates in cells subjected to inhibition of protein synthesis by, for example, cycloheximide or starvation of an essential amino acid, and cell-free systems prepared from such cells show a greatly enhanced ability to initiate new polypeptide chains.

The evidence available to date indicates that the RNA species involved