RÉSUMÉ

Visible benefit

WHEN trichromatic colour vision has such obvious evolutionary advantages, why should some 2 per cent of males in a human population be dichromats (that is, unable to distinguish between red and green)? The question is posed by M. J. Morgan *et al.* (*Proc. R. Soc.* B**248**, 291–295; 1992), who return to the idea mooted during the Second World War that dichromats can 'see through' camouflage that foxes the colour-normal observer. In simple but ingenious tests, colour was used to mask targets demarcated from a background by the orientation or size of their texture elements. Dichromats were indeed significantly better at spotting the camouflaged region. But although this ability in disability is undoubted, the authors allow that the polymorphism of colour vision may be maintained purely by the genetic mechanism of unequal crossing-over.

In season

SATURN's moon Titan, the second largest satellite in the Solar System and the only one with an appreciable atmosphere, has seasons, according to new observations from the Hubble Space Telescope (J. Caldwell *et al. Icarus* **96**, 1–9; 1992). In 1990, when the observations were made, Titan's Northern Hemisphere was brighter than its Southern Hemisphere, the reverse of what Voyager 2 saw in 1981, a third of a Titan year earlier. The role of 'seasons' in modulating Titan's atmosphere and causing slow variations in brightness and the North–South asymmetry was suspected in 1981, but a competing role for the 11-year solar cycle was also implicated. Related observations show that what changes you see depend on the wavelength you look at, as different parts of the spectrum reveal different parts of Titan's atmosphere.

Current communication

Gymnotus carapo is territorial, and can distinguish between its neighbours' voices and associate them with the appropriate territories. *G. carapo* is not a songbird — it is a fish and uses electrical pulses for its 'song' (P. K. McGregor and G. W. M. Westby, *Animal Behaviour* **43**, 977–986; 1992). The pulsed signals are separated by timed silences or 'interpulses', whose lengths are inversely proportional to dominance status. Yet even with interpulses removed from playbacks, fish respond in characteristic ways, because the waveforms are as characteristic of individual fish as songs are of birds. The brevity of each pulse (just two μs) is close to the speed of nervous transmission, however, so it is hard to understand how the fish can tell between any two — it could be that they respond to the 'beat' frequency differences against their own signal.

INFLUENZA VIRUS

Amantadine blocks the channel

J. J. Skehel

THE membrane components of viruses such as influenza encounter acidic cellular compartments at two stages of virus replication. At the beginning of infection viruses are taken into endosomes; there their fusion glycoproteins are activated at low pH to fuse virus and endosomal membranes, allowing the genome–transcriptase complex to enter the cell. Later, newly synthesized fusion glycoproteins and other virus membrane proteins are transported to the cell surface through the acidic *trans*-Golgi. It is thought that in both of these environments one of the influenza virus membrane proteins (M$_2$, which consists of 97 amino acids) functions as an ion channel, and this property of the protein is addressed by Pinto *et al.* in *Cell*[1].

Using voltage-clamp procedures to analyse the total membrane currents of oocytes injected with M$_2$ messenger RNA, the authors show that expression of M$_2$ at the cell surface correlates with the activity of a novel ion channel, and that the current carried by the channel is regulated at low pH. They also report that channel activity is blocked by the anti-influenza drug amantadine, and that the channel properties of mutant M$_2$ proteins (which have been reported to confer resistance to amantadine during virus infections) are unchanged in amantadine-treated oocytes. Studies of such mutants and of the mechanisms of action of amantadine have formed the basis for proposals that, during virus replication, M$_2$ functions as a channel in two stages — initially as a virus membrane component, which allows acidification of the virus core; and subsequently as a *trans*-Golgi membrane component, which relieves the pH gradient in this compartment[2,3].

The anti-influenza activity of amantadine (1-amino adamantane hydrochloride) was first described in 1964 (ref. 4). Since then, it has been shown to be effective in clinical trials[5] but has had limited general use, for two main reasons. One is that it can cause neurological side effects[6]. The other is that its high specificity for influenza A viruses and lack of effect on influenza B (ref. 4) requires identification of the virus concerned before correct prescription. From the time of the first reports of its activity, it has been known that addition of amantadine to cells before infection blocks an early event in influenza replication. The possibility was therefore considered that, as a weak base, it increases endosomal pH (ref. 7) and prevents the low pH-activation of the membrane fusion potential of the haemagglutinin fusion glycoprotein. The isolation of amantadine-resistant mutants containing haemagglutinins which fused membranes at higher pH than wild-type virus was consistent with this possibility[8].

However, several studies[9,10] have shown that at much lower concentrations, which do not influence endosomal pH, amantadine prevents the disassembly of the virus core. As a consequence it blocks virion transcriptase activity and inhibits its transfer to the nucleus where virus mRNA synthesis normally occurs. Virus mutants resistant to this blockade all contain mutant M$_2$ proteins with amino-acid substitutions in their transmembrane regions[11]. Amantadine can also prevent virus replication at a later stage, and it is primarily from studies of this event that the proposed ion-channel function of M$_2$ is derived[12].

In this case, treatment of infected cells with amantadine leads to the detection of haemagglutinin molecules in the *trans*-Golgi and at the surface of infected cells in a conformation characteristic of the conformation they are induced to form at the low pH of virus–membrane fusion. Viruses containing a mutant haemagglutinin which is more stable than wild type, and which is insensitive to premature activation at *trans*-Golgi pH, are resistant to this effect of the drug[13]. But more importantly, the same mutations in M$_2$ which override the early block in replication also lead to drug resistance[12].

Three conclusions have been drawn from these results. First, that by blocking M$_2$ function amantadine maintains the *trans*-Golgi at its normally low pH; second, that the initial inhibition of virion core disassembly results from blockage of the same function; and third, that M$_2$ functions as an ion channel in both cases, mediating the transmembrane export of H$^+$ from the *trans*-Golgi and the import of H$^+$ to the interior of infecting virus particles in endosomes.

The observations of Pinto *et al.*[1] — that amantadine blocks the ion-channel activity of wild-type M$_2$ in oocytes and is without effect on the channel properties of the M$_2$ mutants — provide strong support for these conclusions. In addition particular attention is given to the question of whether M$_2$ functions independently as a channel, as might be expected if the proposal that it functions as a virion channel component is correct, or whether it in some way modifies the properties of an endogenous channel. Using two mutant M$_2$ proteins with either an additional amino acid or a deletion of four amino acids in the transmembrane region, which they pre-