plastid preparations. On the other hand, tobacco rattle virus (TRV) associates with mitochondria. Dr B. D. Harrison (Scottish Horticultural Research Institute, Invergowrie) showed how the X-bodies associated with infection by a defective strain of TRV (one which exists as free nucleic acid and does not form coat protein) consisted of clumps of deformed mitochondria; non-defective strains did not induce X-bodies to such an extent. He suggested that the mitochondrial damage might be due to the continued synthesis of RNA in the defective strain and that this RNA synthesis might be associated with the mitochondria.

Aggregates of virus particles or protein are frequently found in infected cells. Dr R. Hull (John Innes Institute, Norwich, England) showed that there are four *in vivo* aggregation forms of alfalfa mosaic virus particles and that these are strain specific. He found that in double infections the two characteristic aggregates associated with two strains could be found side by side within the same cell.

ENZYME REGULATION

Allosteric Cosmos

from our Molecular Biology Correspondent

To judge from the current literature, it is still an allosteric world, and indeed it is not difficult to apply the term to any situation involving interrelated equilibria. None the less, when a mandarin of physical chemistry expounds an allosteric hypothesis to unify three of the most challenging, but seemingly disparate, biochemical systems, one can scarcely avoid paying attention. The title of T. L. Hill's article (*Proc. US Nat. Acad. Sci.*, **64**, 267; 1969) is "A proposed common allosteric mechanism for active transport, muscle contraction and ribosomal translocation", no less.

The mechanism that Hill envisages involves the presence in each system of a protein capable of existing in two different conformational states, and of utilizing ATP or GTP both as activator and substrate. The isomerization of the protein brings about the transfer, in effect, of another ligand, and the energy for the whole cycle is provided by the hydrolysis of the triphosphate. In active transport, the relevant protein is designed to swivel in some manner which will allow the crucial binding sites to give on one side or the other of the membrane. These two positions are seen as conformational states. In order for the ionic ligand to be taken up by the one state and released by the other, a set of thermodynamic conditions such as the following must be fulfilled: one conformation state is much more stable than the other, but the relative stabilities are reversed when ATP is bound. The isomer with high ATP affinity is also a good catalyst for the hydrolysis; the product, ADP, is not strongly bound by either state. The binding of ATP and of the ligand to be transported are high-affinity processes, rapid compared with the conformational change. The hydrolysis of the ATP is rapid compared with the dissociation of the substrate and the other ligand, but the loss of the product, ADP, and the ligand occurs rapidly relative to the conformational reversion of the protein–ligand complexes to the initial conformation state of the protein. With two forms of the protein and liganded status variantly involving the transport ligand, ATP and ADP, twelve thermodynamic states of the system can be defined. The net result is transport of ligand and elimination of ATP, so that the cycle can begin once more.

With muscular contraction, actin is seen as the ligand that is transported, and the active protein is the myosin bridge which can swing between two positions relative to the filament, in response to the attachment of ATP at the tip. With all units acting cooperatively, a force is generated, leading to relative motion between the actin and myosin filaments, which in turn causes the bridges to return to their initial position. Again, sets of possible conditions for the cycle to proceed can be formulated. The bridges are envisaged to command a continuum of states, in which two positions represent conformations of maximum probability.

In translocation, a factor, G, is taken up from the medium by the ribosome–messenger–tRNA complex. It functions as a bridge between the ribosome and tRNA, and on taking up GTP undergoes an isomerization, which causes the messenger to be displaced relative to the ribosome. This dislodges the tRNA occupying the donor site, and brings in, in its place, the tRNA of the complex.

Whether, when the dust has cleared, the three citadels will be found to have fallen before the new instrument of theory is open to doubt, but one may hope that it will suggest new directions of attack and a re-evaluation of older ideas. Hill indicates with some nonchalance that other processes, including ciliary motility, mitosis and RNA and DNA synthesis can be encompassed by his scheme.

A more sober but no less interesting account of kinetic effects, this time in enzyme regulation, comes from Huang and Frieden (*Proc. US Nat. Acad. Sci.*, **64**, 338; 1969). Earlier work from Frieden's laboratory had shown that the function of the enzyme glutamate dehydrogenase is controlled by a reversible aggregation, governed by ligands. By the use of stopped-flow methods, the disaggregation kinetics have now been analysed, and it emerges that the rate constants vary over three orders of magnitude, according to which co-factor and nucleotide (inhibitor) are present. The situation in which the interconversion between high and low-affinity states of an enzyme (here defined by the degree of association) may be slow compared with the catalytic process has never previously been envisaged. In such a case this rate will be the factor controlling the effective velocity of catalysis. With GDP and NADH as inhibitor and cofactor it is thought that this condition may obtain in glutamate dehydrogenase.

LABORATORY ANIMALS

Infections in Laboratory Monkeys

from a Correspondent

BECAUSE sub-human primates are used increasingly for medical and paramedical studies, there is a greater awareness of the problems inherent in experimenting with captured wild animals. Moreover, the close phylogenetic relationship of these animals to man, with the consequent advantages for research on human problems, brings special hazards of zoonoses. An international symposium devoted to the problems of