out the dendritic tree distal to the MBP would produce 5·5–7·6 mV depolarization at the soma if it were 250μ away, which is comparable with the depolarization known to be produced by strong stimulation of the non-specific thalamic system, the fibres of which end on apical dendrites in the upper cortical layers. If the MBP were 750μ from the soma, then the equivalent depolarizations would be 0·4 to 0·6 mV, which would still be sufficient to modulate spike frequency, though insufficient to cause spike initiation unaided.

VIROLOGY

Cleaving Viral Proteins

from our Cell Biology Correspondent

THE encapsulation of polio virus RNA genomes in capsid protein apparently involves a most intriguing mechanism, the specific cleavage of viral protein. In the latest issue of *Proc. US Nat. Acad. Sci.* (**61**, 77; 1968). Jacobson and Baltimore report that none of the three viral coat proteins (VPO, VP1 and VP3) is a primary gene product, but that all three are produced by cleavage of a precursor protein, NCVP1. The evidence for this is that in a pulse-chase experiment radioactivity is lost from NCVP1 and at the same time there is a large increase in the radioactivity in the three coat proteins. To clinch the argument, tryptic digests of the four proteins are being made and they should provide unequivocal evidence of the precursor product relationship between NCVP1 and the capsid proteins. None of these experiments, of course, necessarily implies that the three polio capsid proteins exist as separate entities *in vivo*, for although they can be separated on polyacrylamide gels, *in vivo* the chain of NCVP1 could be folded and cross-linked so that the products of its cleavage are held together.

Recently Holland and Kiehn (*Proc. US Nat. Acad. Sci.*, **60**, 1015; 1968) demonstrated a similar cleavage process during the replication of several enteroviruses, and Baltimore and his colleagues have followed this up and report briefly that, during mengovirus replication, a protein of about the same size as the polio protein NCVP1 is cleaved to yield viral specific proteins. Thus the cleavage of primary gene products seems to be a general phenomenon in the replication of some RNA mammalian viruses and is not restricted to the encapsulation process. Indeed, Jacobson and Baltimore suggest that all the major species of the fourteen polio virus polypeptides which can be identified in extracts of infected HeLa cells are cleavage products either of nascent or of complete polypeptide precursors. And they speculate, reasonably enough, that the polio virus RNA genome, a single stranded RNA molecule, may be translated as a few and perhaps even as just a single polypeptide chain which is then specifically cleaved.

A comparison of the structure and translation of the genetic material of the three other types of mammalian RNA viruses with that of the polio virus type is interesting in the light of this speculation. Viruses of the reovirus type contain a number of fragments of double stranded RNA, each of which acts as template for synthesis of separate *m*RNA molecules. Viruses of the influenza type contain a number of single stranded fragments which are presumably translated independently. Viruses of the Newcastle disease type contain a very large single stranded RNA molecule, but apparently shorter *m*RNA molecules complementary to the genome RNA are synthesized and then translated. One possible interpretation of these three types of organization is that they are all mechanisms for packaging genetic information in small units and so allowing control of gene expression; mechanisms which have evolved to circumvent the fact that in mammalian cells, unlike the case of bacteria, it seems impossible to initiate translation of a *m*RNA molecule internally but only at the 5′ end. Polio virus, on the other hand, pays the consequence of not packaging its genetic information in small units; the whole genome is translated as a single polypeptide chain which then has to be cleaved. This means, of course, that there is little scope for a flexible control of the time of gene expression during the infective cycle.

These intriguing arguments hang on the claim that in mammalian cells there is no internal initiation of translation, and Jacobson and Baltimore have marshalled some convincing evidence in support of it. In brief, internal initiation is thought of as a mechanism, in bacteria, for the translation of polycistronic *m*RNAs, but in mammalian cell all the evidence points to monocistronic messengers. Polysomes making haemoglobin, myosin and actin, for example, seem to contain monocistronic messengers. In at least some mammalian cells there is a linear relationship between the number of ribosomes in a polysome and the average length of the nascent protein per ribosome. Such a relationship is incompatible with internal initiation and is not found in bacteria. Finally, in uninfected HeLa cells there is little evidence for the cleavage of HeLa proteins, which implies that, unlike polio *m*RNA, the host cell *m*RNA is monocistronic. In general, then, in mammalian cells there is no need for internal initiation because messengers specify only one species of protein. It will be interesting to see how many of Jacobson and Baltimore's stimulating ideas stand up to critical experimental tests.

MOLECULAR BIOLOGY

Polymorphic Polynucleotides

from our Molecular Biology Correspondent

THE chemistry of the polynucleotides has, regrettably perhaps, passed from its age of innocence, when there was only base pairing to consider, to one of sophistication and complexity—of stacking, loops, slippage and tertiary structure. The interest of these developments goes well beyond their capacity to entertain the physical chemists, as several new studies in the current literature show.

Scheffler, Elson and Baldwin (*J. Mol. Biol.*, **36**, 291; 1968) have studied a series of oligomers of alternating dAT, of the type $d(pTpA)_n$, where n is 4 or greater. Fractions, each with a unique value of n, have been obtained, as shown by end-group analysis and molecular weight determination by sedimentation equilibrium. The temperature melting profiles of these molecules show some remarkable effects. At low salt concentrations, the curve is simple, with a mid-point and breadth which depend in the expected manner on chain length, and the melting process is rapidly reversible on cooling. The melting curve, as molecular weight measurements show, is in fact that of single chains, folded back on themselves in a hairpin, in which only