

protein associated with *mRNA* released from polysomes has yet to be shown to be identical with the protein in the free cytoplasmic "informosomes". In these circumstances, there is little point in speculation about the possible function of the protein, and a rigorous proof of the "informosome" model seems as far away as ever.

Also in the latest issue of *J. Mol. Biol.* (36, 305; 1968), Shinozawa, Yanara and Imanori report the curious observation that polyvinyl sulphate (PVS) interacts with ribosomes, competing with *mRNA* to form polysome-like structures. Their original observation was that PVS (known to be an inhibitor of RNase), added to an *E. coli* cell free system in an attempt to block RNase activity, inhibited protein synthesis instead. Following this up they have now shown that the PVS binds preferentially to the 30S ribosome and mimics *mRNA* by forming polysomes with 30S and 50S ribosomes.

PVS inhibition of protein synthesis in a cell free system can be prevented only if the ribosomes are preincubated with *mRNA*, *tRNA* and GTP, presumably because once an initiation complex has been formed the binding sites for which PVS competes are occupied. In the last issue of *Nature* (220, 244; 1968) Kolakofsky, Ohta and Thach reported a further step in their analysis of the role of GTP at initiation. It was known that GTP was required for, but not hydrolysed in, the first step, the *mRNA* directed binding of Fmet-*tRNA*_F to the 30S ribosome, but ATP is hydrolysed during the activation of the Fmet-*tRNA*_F on the 70S ribosome before peptide bond formation. They asked whether the hydrolysis of GTP is involved in the combining of the 30S and 50S subunits to form the active 70S ribosome; the answer seems to be that it is not. Essentially the experiment consisted of showing that a 70S ribosome will form from the two subunits, *mRNA* and Fmet-*tRNA*_F in the usual conditions when GTP is replaced by an analogue GMP-PCP, which substitutes for GTP in the first step of initiation, but cannot be hydrolysed so that the second step peptide bond formation is blocked.

MICROBIOLOGY

Hypercholesterolaemia

from our Microbiology Correspondent

Gordon and Schaeffner's findings that orally administered polyene macrolide antifungal antibiotics have profound effects on the prostate gland and on prostatic hyperplasia in dogs have been discussed recently (*Nature*, 220, 120; 1968). A possible mode of action of these antibiotics was considered to be associated with their effect on the metabolism of steroid hormones, and subsequently Schaeffner and Gordon (*Proc. US Nat. Acad. Sci.*, 61, 36; 1968) have provided additional evidence for the hypocholesterolaemic activity of polyene macrolides. The haptene macrolide candicidin produced a maximum average decrease in the concentration of serum cholesterol of 34 ± 14 per cent at an oral dose rate of 5 mg/kg body weight during three weeks. Similarly, another haptene macrolide, amphotericin B, and a pentaene, filipin, reduced serum cholesterol by 45 ± 7 per cent and 50 ± 5 per cent respectively. On the other hand, unequivocal hypocholesterolaemic activity of nystatin (a tetraene macrolide) was not demonstrated. There was difficulty in establishing a

dose response relationship from the data, because such different base line concentrations of serum cholesterol were found within the large sample of dogs used. Indeed, Schaeffner and Gordon grouped their dogs for the various drug treatments according to their basal cholesterol titre and, in effect, were studying different populations. For example, those dogs treated with amphotericin B and filipin were much more hypercholesterolaemic than those exposed to candicidin or nystatin. But when population percentiles are examined in relation to serum cholesterol concentrations before and after drug treatments, it is clear that the post-treatment range of cholesterol is much narrower than the corresponding pre-treatment range. As Gordon and Schaeffner remark, this result suggests a greater homeostatic control of serum cholesterol after the administration of polyene macrolide.

Polyene macrolides are only sparingly soluble in aqueous systems and are very poorly absorbed from the gastro-intestinal tract. How then do these substances exert their hypocholesterolaemic effect? The prevention or reduction of absorption of exogenous cholesterol from the gut, and/or resorption of endogenous cholesterol, are obvious possibilities, and Schaeffner and Gordon claim to have studies in progress that support such a hypothesis. Whatever the mode of action, the effects of these antibiotics on serum cholesterol concentrations and on prostate abnormalities are likely to be closely associated, because the relationship of cholesterol to the synthesis of steroid sex hormones is well established. If polyene macrolides can eventually be used for the treatment of prostatic and lipid metabolic disorders, a group of immensely important microbiological agents will have been added to the arsenal of therapeutic drugs.

NEUROPHYSIOLOGY

Fluorescent Neurones

from our Neurophysiology Correspondent

A KNOWLEDGE of precise cellular geometry is often important in understanding the nervous systems of animals with relatively small numbers of neurones where individual patterns of connexion are probably fixed genetically. This is true of many invertebrate nervous systems, particularly when neurones can be identified as homologous in different individuals of the same species. Degeneration techniques have often failed, sometimes because more than one cell body is associated with what appears to be a single fibre, while conventional staining suffers from the apparent randomness with which neurones are stained. Another method is to inject cells with dyes, which must diffuse throughout a cell and its processes without escaping through the membrane; a suitable group of dyes was first used by Kravitz and his colleagues. These are the Procion, fluorescent derivatives of cyanuric chloride, which form covalent bonds with carbohydrates and proteins. Stretton and Kravitz have reported their results from injecting Procion-Yellow into cells of the lobster abdominal ganglia (*Science*, 162, 132; 1968). They were able to stain corresponding cells in several individual lobsters and to follow, with light microscopy, processes of single cells with diameters of less than 1μ . In one cell, I_2 , of the second abdominal ganglion, they showed that there is bilateral symmetry