RIBOSOMES

Translation

from our Cell Biology Correspondent

ELUCIDATION of many of the outstanding questions about the fate of messenger RNA–ribosomes complexes at the termination of translation has been hampered by lack of a suitable system in which complexes of single ribosomes with *m*RNAs can be generated. Webster and Zinder at the Rockefeller University, however, now report (*J. Mol. Biol.*, **42**, 425; 1969) an ingenious trick by which translation of f2 phage RNA by single ribosomes can be monitored. They incubated f2 RNA with a cell free protein synthesizing extract which had been depleted of the amino-acid asparagine by incubation with asparaginase. In these conditions a single ribosome binds to the phage RNA and begins translating the coat protein cistron but is halted at the position of the first asparagine residue in the coat protein, which is the third amino-acid in the chain. Further synthesis of coat protein is then entirely dependent on added asparagine.

Using this system and RNA obtained from a wild type and a mutant phage, which has an amber codon in place of the codon for the sixth amino-acid, glutamine, in the coat protein cistron, they have been able to show, first, that the rate of synthesis is about twenty-five to thirty amino-acids a minute, and second, that when the amber mutation is allowed to act as a chain terminator the *m*RNA is released from the complex with ribosomes within 0·75 minutes. This release occurs at the same rate when the amber codon is at position six or position seventy in the coat cistron. When, however, the ribosome is allowed to translate the whole coat cistron (specifying 128 amino-acids) until it reaches the natural termination signal, there is a rapid but only partial release of the *m*RNA from the complex. This suggests that if translation of a messenger is terminated prematurely the ribosome–*m*RNA complex is broken, whereas after normal termination at least some of the ribosomes may remain attached to a polycistronic messenger and begin to synthesize the next cistron. The proximity of an initiation site to a terminator may decide whether the ribosome–*m*RNA complex dissociates or remains intact.

Webster and Zinder's experiments fit in well with current ideas about the cyclical dissociation of ribosomes into subunits after each round of protein synthesis. But 70*S* ribosomes can be isolated from bacterial cells and there is currently an argument about whether or not these are artefacts of extraction. Kelley and Schaechter (*J. Mol. Biol.*, **42**, 603; 1969) report that the free 70*S* ribosomes isolated from *Bacillus megatherium* differ from the 70*S* ribosomes which, with *m*RNA, constitute polysomes; the free 70*S* particles dissociate into subunits at higher Mg^{++} concentrations than the polysome 70*S* ribosomes. This argues strongly that the free 70*S* ribosomes extracted from cells are not just the remains of polysomes fragmented by shear forces during isolation.

One of the chief remaining problems of chain initiation is how a ribosome selects the correct AUG or GUG codons for initiation because, internally, these codons specify methionine not formyl-methionine, the initiating amino-acid. Bretscher's work (*ibid.*, 595) with a circular DNA molecule seems to have eliminated the most obvious suggestion, namely that the ribosome starts at the beginning of an *m*RNA and works along until the first AUG or GUG codon and then initiates protein synthesis. He finds that with the circular fd phage DNA acts as messenger and yet it has no free ends.

STEROIDS

Central Nervous Activities

from a Correspondent

THE common complaint that insufficient time is set aside for discussion at scientific meetings, particularly when the topics chosen prove more interesting than the organizers anticipated, could not be made of the meeting of the Steroid Biochemistry Group of the Biochemical Society at Oxford on July 11. In this case discussion of techniques and interpretations was an important feature.

Some of the problems arising in the study of the feedback action of steroids on the brain were outlined by B. T. Donovan (Institute of Psychiatry, London), who pointed out that until quite recently the secretion of gonadotrophin by the human pituitary was presumed to wax and wane during the menstrual cycle and to be linked with the rhythmic secretion of sex hormones. But the results of sensitive immunological assays of gonadotrophin now indicate that notable amounts of hormone are secreted only at ovulation, and that much smaller and near constant quantities are detectable at other times. With the weakening of evidence for a feedback action of gonadal steroids on the brain during the menstrual cycle, it becomes more difficult to account for the regular occurrence of ovulation, except on the basis of the presence of a twenty-eight day clock in the brain.

No doubt this represents an extreme view adopted to provoke discussion, for other evidence was cited which establishes that the secretion of gonadotrophin is controlled by the sex hormones. Thus, as described by B. A. Cross (University of Bristol Medical School), the changes in the activity of nerve cells in the hypothalamus brought about by sex hormones can be followed by tracing the firing rate of neurones in different conditions. To abolish the influence of stimuli reaching the hypothalamus of the rat from other parts of the brain, the surrounding tissue can be removed to form an island and the effect of steroids can be followed, as it were, in isolation. Not all units are affected in the same way by sex hormones, for some fire more rapidly and some slow down, while the discharge rate of others remains unaltered. Overall, however, the unit activity of hypothalamic islands changes in phase with the oestrous cycle, and is highest in the anterior hypothalamus during pro-oestrus, as might be expected with ovulation impending.

The way in which androgen causes masculinization of the mechanisms governing sexual behaviour and gonadotrophin secretion in the male was another problem raised. This was the gist of the contribution from S. Levine (Stanford University). Male rats castrated immediately after birth are functionally female in the behavioural sense when mature, and display lordosis—forward curvature of the spine—and allow mounting by other males when treated with oestrogen and progesterone. Conversely, treatment of newborn female rats with androgen prevents the development of female sexual behaviour and favours the manifesta-