in the first place. It was a great surprise to find that lysozyme and α -lactalbumin, which have no apparent common function, show a high degree of homology in primary structure.

In his discussion on lysozymes, P. Jollès of Paris took the opposite case—analogue proteins, where convergent evolution from quite different ancestry produces proteins of different primary structures, all performing similar functions. The French group have purified three types of lysozymes: from bird (or man), Papaya latex and phage. All three proteins are capable of hydrolysing bacterial cells walls, but their primary structures are very different.

In his talk on the heterogeneity of immunoglobulins, Dr C. Milstein of Cambridge pointed out that he was dealing with a heterogeneous system to the tune of more than 10^5 different homologous proteins. This formidable picture has been greatly simplified in recent years, although the genetics of the system are by no means clear. The immunoglobulin molecule is known to consist of two pairs of polypeptide chains, each pair containing a heavy and a light chain, and it now appears that the basic building block in both these chains may be a 60 residue loop, closed with an intrachain disulphide bridge. The light chains can be visualized as two such loops in series, a C-terminal "constant" section and an N-terminal "variant" section. The heavy chains may contain four such loops, of which two in the C-terminal half (the Fc fragment) and one in the N-terminal half (the Fd fragment) are also "constant". The key problem is to relate this simple basic pattern to the enormous number of different antibodies which can be produced. In the first place it is the "constant" sections that are responsible for the so-called isotypic variants, common to all members of a species, but serving to differentiate classes of immunoglobulins in terms of complement fixation and placental passage. By contrast, it is the comparatively short "variant" sections, comprising only a single loop, that give the so-called idiotypic variants responsible for each individual antibody. Genetically, at least three non-allelic genes and some somatic hypermutation are thought to be responsible for this part of the molecule.

The generous bonus of answers predicted (*Nature*, **219**, 330; 1968) after publication of the X-ray analysis of α -chymotrypsin is already extending to proteases originating outside the pancreas. This was clear from S. Magnusson's comparison of thrombin (from prothrombin, produced in the liver) and the pancreatic serine proteases trypsin, chymotrypsin and elastase. Thrombin qualifies as a serine protease because its specific hydrolysis of the arg-gly bond in fibrinogen is inhibited on blocking a single serine with DFP. But the similarities may go much deeper than this: both the tertiary structure and the mode of activation from prothrombin show signs of resembling that of the pancreatic enzymes. Activation of prothrombin produces two chains, a 49 residue A chain bearing no apparent homologies with the pancreatic enzymes, and a B chain (about 270 residues) which has extensive sequence homologies with chymotrypsin, particularly in the buried regions around the methionine loop and the active serine. Further, the N-terminal isoleucine of thrombin, trypsin and chymotrypsin all correspond to ile 16 in the zymogen. Therefore in both mode of activation and tertiary structure, α -chymotrypsin

may prove a model for a wide range of serine proteinases.

NEUROPHYSIOLOGY

Corollary Discharge?

from our Neurophysiology Correspondent

THE visual world shows great stability even though the eyes through which it is observed are continually moving. On the other hand, during passive eye movements the visual world is unstable, appearing to move in a direction opposite to eye motion: this is easily verified by tapping one eyeball with a finger and was well known to Helmholtz (*Physiological Optics*, III, 243, Dover: 1962). When the extraocular muscles are anaesthetized the visual world appears to move in the same direction as an attempted, voluntary, eye movement. It is clear that the information necessary for establishing the direction of gaze must therefore derive from the motor outflow to the extraocular muscles rather than from proprioceptors in the muscles themselves. It was suggested that a "corollary discharge" signals the difference between present and past eye positions and allows anticipation of and correction for the change in sensory input due to eye movement. Until recently there has been no direct evidence of such a discharge.

In 1966, Bizzi (*J. Neurophysiol.*, **29**, 1087) made microelectrode recordings from the cat's lateral geniculate body and found units which fired during the rapid eye movements of sleep. Because these were obviously not excited by changing retinal input he postulated that the corollary discharge might be responsible for their activity. More recently he has found units in the frontal lobes of unanaesthetized macaques which also fire during eye movements. The frontal lobes are known to be involved in some way in oculomotor function: Ferrier in 1875 showed that electrical stimulation of the frontal lobes in a monkey could cause conjugate horizontal and vertical eye movements, although lesions of the frontal lobes do not seem to produce gross, permanent, oculomotor disturbance. Bizzi found two types of neurone (*Exp. Brain Res.*, **6**, 69: 1968). Those in class I fired during voluntary saccades and the fast phase of nystagmus, but not during slow pursuit movements or the slow phase of nystagmus. Class II neurones discharged steadily when the eyes were pointed in a specific direction and also fired during slow pursuit movements when these caused the optic axes to coincide with their preferred direction, but they remained silent during saccades. Out of seventy neurones of both classes, only two were found to fire before the initiation of a rapid eye movement, so it is unlikely that these neurones were involved in initiation of eye movements. Neither class of neurone was affected by change in background illumination, so the source of their activity could not have been retinal. Although it would be possible to explain the discrimination shown by class I neurones as the effects of differential gamma efferent activity if their firing were due to afferent stimulation from stretched eye muscles the same could not be said of class II. Bizzi suggests that both types are representing the corollary discharge. It would be useful to know whether changes in head position also affected the activity of these neurones, for this must also be signalled in the corollary discharge, should it exist.