nuclear DNA. Nuclei with more than 40 per cent of their DNA in chromocentres and those with less than 1 per cent condensed, as well as those in intermediate states, can each be found among cells in G_1 or G_2 and the sequence of changes in condensation and diffusion has still to be correlated with the cell cycle.

Perhaps the most striking feature of the symposium as a whole was the contrast between the wealth of relevant information and ideas presented, and the fragmentary state of our understanding of entry into mitosis, considered as a process. There were many beautiful pieces for the jigsaw puzzle; the picture is still hard to discern.

PROTEIN CHEMISTRY

Probing Heavy Metals

from a Correspondent

PARKINSON'S Law of Biochemistry states that the importance of studying a system is inversely proportional to the ease of doing so. The biological roles of Na^+, K^+, Mg^{2+}, and Ca^{2+} are good examples of this because their closed electron shells mean that they have few accessible spectral properties. But several recent articles have shown that heavier elements such as the trivalent lanthanides and monovalent thallium, which all have spherically symmetrical outer electron shells, may bind to the same sites in macromolecules as do the lighter metals. The spectroscopic properties of these ions may then be studied to probe the nature of the binding site.

Eisinger and Lamola (*Biochim. Biophys. Acta*, **240**, 313; 1971) have studied intersystem crossing in mononucleotides by observing energy transfer from the triplet state to Eu^{III} which then re-emits light at 590 nm. The information which they gain about the excited singlet and triplet states is important in understanding the photochemistry of the nucleic acids, and cannot easily be obtained by more conventional techniques such as fluorescence because of the very short lifetime of the singlet state—about 10 ps.

Luk (*Biochemistry*, **10**, 2838; 1971) has studied the fluorescence properties of various lanthanides bound to transferrin. From the absorption spectrum of the complex he suggests that the binding site for Tb^{III} involves a tyrosine residue and further concludes that the two Fe^{III} binding sites must be more than 4.3 nm from the Tb^{III} site because no energy transfer takes place from the Tb^{III} to the Fe^{III}. A similar study on the K^I and Mg^{II} activated enzyme pyruvate kinase by Kayne and Reuben (*J. Amer. Chem. Soc.*, **92**, 220; 1971) used the effect of the paramagnetic ion Mn^{II} (which binds at the Mg^{II} site) on the NMR line width of Tl^I (which binds at the K^I site) to show that these sites must be less than 0.74 nm apart, and are therefore presumably bound at the active site.

Most of the lanthanides are paramagnetic as a result of their partly filled 4f shell and cause an increase in the proton relaxation rates of ligands bound to them. Reuben (*Biochemistry*, **10**, 2834; 1971) has used this effect to examine the binding of Gd^{III} to bovine serum albumin and shows that there are four binding sites for the metal, while Dwek and his colleagues (*Eur. J. Biochem.*, **21**, 204; 1971) have shown that Gd^{III} binds at the active site of lysozyme and have calculated the distances from the metal to various substrate analogues.

Heavy metals have so far been used to form derivatives for X-ray structure determination. One as yet unrealized advantage of the lanthanides is that they are heavy enough to be used in this way. This means that it may now be possible to locate a probe molecule precisely, a great improvement over such nebulous criteria as "probes for hydrophobic areas".

PROTEIN HORMONES

Function of Structure

from a Correspondent

THE cross-reactivity between the glycoprotein hormones in biological and immunological systems is becoming more explicable in the light of recent advances in knowledge of their structure. It now seems that luteinizing hormone (LH), thyroid stimulating hormone (TSH), follicle stimulating hormone and human chlorionic gonadotrophin (HCG) may each be dissociated into two subunits (α and β) of about half the molecular weight of the original molecule. Discussions on their properties occupied one day of the second international symposium on protein and polypeptide hormones held in Liège from September 28 to October 1, the main theme of which was relationships between structure and activity.

Hormone specificity is carried by the β subunit of each hormone and the α units are non-specific. The subunits themselves possess little, if any, biological activity but when they are incubated together they reassociate and biological activity is restored. Even more interesting are the numerous observations that hybrid molecules may be produced; for example, when TSH–α is combined with LH–β, LH activity is generated and LH–α and TSH–β give TSH activity.

There was good agreement regarding the primary structures of the subunits of ovine LH reported by Dr H. Papkoff (University of California, San Francisco) and by Dr D. N. Ward (University of Texas). The amino-acid sequence of the α unit is dissimilar from the β sequence but strikingly similar to TSH–α. This is not surprising in view of the interchangeability of the α units. Initial work on the immunological properties of the subunits by Professor S. Berson (Veterans Administration Hospital, Bronx), Dr G. T. Ross (US National Institutes of Health, Bethesda) and Dr G. Hennen (University of Liège) bears out the specificity of the β units and the non-specificity of the α units. Antisera raised to native hormones are likely to contain antibodies directed against parts of the molecules common to all the glycoprotein hormones: there is a better chance of developing specific radioimmunoassays by making use of the β units. Professor P. Franchimont (University of Liège) produced evidence for the presence of α and β subunits of HCG in the blood and urine of pregnant women based on radioimmunoassays using the subunits.

Determination of structure is a step towards explaining the mode of action of a hormone. Conformation as well as primary structure is important in any consideration of a receptor. A beautiful example of how X-ray crystallography has been applied to establish the conformations of the insulin monomer, dimer and hexamer was presented by Dr T. L. Blundell (University of Oxford).

Much of the speculation regarding hormone receptor sites and target cells has been based on analogies with drug action. There was much discussion of the location of receptors, their nature and specificity and how they function. The best known theory is that hormones (first messenger) interact with adenyl cyclase at the receptor site bringing about an increase in cyclic AMP (the second messenger) within the cell. This gave a simplified, but incomplete, picture of hormone action illustrated for glucagen by the work of Dr M. Rodbell (US National Institutes of Health). Professor O. Hechter (Northwestern University, Chicago) gave the example of ACTH and a plea for his cybernetic approach as a basis to provide a set of first principles for understanding fundamental aspects of hormone action on target cells.

Widespread use is being made of labelled preparations of hormones in the study of biologically significant sites. Competition for binding sites with unlabelled hormones forms the basis of a new type of assay analogous to those used for steroid hormones. Already examples are available for ACTH (Dr J. Roth, US National Institutes of Health), angiotensin (Dr T. Goodfriend, University of Wisconsin) and HCG (Professor R. Canfield, Columbia University, New York; Dr K. Catt, US National Institutes of Health). These promise to be as sensitive as radioimmunoassays and are a step nearer to a measure of the biological action of the hormone.