pressed, presumably in a highly specific manner, so that only a small fraction of the base sequences is available for transcription and, furthermore, there is some evidence from DNA–RNA hybridization experiments that the RNA transcribed off native chromatin in an *in vitro* system is the same as that transcribed *in vivo*. The experiment to test the effect of chromosomal RNA on the specificity of histone repression is to dissociate and then reconstitute chromatin in the presence and absence of chromosomal RNA and monitor the RNA transcribed off the native and reconstituted chromatin by hybridization. Both groups now claim that if reconstitution is performed in the absence of chromosomal RNA the pattern of repression is not that of native chromatin, but in the presence of chromosomal RNA specific repression is achieved on reconstitution.

On the face of things, these experiments strongly support the notion that chromosomal RNA confers specificity on the histones. The RNA is apparently firmly bound to the histones and at the same time is resistant to digestion by ribonuclease, which implies it is in a double stranded form, presumably hydrogen bonded to DNA. It must be said, however, that not everyone working on this topic accepts these experiments at face value, chiefly because everything hangs on the sensitivity of the RNA–DNA hybridization competition techniques that are used to determine which DNA sequences are being transcribed off native and reconstituted chromatins. The crucial question is whether the systems are clean enough to allow the distinctions to be made. They probably are, but sceptics may not be convinced until the base compositions, or, better still, the sequences, have been determined.

ACTIVE TRANSPORT

Crossing the Membrane

from a Correspondent

ACTIVE transport across biological membranes retains its mysteries, but one new approach—the study of the enhanced membrane permeability induced by some peptide antibiotics—has already produced surprises, and looks increasingly hopeful for the future. Valinomycin, nonactin and gramicidin are examples of these antibiotics: they are macrocyclic peptides which increase the cation permeability of several membrane systems, both natural and artificial. They form cation complexes with extreme selectivity; for example, valinomycin can develop a 300-fold preference for K^+ over Na^+.

The structural basis of this selectivity has been clarified in the case of the K-specific antibiotic nonactin. X-ray analysis of the crystalline nonactin-K complex shows that the anhydrated K^+ ion fits snugly in a hydrophilic pocket in the centre of the molecule and the peptide chain wraps round the ion like the seam of a tennis ball. To determine the state of such complexes in solution, Haynes, Kowalsky and Pressman have now analysed the nuclear magnetic resonance spectra of valinomycin in various states of complexation (*J. Biol. Chem.*, **244**, 502; 1969).

When valinomycin, dissolved in deuterated chloroform, combines with KCNS or CsCNS all its proton resonances move significantly, indicating a general conformation change in the molecule. The spectra of the K^+ or Cs^+ complexes themselves are materially different. Added water causes little change in the spectrum of the K^+ complex, and integrations of the water resonance peak show that less than two water molecules can be carried by each complex molecule in a low dielectric medium. The metal ion is thus more or less unhydrated.

Molecules like valinomycin may act as channels—by stacking together in columns and breaching the membrane—or carriers—by moving freely through the lipid interior of the membrane, and collecting and discharging their ion at the interfaces of the membrane. Haynes and his colleagues provide two pieces of evidence that favour the carrier mechanism. First, there is no sign in the nuclear magnetic resonance spectrum that the valinomycin complexes have any tendency to associate in a non-polar medium. Second, a study of the line broadening induced by the exchange reaction

valinomycin–KCNS + valinomycin* =
valinomycin + valinomycin*–KCNS

reveals that K^+ exchange is undetectable in $CDCl_3$, though quite fast in the more polar solvent 80 per cent CH_3OH/20 per cent $CDCl_3$. The unwillingness of K^+ to leave its hydrophilic pocket when the whole complex is immersed in a non-polar fluid clearly counts against a channel mechanism, which would involve a rapid shuttling of K from molecule to molecule of peptide within the membrane.

The relevance of these molecules to the natural process of active transport is fascinating, though very much *sub judice* at the moment. The ion-carrying antibiotics are also grist to the mills of the chemiosmotic theory of mitochondrial action. Mitchell and Moyle report that they have used valinomycin-induced K^+ permeability to measure the electric potential across mitochondrial membranes (*Europ. J. Biochem.*, **7**, 471; 1969). This, combined with values for the *p*H difference across the same membranes, allows Mitchell and Moyle to argue that protons fulfil both the kinetic and thermodynamic requirements of an intermediate between respiration and ATP synthesis.

MOLECULAR BIOLOGY

Original *Syn*

from our Molecular Biology Correspondent

ONE of the features defining the stereochemistry of the nucleotides is the configuration about the glycosidic bond, which may be either *syn* or *anti*, the one being transformed into the other by a rotation of the base through 180°. In the *syn* form there is more steric crowding, and it is by now well enough established that the standard nucleotides in their free and polymerized states exist in the *anti* form. A different situation, however, seems to obtain in the adenosine analogue, formycin.

This is an antibiotic, which differs from adenosine in that the carbon atom of the five-membered ring of the purine is interchanged with the glycosidic nitrogen. The glycosidic C–C bond is longer than the C–N of purine nucleosides, and this, together with the absence of a hydrogen on what in adenosine is the C–8, are evidently enough to cause the *syn* configuration in this molecule to be favoured, for it was established some time ago that this is the structure in the crystal. It is also known that the triphosphate will in certain