but there is no effect on the number of breaks induced in chromosomes free of BUdR.

Repairing DNA

from our Molecular Genetics Correspondent

DURING the past six months an exciting addition to our knowledge of DNA synthesis has appeared, most of it from the work of four groups in the United States. These groups have discovered enzymes able to join a break in one strand of a DNA helix. This enzyme activity has been detected and the enzyme purified from *E. coli* and *E. coli* infected with T4 or T7 bacteriophages. The detection of this enzyme, which has been named a DNA sealase or DNA ligase, requires a rather sophisticated substrate. Basically two types of substrates have been used. Phage λ DNA molecules which are either hydrogen bonded to one another or hydrogen bonded to themselves into a circular DNA molecule can be covalently sealed giving covalent dimer DNA helices or covalently intact circular DNA helices. Alternatively, double-stranded DNA from a variety of sources can be "nicked" with an endonuclease, thereby producing a few single breaks in the helix. These breaks can be labelled specifically with radioactive phosphate using the enzyme polynucleotide kinase and γ -labelled adenosine triphosphate, ATP. The breaks can then be rejoined by the ligase. Once the ligase has joined the labelled phosphate into the chain, the phosphate can no longer be removed from the DNA by the enzyme alkaline phosphatase.

The ligase isolated from *E. coli* has the surprising requirement for the co-factor diphosphopyridine nucleotide, DPN. The DPN has been shown to combine with the DNA ligase in the absence of DNA, forming an enzyme-adenylate complex and free nicotinamide nucleotide. This ligase-adenylate complex will now join a single-stranded break in a DNA helix, concomitantly releasing adenylic acid. The enzyme isolated from phage-infected cells requires ATP as a co-factor, and again forms an enzyme-adenylate complex in the absence of DNA, releasing pyrophosphate.

These enzymes, from whichever source they are isolated, apparently repair breaks in a DNA double helix only when the break has a 5' phosphate and a free 3' hydroxyl group in the break. It is likely that these enzymes play an important part in genetic recombination, the repair of radiation-induced damage, and DNA synthesis, but exactly how is unknown. (References: Gellert, M., *Proc. US Nat. Acad. Sci.*, **57**, 148 (1967); Weiss, B., and Richardson, C. C., *Proc. US Nat. Acad. Sci.*, **57**, 148 (1967); Olivera, B. M., and Lehmann, I. R., *Proc. US Nat. Acad. Sci.*, **57**, 1426 (1967); Geftter, M. L., Becker, A., and Hurwitz, J., *Proc. US Nat. Acad. Sci.*, **58**, 240 (1967); Becker, A., *et al.*, *Proc. US Nat. Acad. Sci.*, **58**, 1996 (1967); Little, J. W., *et al.*, *Proc. US Nat. Acad. Sci.*, **58**, 2004 (1967).)

Neurone Geometry

from our Neurophysiology Correspondent

FIVE papers in the current issue of the *Journal of Neurophysiology* deal with the location of excitatory

and inhibitory synapses on motoneurons. (Smith, Wuerker and Frank, *J. Neurophysiol.*, **30**, 1072-1096, 1967; Nelson and Frank, *ibid.*, 1097-1113; Burkem, *ibid.*, 1114-1137; Rall, *ibid.*, 1138-1168; Rall, Smith, Frank, Burke and Nelson, *ibid.*, 1169-1194.) Rall has proposed a model for the contribution of dendritic potentials to postsynaptic excitation and inhibition measured at the motoneurone soma which is in several respects at variance with Eccles's model of the postsynaptic membrane. Eccles's model implies that to be effective in changing neuronal excitability a synapse must be located close to the neurone soma. Using this model Fatt showed how relatively ineffective synapses located on distant dendrites would be (Eccles, *The Physiology of Synapses*, Springer, Berlin, 1964). Several predictions can be made from the model: the maximum amplitude of a postsynaptic potential (PSP) should be linearly related to the postsynaptic membrane potential; there should be an equilibrium potential at which no postsynaptic currents would flow and no postsynaptic potential therefore be generated; and it should be possible to reverse the postsynaptic potential when the equilibrium potential is surpassed. These predictions are satisfied by the neuromuscular junction, which has become the "model synapse", but there are several discrepancies in motoneuronal behaviour. While inhibitory postsynaptic potentials (IPSPs) fit the Eccles model well, excitatory potentials (EPSPs) do not.

On the basis of their experiments, Rall and his colleagues contend that, while inhibitory synapses are located on, or close to, the motoneurone soma, excitatory synapses may be largely located on the dendrites. They measured changes of membrane impedance during PSPs and found that, while the majority of IPSPs were accompanied by impedance changes of the somatic membrane, EPSPs were accompanied by a variable degree of impedance change, less than half, in fact, producing a measurable change at the soma. If Eccles's model were correct, all PSPs should produce measurable impedance changes at the somatic membrane; however, if some excitatory synapses were dendritically located, then the impedance changes they produced would be extremely small or even too small to measure. Similarly, when the somatic membrane was hyperpolarized, the effect on EPSPs was extremely variable and was quite consistent with the suggestion that excitatory synapses are located on remote dendrites, making their EPSPs relatively immune to the effects of current passed through the somatic membrane. Furthermore, it seemed that EPSPs, unlike IPSPs, could have a quite complicated composition, reaching maxima and decaying over a wide range of times. This would be entirely consistent with the remote location of some dendritic synapses which would affect the somatic membrane electrotonically, and whose potentials would therefore be "smoothed" to a varying extent dependent on the area of neuronal membrane between the synapses and the soma.

All these experimental results fit Rall's theoretical calculations well, and are good evidence for his hypothesis that remotely located synapses contribute significantly to potentials measured at the motoneurone soma. This hypothesis has been developed for several years and is quite comprehensively discussed in one of Rall's earlier papers (Rall, *Biophys. J.*, **2**, 146-147; 1962).