NUCLEIC ACIDS

Complex Forks

from our Cell Biology Correspondent

IN the current issue of the *Journal of Molecular Biology*, two groups, Huberman, Kornberg and Alberts (**62**, 39; 1971) and Sinha and Snustad (*ibid.*, 267), report experiments which strongly suggest that the protein specified by gene 32 of bacteriophage T4 plays a structural part in the replication of T4 DNA. At least nineteen genes of phage T4 participate in the replication of its DNA. Gene 43 codes for T4 phage specific DNA polymerase which like *Escherichia coli* DNA polymerase requires a primer and uses as substrate the nucleoside tri-phosphates. Gene 32, on the other hand, is required in stoichiometric rather than catalytic amounts and must be present throughout the phage's replicative cycle. Alberts and his colleagues (for example, Alberts and Frey, *Nature*, **227**, 1313; 1970) have purified gene 32 protein and shown that it binds tightly and co-operatively to single stranded DNA. They have suggested therefore that the role of this protein is to denature double stranded T4 DNA and so provide the aligned, parental single DNA strands required as template by the T4 polymerase. The experiments which Huberman *et al.* report are certainly consistent with that picture.

Huberman *et al.* find that *in vitro* gene 32 protein stimulates by some five to ten-fold the rate of DNA synthesis by T4 DNA polymerase programmed with single stranded T4 DNA. Moreover, this stimulation *in vitro* by a temperature sensitive gene 32 protein is temperature sensitive. The stimulation does not result from an increase in the rate of chain initiation and it is greatest at low temperature, at high ionic strength and when enough gene 32 protein is present to saturate the template DNA. These findings indicate to Huberman *et al.* that the protein most probably acts *in vitro* by eliminating regions of secondary structure formed when the template single stranded DNA chain imperfectly base pairs with itself; such secondary structures are presumably inhibitory to the T4 polymerase. There is also the possibility that some specific interaction between gene 32 protein and molecules of T4 polymerase is involved in the stimulation because in the absence of DNA the two proteins interact to form a weak complex.

Sinha and Snustad (*ibid.*, 267) have ingeniously exploited a gene dosage experiment to show that *in vivo* the role of gene 32 protein is stoichiometric rather than catalytic. They infected amber restrictive *E. coli* with mixtures of various proportions of wild type T4 phage and strains carrying an amber mutation in gene 32. In such infections the rate of T4 DNA synthesis and the burst size falls off rapidly as the proportion of wild type phage is decreased. In other words, the number of copies of functional gene 32 protein present seems to determine the rate of T4 DNA synthesis and hence the burst size.

Together with the data reported by Huberman *et al.*, Sinha and Snustad's findings lead to the conclusion that the T4 replication fork contains, in addition to, indeed in advance of, the T4 DNA polymerase, a run of gene 32 protein molecules bound to the template DNA. And according to the calculations of Huberman *et al.*—because there are about sixty T4 replication forks in an infected cell and about 10,000 molecules of gene 32 protein—each fork must contain of the order of 170 gene 32 protein molecules. It might even be imagined that not until this run of gene 32 proteins has associated with the T4 DNA can replication commence.

NUTRITION

Effects of Alcohol

from a Correspondent

AT a symposium on alcohol in nutrition, organized by the Nutrition Society at the Middlesex Hospital Medical School, London, on December 3, the chairman, Professor Sir Charles Dodds, in his opening address stressed the importance of improving knowledge and understanding of the effects of alcohol in man, its use and abuse in society, and its role in nutrition and medicine. Professor F. Aylward (University of Reading) traced the history of the use of alcoholic beverages by man since early times in various societies and its consumption in different countries and noted that the consumption of wine had increased in the United Kingdom in recent years.

Dr G. L. S. Pawan (Middlesex Hospital Medical School, London) described the pathways of alcohol metabolism in man and his experiments to discover what procedures, if any, would significantly increase the rate of alcohol metabolism and "sober up" an intoxicated person. In his experience, intensive physical exercise, vitamins, caffeine or strong coffee, thyroid hormones and other substances are without effect, but of the sugars tested, fructose significantly increases the rate of alcohol metabolism and helps to "sober up" the intoxicated subject. Adaptation to a high fat diet, starvation for some days, and administration of 4-methyl pyrazole decrease the rate of alcohol metabolism.

Professor C. W. M. Wilson (Trinity College, Dublin) described some of the pharmacological actions of alcohol, and discussed the factors which affect the taste threshold of this substance in man. Mr J. C. McKenzie (Food and Drink Research Ltd, London) reviewed the important social implications of alcohol consumption. In his opinion, social rather than metabolic factors are the most important in the development of alcoholism.

Professor J. Tremolières (Hôpital Bichat, Paris) discussed the metabolic basis of ethanol toxicity. He presented evidence for an alternative peroxidase pathway of ethanol metabolism, not involving either the alcohol dehydrogenase nor the microsomal ethanol oxidizing systems, which in certain conditions may be important in man.

The Earth's Atmosphere and Quasar Redshifts

THE distribution of quasar emission line redshifts is intriguing because it can be used to support a wide number of ideas about the universe, depending on the assumptions used in its interpretation. But one assumption which is common to all attempts to use quasar redshifts as a means of probing the universe is that the effects producing the observed distribution are properties of quasars and their position in the universe. R. C. Roeder and C. C. Dyer point out in next Monday's *Nature Physical Science* (January 3) that this may not be a valid assumption, and that the Earth's atmosphere probably produces an "ease of measurement effect".

This work extends Roeder's earlier investigation of the origin of quasar redshifts (*Nature Physical Science*, **233**, 74; 1971). It seems that the effect is manifested by a tendency for more quasar redshifts to be determined for values close to existing humps in the distribution. It may be that these redshifts are simply easier to measure or, more subtly, that observers are more confident in announcing observations which have a superficial resemblance to results already in the literature. In their latest work, Roeder and Dyer lean towards the first view.

Night sky lines will probably have an effect on redshift measurements when the quasar spectra are shifted so that their lines are close to those of the night sky. One plausible example is the line CIV 1549 which could easily be shifted by redshift $z=1.61$ to interfere with Hg 4047 from the sky. The Hg lines are particularly significant in the spectra taken at the Hale Observatories and Lick Observatory, and OI and NaI are often seen in spectra obtained at Kitt Peak. Quasar lines should be more easily identified when there are many more quasar lines in the optical window than the number of night sky lines.