GENETICS

Promoting Gene Activity

from our Molecular Genetics Correspondent

WITH the mechanisms by which operons are switched off by repressor proteins becoming well characterized, one of the most pressing problems in regulation of gene expression is to define the interaction which takes place between RNA polymerase and the promoter of an operon to allow its transcription into RNA and hence translation into proteins. The discovery that at least one promoter of phage λ comprises a complex structure, with a site where RNA polymerase binds separated by 200 nucleotides from the site where transcription is initiated (see *Nature*, **237**, 426 ; 1972), shows that the sequence of events leading to expression of the genes of an operon may be a complex one.

The promoter of the lactose operon also appears to comprise two sites, as Beckwith, Grodzicker and Arditti report in the *Journal of Molecular Biology* (**69**, 155; 1972), although in this case they seem to lie adjacent to each other. Several different mutations in the region between the *i* regulator gene and the operator of the lactose operon reduce the level at which the enzymes of the operon can be produced; these have been taken to define the site at which expression of the operon is initiated. Two proteins must interact at this initiation site if the lactose operon is to be switched on; RNA polymerase must bind to the site to initiate synthesis of RNA, but this action depends on the presence of a further protein, the cyclic AMP binding protein, which is activated by the cyclic nucleotide.

A deletion in the left end of the promoter reduces transcription of the operon to 2 per cent of its usual level, but this residual activity does not depend on mediation of the cyclic AMP system. This suggests that RNA polymerase can bind to the right end of the promoter, albeit weakly, of its volition, and can initiate transcription there. And mutants which lack an active cyclic AMP system can also express the operon at this low level, presumably by utilizing only this part of the promoter. But these strains, which either lack an active cyclic AMP binding protein or which cannot synthesize cyclic AMP, might be leaky so that residual expression depends on this system after all. By constructing double mutants, which can neither make cyclic AMP nor utilize added cyclic AMP, Beckwith *et al.* have excluded this possibility and have shown conclusively that the lactose operon can be expressed at 2 per cent of its usual level without mediation of the cyclic AMP system.

The immediate prediction suggested by these results is that mutants should exist in the right end of the promoter which do not influence the interaction with the cyclic AMP system, but which reduce initiation of transcription of the operon. It is the properties of these mutants that will solve a long standing question: does the sequence of the promoter where RNA polymerase binds overlap that of the operator where repressor protein binds? Biochemical experiments have suggested that RNA polymerase and represser do not compete for binding to DNA, but that represser acts as a block to the progress of polymerase into the structural genes of the operon. The genetic conclusion—which seemed to buttress this idea—that promoter mutants do not influence the activity of the operator now seems, however, to have been based on the use of mutants which affect only the activity of the cyclic AMP binding system. It is mutants which affect the binding of polymerase which must now be used to re-investigate this idea.

To discover the sequence of DNA base pairs which makes up the promoter and operator is, of course, one of the most important experiments to be performed; but attempts to protect DNA by binding these proteins to it so that the binding sites can be recovered and sequenced have not proved successful. A more subtle approach to deducing the sequence of a promoter is offered by the results now reported by Jackson and Yanofsky (*J. Mol. Biol.*, **69**, 307; 1972), who have mapped the internal promoter of the tryptophan operon in its second gene.

In cells which are repressed for the tryptophan enzymes, the first two genes of the operon are inactive, but the last three are expressed at a low level because a weak promoter seems to be located within the operon. Genetic mapping experiments now show that this site is located close to the end of the *trpD* gene, the second of the five tryptophan genes. This means that a sequence of DNA which codes for protein must also act as a site for binding RNA polymerase and initiating transcription. If mutants in this promoter can be isolated, characterizing the sequence of the protein which is made and comparing it with the wild type enzyme may reveal the nucleotide sequence which makes up this recognition region. Sequencing DNA directly seems unlikely to resolve promoter and operator sequence; and if the sequence of the tryptophan operon promoter can be deduced in this way, it will no doubt not be long before genetic tricks are used to turn other regulator sequences into proteins which can be sequenced.

MID-ATLANTIC RIDGE

Conflict at 43° N

from our Geomagnetism Correspondent

THE spreading history of the mid-Atlantic ridge at latitude 43° N is in doubt because there is a conflict between magnetic anomaly evidence and plate tectonic evidence. If the magnetic anomaly profile at that latitude is to be consistent with seafloor spreading, the spreading rate out to 30 km (4 million years) from the ridge crest and beyond 150 km (11 million years) must have been about 0.75 cm yr^{-1}, whereas between 30 and 150 km it must have been about 1.65 cm yr^{-1}. In short, there was apparently a period of about 7 million years when the rate of spreading more than doubled. Plate tectonic evidence, on the other hand, indicates no such anomaly. If plate motions based on the strike of fracture zones and spreading rates extrapolated from other parts of the ridge are used to calculate the spreading rate at 43° N, the answer turns out to be about 0.75 cm yr^{-1}, whether the extrapolation is from the South Atlantic or from the Reykjanes ridge and the Arctic Ocean.

Another Way to Reduce Drag

ALTHOUGH it is well known that drag in turbulently flowing liquids can be reduced by adding polymer solutions, soap solutions or even solid suspensions to them, each additive has its own particular disadvantage. Polymer solutions, for example, are quite easily degraded mechanically.

In *Nature Physical Science* next week (September 11), Zakin and Chiang report that yet another type of additive —a non-ionic surface active agent together with a salt—can reduce drag, and that it is both mechanically and chemically stable. The particular surface active agent used was a mixture of polyoxethylene and two saturated hydrocarbons.

Tests on a 1 per cent solution of the agent in water, containing varying amounts of Na_2SO_4, revealed significant drag reduction at Na_2SO_4 normalities greater than about 0.3. With 0.3 and 0.35 N solutions drag reduction dropped off at the higher Reynolds numbers but 0.4 N solutions displayed both the greatest relative viscosity (2.80) and the greatest drag reducing capability in any of the experiments. (A drag reduction of 57 per cent was measured at a Reynolds number of 11,000 under these conditions.) At higher concentrations of the salt, the drag reducing behaviour was little altered, but the viscosity was considerably smaller (1.60 at a normality of 0.50).

© 1972 Nature Publishing Group