native enzyme has the structure $A_4B_4C_8$.

The A and B chains can be separated on a preparative scale from the smaller C chains by chromatography in sodium dodecyl sulphate solution (Hayakawa *et al.*, *ibid.*, 574) and the approximate molecular weights were confirmed by sedimentation equilibrium. The activation of the enzyme by incorporation of phosphorus from labelled ATP was found to implicate both the A and the B, but not the C, chains. Phosphorylation of the B chains occurred much more rapidly, but the activity continued to rise as incorporation progressed to the A chains. Activation can also be occasioned by exposure of the phosphorylase kinase to trypsin, and this again affects only the A and B subunits, both of which are broken down to fragments of lower molecular weight. Hayakawa *et al.* hazard the view that C, which is unaffected by any of these treatments, may be the catalytic subunit, which is regulated by A and B. Moreover, the trypsin-activated enzyme can, as Graves *et al.* (*ibid.*, 580) report in the third article, be dissociated in the presence of ATP, by a slow process to smaller species, sedimenting at 9S and 16S, which possess activity, and in the smaller of which no part of the A subunit can be detected. The native, undigested, kinase cannot be made to dissociate under any but denaturing conditions, yet it seems that the very large cluster of subunits that comprises the native enzyme is not a condition for enzymatic activity.

Another curiosity, and the subject of a painstaking study by Roseman and his colleagues, is a bacterial protein involved in the transfer of phosphorus to lactose (Hays *et al.*, *J. Biol. Chem.*, **248**, 941; 1973). The sites of phosphorylation are histidine residues. This protein has a molecular weight of 35,000 by sedimentation equilibrium, and has an unusual trimeric structure, being made up of three seemingly identical subunits of 12,000 molecular weight apiece.

TRANSCRIPTION

Elusive Sigma Factor

from our Cell Biology Correspondent

THE hopes of divining how RNA polymerase knows which DNA to transcribe and which DNA to leave untranscribed, that were raised among molecular biologists two and three years ago by the discovery of a subunit of *Escherichia coli* RNA polymerase called sigma factor, have slowly evaporated. And the article by Greenleaf, Linn and Losick in the current issue of the *Proceedings of the National Academy of Sciences* (**70**, 490; 1973) seems like a haunting voice from the past. During the heydays of sigma factor Losick and his colleagues confidently anticipated that during the sporulation of the bacterium *Bacillus subtilis* the change in pattern of transcription of the bacterial DNA would prove to result from changes in the RNA polymerase molecule, and at that time (1969) it seemed plausible to suggest that the sigma factor responsible for programming the transcription of genes expressed during the vegetative phase of the life cycle was replaced by a new sigma factor programming the transcription of different genes expressed specifically during sporulation.

Losick and his colleagues found that the vegetative sigma factor is indeed lost early during sporulation, a fact which could account for the turnoff of ribosomal RNA synthesis and the failure of the sporulating cells to support the growth of phage φe. They also found that one of the other polypeptide chains of the vegetative enzyme (the β subunit) is replaced by a smaller polypeptide during sporulation. Egged on by these discoveries, and in particular the loss of the vegetative stage sigma factor at the start of sporulation, Losick and his colleagues began to search for the putative new sigma factor characteristic of the enzyme in sporulating cells. The report in the February issue of the *Proceedings* describes the results of this search which, frankly, are disappointing.

If a new sigma factor is made during sporulation the obvious place to look for it is in the RNA polymerase from sporulating cells, of which the factor should be a component. Greenleaf *et al.* therefore prepared antibody against the core polymerase of vegetative cells (core polymerase lacks sigma factor). They then challenged RNA polymerase from sporulating cells with the anti-core polymerase antibody and found that a polypeptide with a molecular weight of about 70,000 coprecipitated with the polymerase from sporulating cells. Clearly this coprecipitating polypeptide not present in the vegetative core enzyme might well be a sporulation sigma factor. Greenleaf *et al.* therefore purified the 70,000-dalton polypeptide and established that it binds specifically to core RNA polymerase, a property which a putative sporulation sigma factor must have; depending on the conditions, 0.3 to 2 molecules of 70,000-dalton polypeptide bind to each core polymerase. Furthermore, this polypeptide first appears about 3 h after the start of sporulation and persists for about at least a further 3 h and it cannot be detected in RNA polymerase extracted from a mutant of *B. subtilis, rfr10,* which cannot sporulate and which is rifampicin resistant; cell extracts from this mutant also lack the 70,000-dalton polypeptide.

With such a body of circumstantial evidence it must have been hard for Greenleaf *et al.* to resist the temptation to send out for a corkscrew, but the celebrations would have been premature, for the last sentence of their report reads: "Attempts to demonstrate a role for the 70,000-dalton binding protein in the transcription of sporulation genes have not yet been successful."

Hatched from the Same Egg

THE evidence, based on sequence homologies, that several proteins have a common evolutionary origin brings a measure of conviction. Is the same true of non-translated gene products, namely ribosomal and transfer RNA? Mullins *et al.* have investigated this question and in next Wednesday's *Nature New Biology* (March 21) they report their comparison of the pre-modified sequences of non-informational RNAs including twenty-two tRNAs and 5S RNA.

Mullins *et al.* found that $tRNA^{tyr}$ and $tRNA^{gln}$ from *Escherichia coli* show a remarkable homology with 5S RNA from the same species and that several other tRNA sequences are only a little less homologous. Although several insertions and deletions are required to make these homologies manifest, they are apparently well above chance expectation. Nevertheless they show a peculiar pattern—which Mullins *et al.* term "displaced linear homology"—in that the first half of the tRNA sequences are homologous with the last third of the 5S sequence and the second half of the tRNA with the first third of the 5S. Moreover, the extra sequence of forty-one nucleotides at the 5′ end of the precursor form of $tRNA^{tyr}$ shows homology with the middle third of the 5S RNA sequence.

Mullins *et al.* interpret these results ingeniously, using the observation of Brownlee, Sanger and Barrell (*Nature*, **215**, 735; 1967) that for *E. coli* 5S RNA the first nine residues show homology with the last nine and that region 10–60 is homologous with region 61–110; in other words, the molecule has a palindromic structure with the pattern ABBA. Mullins *et al.* postulate a proto-non-informational RNA consisting of about sixty residues with the pattern AB. They suggest that this gave, by processes of partial gene duplication, a sequence first with the structure ABB and then with the structure ABBABB. This, they suggest, gave by a similar process a sequence with the structure ABBA corresponding to 5S RNA and alternatively a sequence BAB, which after truncation would correspond to tRNA.

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