The chain contains two substituted lysine residues: an acetyllysine at position 16 appears in half the molecules, and position 20 is occupied by methyllysine in a quarter of the chains and dimethyllysine in the rest. The modification of side chains ensues after synthesis of the chains has been completed, and the Rockefeller group, which discovered this phenomenon, has now found that some histones also contain 3-methylhistidine (Gershey *et al.*, *ibid.*, 4871). This amino-acid is known also to occur in muscle proteins. It was found, in very small amounts, in histone fractions I and V, after incubation of the cells with labelled methionine, which functions as the methyl donor. Although it is not unreasonable to conjecture that substitution of basic groups will modify the strength or nature of the interaction between the histone and DNA, any more detailed speculation concerning the function of the methylation reaction is still only whistling in the dark.

It is possible that variations in the extent of modification of the lysines may have played their part in bedevilling attempts to prepare homogeneous components. Microheterogeneity—not apparently arising from methylation, for no unusual side chains are reported—has been studied in the lysine-rich fraction from rabbit thymus by Bustin and Cole (*ibid.*, 5286). They have prepared nine fractions by ion-exchange chromatography, which (with one exception) they hold to be homogeneous, and they give reasons for believing that their procedure gives a true analysis of the number of components. As this and earlier work shows, the fractions are all very similar in composition and all have blocked N-termini and two adjacent lysines at the C-terminal end. Chemical cleavage of the chains near the middle, at the solitary tyrosine residue present in each (Bustin and Cole, *ibid.*, 5291), makes it possible to show that the lysines tend to cluster in the C-terminal half, and that the differences in sequence between the fractions occur principally at the other end, as do those between corresponding histones from different tissues. All this is consistent with the notion that the chain is anchored to the DNA at one end (and that this is where there is little scope for mutational error), though why such an arrangement should profit the organism now becomes merely another of the mysteries of this impenetrable field. The lysine-rich histones seem to be required for the integrity of the chromosome, but the characteristic nucleohistone superstructure depends not on these but on the arginine-rich fraction.

RNA BACTERIOPHAGES

Unexpected Complexity

from our Cell Biology Correspondent

Two years ago it looked as if the RNA bacteriophage bandwagon had almost reached the end of the road. It was obvious that the phage RNA would continue to be used increasingly for studying protein synthesis—phage RNA is still the only source of well characterized messenger RNA—but interest in the process of phage RNA replication was dwindling and many of the chief workers were moving into new fields. It all seemed so straightforward; the phage RNA is injected into the *E. coli* host, where it is translated. One of the products of translation, RNA synthetase, catalyses the synthesis

of a complementary RNA strand, the minus strand, the sequence of which is determined by the sequence of the parental plus strand. This minus strand can then act as template for the synthesis of many progeny RNA plus strands identical to the infecting parental plus strand.

But in the past two years, it has become increasingly obvious that this picture is over-simple. Leaving aside the red herring introduced by Spiegelman's group, which at one stage suggested that the minus strand does not play a part in phage replication, a whole series of totally unexpected features has been uncovered. August's group, for example, discovered that the phage Q β RNA synthetase requires two cofactors which are present in uninfected bacteria. Then it was discovered that although the 3' terminal sequence of Q β plus strand RNA is CpCpA, the 5' terminal base of the minus strand, which might be expected to base pair with the 3' terminal base of the plus strand, is G and not U as expected. In other words, the terminal A residue of the plus strand must be added by some process other than Watson-Crick base pairing. Kamen then discovered that Q β RNA clipped of its 3' terminal A residue was infectious, but if the penultimate C residue was also removed infectivity was lost. The latest word from August's laboratory is that the terminal A is added to the plus strand by RNA synthetase, rather than by a host enzyme, but the enzyme does this without the requirement of a complementary template.

Several groups, including August's, have also turned up another curiosity of RNA phage replication; when *E. coli* is infected with an RNA phage, a small RNA molecule sedimenting at 6S accumulates. Since 1965 there have been several reports of the occurrence of this small RNA and as many inspired guesses as to its function, but it has only just been characterized in any detail. In the current issue of *Journal of Molecular Biology* (45, 181; 1969), Banerjee, Rensing and August report that during infection of *E. coli* with Q β , the 6S RNA which accumulates has a chain length of approximately 130 nucleotides, is highly resistant to RNase (which suggests it has a double stranded structure) and can be isolated from partially purified RNA synthetase fractions. Like Q β minus strands, the small RNA can be replicated *in vitro* by purified RNA synthetase in the absence of the two bacterial cofactors that are essential for replication of the plus strand. Moreover, the 6S RNA has a markedly different base composition from that of plus strands, with considerably more G and C residues, but, like both plus and minus strands, its 5' terminus is pppGp.

Both the origins and functions of this RNA are completely obscure; with the available assays it cannot be detected in uninfected cells, which suggests that it is of phage origin, but not even that is certain. It is always possible that a few molecules of 6S RNA are present in uninfected *E. coli* but cannot be detected until they have been replicated by the phage RNA synthetase. But irrespective of whether this curious molecule is a host nucleic acid, or a device for replicating a small portion of the phage genome, or a degradation product or something else again, it should prove very useful for elucidating the molecular chemistry of RNA synthetase which is a fastidious enzyme. 6S RNA clearly shares with Q β RNA plus and minus strands the initiation signal recognized by the synthetase, and elucidation of its primary and secondary structure ought to reveal just what that signal is.