The new evidence which supports this idea comes from a study of sunspot variations from 1966 to 1969. In each of the four years (that is, every thirteen Carrington rotations) the number of spots varies in a way which is clearly related to the magnetic field variations observed by Severny at different latitudes. According to Tuominen, about half of the total solar magnetic field of ~1 gauss is related to the activity of visual sunspot leaders.

NUCLEOTIDE SEQUENCES

## Bigger and Better

from our Molecular Biology Correspondent

THE determination of ever longer tracts of nucleotide sequences of viral and ribosomal RNAs has created as many questions as it has answered. The most striking achievements so far have centred on the RNA of the small phages of the R17 group. Adams, Spahr and Cory (*Biochemistry*, **11**, 976; 1972) have now consolidated and extended the sequence at the 5′ end of R17 RNA so as to locate precisely the beginning of the first protein cistron, which occurs after a long leader sequence of unknown purport.

The R17 RNA has a built-in end-group label, in the form of a triphosphate group on the terminal guanosine residue, and 5′ terminal fragments in a limited nuclease digest can therefore be identified by the appearance of a unique spot in electrophoresis patterns of total hydrolysates of the isolated components. Four such terminal fragments were in fact found in a mild ribonuclease IV digest, the longest of which proved to contain 117 residues. This is the tract for which Adams *et al.* now give the complete sequence, and it turns out to be just sufficient to establish the overlap with the fragment containing the start of the A-protein cistron, which was fully sequenced earlier. The first seven residues of the latter coincide with the last eight of the 117-residue terminal fragment.

In view of the vanishing low probability that a given sequence of eight nucleotides will appear twice in an RNA of moderate length, and the reported finding of an overlapping piece by the Cambridge group, there thus seems no doubt that the first cistron begins with an initiation codon, starting at position 130. This is precisely the result obtained for the RNA of the closely related phage, MS2, by Fiers's group in Belgium who a few months ago completed the sequence of the first 125 residues (and for another member of the same family, *f*2, the first seventy-four residues at least are also homologous). With a few dubious looking bulges, a base-pairing scheme of sorts can be constructed by making a hairpin of the sequence, but the longest unbroken Watson–Crick sequence is only five base pairs, and one would therefore expect its stability to be relatively marginal.

The purpose of the long leader sequence in these RNAs remains an absorbing mystery. That such strict homology is maintained in variants of the phage isolated in different parts of the world suggests a specific functional significance. The essentially unrelated phage, Qβ, also has a long untranslated sequence at its 5′ end, and within this Adams and Cory found two sizable segments that had closely similar counterparts in the same region in R17. Adams *et al.* feel that it may be involved in replication, providing, for instance, polymerase initiation sites. Another striking feature is that four initiation codons occur in the leader region, but are evidently in themselves insufficient to attract the ribosome. Other as yet unrecognized signals must therefore be implicated in the initiation process.

On the ribosomal RNA front, an important advance comes from Santer and Santer (*FEBS Lett.*, **21**, 311; 1972), who have sequenced both a twenty-six-nucleotide fragment split from the 3′ end of *Escherichia coli* 16S RNA by $T_1$ ribonuclease, and the fifty-nucleotide fragment specifically knocked off the 3′ end *in situ* by colicin $E_3$. The terminal segment has some curious features, most of all the remarkable density of methylation in this region. In an RNA containing few methyl groups, it is surprising to find no less than five within a group of a few nucleotides, four of them in two adjacent residues, a dimethyladenine and a dimethylguanine. There is an antibiotic, kasugamycin, that evidently recognizes this sequence—which, as the lethal effect of colicin $E_3$ also demonstrates, is vital for ribosomal activity. Dahlberg and his colleagues showed last year that in a mutant devoid of the two dimethylated bases kasugamycin is without effect. The resistant strain is thought to lack a methylase which presumably recognizes a tract of sequence in this region.

The action of colicin $E_3$ on the ribosome is, in fact, a rather complex matter. The removal of the terminal nucleotide segment *in vitro* was established by work from Nomura's laboratory, and also by Boon, who now gives some further details (*Proc. US Nat. Acad. Sci.*, **69**, 549; 1972). A curious feature is that the colicin will not work on the 30S subunits alone in the absence of the larger subunit. When the 50S subunits are added back, the colicin at once takes effect. The agent of cleavage is not the 50S subunit after some form of sensitization by the colicin, for pretreatment of either subunit with colicin produces no effect. Some strains of *E. coli*, especially those that themselves synthesize colicin $E_3$, are resistant, and are known to carry an "immunity factor". Boon has now carried out titrations with preparations of the immunity factor which show that this acts by binding to the colicin, rather than to the ribosomes. Once the colicin concentration exceeds that of the factor, the

## Infectious DNA Proviruses

IF it is assumed that the genetic information of RNA cancer viruses persists in infected cells as a double stranded DNA molecule, the provirus, which is synthesized by viral reverse transcriptase using the single-stranded genomic RNA of the virion as a template, it should be possible to isolate the proviral DNA from transformed cells and perhaps use it to infect and transform other cells. Such an experiment is undeniably ambitious, but according to the report of Hill and Hillova, which is published in next Wednesday's *Nature New Biology* (May 10), it can be done.

Hill and Hillova extracted DNA from rat XC cells transformed by the Prague strain of Rous sarcoma virus (PR.RSV) and from hamster cells transformed by a temperature sensitive mutant strain of Schmidt Ruppin Rous sarcoma virus (SR.RSV) and purified the DNA by centrifugation in caesium chloride gradients. They then repeatedly exposed cultures of fresh chick fibroblasts, previously washed in DEAE-dextran solutions, to aliquots of the DNA from the transformed cells and searched for foci of transformed chick cells and for evidence of the production of progeny PR.RSV or SR.RSV particles. As controls they exposed similar cultures of chick cells either to DNA from transformed rodent cells which had been digested with DNAase or to DNA from calf thymus.

As optimists would have anticipated Hill and Hillova found that only the chick fibroblasts exposed to undigested DNA from transformed cells are transformed and begin to produce virus. Moreover the virus produced is of the same antigenic subgroup as the virus used originally to transform the donor rodent cells and the virus produced by cells exposed to temperature sensitive SR.RSV is temperature sensitive. It seems clear therefore that transformed cells do indeed contain at least one DNA provirus which can be isolated in an infectious state.

With so many research groups now working with the RNA cancer viruses it should not be long before these data are independently confirmed.