a powerful superconducting magent (called a "wiggler" for technical reasons) which will accelerate the electrons in the source so strongly that the spectrum of radiation, currently cutting off at a wavelength around 0.3 Å, will extend down to 0.1 Å.

Although synchrotron radiation sources will soon be widely available in numerous countries, the technique still shows massive potential for further development. The Daresbury ring at full power produces several tens of kilowatts of raw radiation, enough to destroy most experimental specimens. Yet, because the requirement is mainly for spectrally pure radiation, most of the power is dissipated as heat in a monochromator. If by some means the power available could be channelled into radiation of one wavelength a new and even more extraordinary generation of experiments would become possible, investigating nonlinear properties of matter. Perhaps the most radical proposal is to combine the power of synchrotron radiation with the coherence properties of a laser and produce the so-called free-electron-laser. It is gratifying to see UK scientists involved in all phases of the development and exploitation of synchrotron radiation. □

Coding complications

from a Correspondent

READERS will recollect that the celebrated wobble hypothesis of Crick defines the nature of the interaction between the codons of messenger RNA and the corresponding anticodons of tRNA. In short, the codons are read one at a time by tRNA molecules. These form three base pairs between the bases in their anticodon and those in the codon that it responds to. The first two base pairs formed by the codon are standard Watson–Crick A–U or G–C pairs but in the third position G–U pairs are allowed, as are A–I, G–I and U–I where the I residue is in the anticodon.

Although there is considerable evidence that this is the normal mode of codon–anticodon interaction in both eukaryotic and prokaryotic organisms, evidence has been accumulating that things are not always as simple as this. Thus in mitochondria, it would appear that a single base in the third position of the anticodon can 'read' each of the four bases which might occur in the third position of a codon, or to put the matter another way, only the first two bases of the codon are relevant. This state of affairs resembles the 'two out of three' mechanism proposed by Lagerkvist[1]. More evidence for such anomalies now appear in two papers in *Nature* and in two in *Cell*.

Munz *et al.* (see this issue of *Nature*, p. 187) have studied serine specific tRNA in *Schizosaccharomyces pombe*. This organism utilizes two isoaccepting $tRNA^{Ser}$ with anticodons IGA and U*GA (U* is a modified uridine) respectively. The one with IGA should be able to respond to the codons UCU, UCC and UCA and the other only to UCA. By means of some clever genetic manipulations Munz *et al.* were able to show, in essence, that mutants in which the U*GA species is not synthesized are not viable. If the possibility that the missing tRNA had some other essential role to play is excluded, this would seem to imply that UCA codons were not being properly recognized. The anomaly appears when it is noted that the other serine specific isoacceptor with IGA for its anticodon should have been able to recognize this codon according to the rules of wobble. Apparently it does not. The significance of this *in vivo* result is increased when it is realized that the bulk of the evidence for A–I interactions is derived from *in vitro* experiments.

Meanwhile, Diamond, Dudock and Hatfield[2] have isolated and sequenced an unusual tRNA species from bovine liver. This accepts serine but has CmCA for its anticodon, an anticodon normally expected to recognize the tryptophan codon UGG. The anomaly appeared when it was found from *in vitro* binding experiments that the tRNA responded to UGA (which is normally the opal stop signal) but not to UGG or any of the serine codons. It was further shown that the tRNA could act as a suppressor of termination as the first result might suggest. In other words the Cm in the third position had 'read' A rather than G as demanded by the wobble hypothesis. This result for a eukaryote had been anticipated in the work of Hirsch[3] who described a $tRNA^{Trp}$ in *E. coli* which had an anticodon CCA but which responded to UGA codons. Both the eukaryotic and the prokaryotic tRNA molecules also had anomalous features in their sequences in the vicinity of their DiHU stems and the possibility remains that this feature is somehow related to their anomalous codon reading properties.

Another curious anomaly has been discussed by Bienz and Kubli (see this issue of *Nature* p 188). *Drosophila melanogaster* produces two major $tRNA^{Tyr}$ species one of which has the first position of its anticodon occupied by the modified Q base. The one with the unmodified anticodon, GUA, but not the other, is capable of acting as a suppressor to the amber termination codon UAG; in other words it can recognize UAG and insert tyrosine so preventing termination of translation. Again we have a wobble anomaly in that the interaction in the third position is between two G residues. The discovery of this naturally occurring suppressor in *Drosophila* was aided by an interesting assay system for breakthrough or suppression of a chain termination signal. This involved injecting into a *Xenopus* oocyte some of the tRNA to be assayed and some TMV RNA. If suppression occurred, this resulted in the formation of a 160,000 molecular weight protein, identifiable by polyacrylamide gel electrophoresis. Thus Bienz and Kubli also showed that wild type $tRNA^{Tyr}$ from yeast (with no Q base) would also act as suppressor in this system. They suppose that the presence of the Q base somehow inhibits the misreading of the UAG codons involved in this type of suppression.

Finally Bossi and Roth[4] report on a different sort of suppressor effective in the suppression of the effect of a frameshift mutation. A frameshift mutant occurs when an extra base pair is inserted or a normal one left out during the process of replication. In either case the reading of the bases constituting the codons gets out of phase when the site of the mutation is encountered during translation. This results thereafter in a garbled polypeptide. Such a garbling of the message due to an insertion could be corrected if a tRNA was available which read four bases instead of three at a site near to the original mutation. Several mutant tRNA species can be produced which have this effect. Most of them respond to a region of the messenger RNA where there is a sequence of four identical bases; reading of the fourth base, so to speak, takes up the extra inserted base. The mechanism by which this occurs is obscure; maybe four base pairs are involved or maybe there is some sort of ambiguity as to which of the two possible triplets in the run of four the tRNA responds to. Bossi and Roth however, now describe a new suppressor, SufJ, which responds to sequences of four bases: ACCU, ACCC and ACCA (the sequence ACCG has not been tested). In other words it recognizes the triplet ACC but pulls the fourth base through the reading frame. This seems to be a sort of three out of four reading mechanism reminiscent of Lagerkvist's idea.

Simple explanation to account for these puzzling phenomena are not in sight but one thing seems certain: our once clear picture of the mechanism underlying the translation of the genetic message is developing a plethora of unbecoming flaws. □

1. Lagerkvist *Proc. natn. Acad. Sci. U.S.A.* **75**, 1759 (1978).
2. Diamond, Dudock & Hatfield *Cell* **25**, 497 (1981).
3. Hirsch *J. molec. Biol.* **58**, 439 (1971).
4. Bossi & Roth *Cell* **25**, 489 (1981).

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