of both the wild type and the nuclear-disruption deficient phage, these authors put forward a model for the nuclear disruption process. They suggest that the host DNA becomes attached to the cell membrane at several hundred sites during a normal infection. In an uninfected cell it might be attached at about five sites—the origin and terminus of replication and a few replication forks—while in the nuclear-disruption deficient infected cells it is probably attached at fewer than ten sites. Surprisingly, in spite of this major change in the effect of the phage on the host cell DNA, no difference was detected in either the burst size or the growth rate of the mutants and the wild type.

These various results show that the growth and assembly of T4 is still a subject of considerable interest and give hope that some of the intriguing problems may be cleared up soon.

Poly(A) tales

from Tim Hunt

THE November issue of the *Proceedings of the Academy of Sciences of the USA* contains an elegant demonstration that the poly(A) tail of globin mRNA is unnecessary for its translation in cell-free protein synthesising systems. Sipple *et al.* (Columbia) (**71**, 4635; 1974) hybridised globin mRNA with oligo(dT) and then attacked the hybrid with RNase H, a nuclease that specifically digests the RNA strand of a DNA–RNA hybrid. After this treatment, the reaction mixture was passed over a mixed gel filtration and nitrocellulose column to remove the oligo(dT) and undigested hybrids. The mRNA that resulted was shown to be free of poly(A) by its failure to form dsRNA with ^{3}H poly(U).

It would be hard for these authors to be sure that they had removed literally all the poly(A); the possibility that a few residues remain would not, I think, be excluded. Nevertheless, this method for removing the poly(A) has advantages over the use of polynucleotide phosporylase or the 3′ exonuclease from eukaryotic nuclei. These exonucleases are processive enzymes—they do not leave their substrate until it is completely digested; hence, in order to digest all the molecules in a message preparation a molar excess of enzyme must be added, which in turn means that it must be highly pure. In addition, it is hard to stop the enzyme from going past the poly(A) stretch into the structural mRNA. Lastly, the RNase H method has a universal application for the removal of specific pieces of RNA if the complementary piece of DNA is available.

So what happens when you remove poly(A) from mRNA? The answer is generally agreed to be almost nothing. As a template for globin synthesis in cell-free systems (wheat germ, Krebs II ascites extracts, Schreier and Staehelin) the deadenylated mRNA is just as active as its unassaulted parent. This conclusion has been reached before by Williamson *et al.* (*Biochemistry*, **13**, 703; 1974), Bard *et al.* (*Cell*, **1**, 101; 1974) and Soreq *et al.* (*J. molec. Biol.*, **88**, 233; 1974), all of whom used processive exonucleases to remove the poly(A); Williamson *et al.* and Bard *et al.* clearly did some damage to the mRNA beyond removal of the poly(A), but Soreq *et al.* used highly purified enzyme under very restrictive conditions, and their data are extremely similar to those of Sippel *et al.*

They did notice that the activity of the deadenylated MRNA tailed off earlier than that of the native mRNA, although the effect is not dramatic. Sippel's group also report a lowered stability *in vitro*, but the cell-free system itself loses a lot of activity over the same period of time, and the decay of the message has curious linear kinetics which is unusual; normally mRNA decays exponentially. In any case, it may be dangerous to argue from cell-free experiments to the situation within living cells, and with this caution in mind, Soreq's group arranged for their mRNA to be injected into *Xenopus* oocytes (Huez *et al.*, *Proc. natn. Acad. Sci. U.S.A.*, **71**, 3143; 1974). They found that both the activity and the stability of the deadenylated mRNA were apparently impaired. I think there are problems in the interpretation of these kinds of experiment, although the experimental data are impressive. The trouble lies in knowing how to quantitate the amount of protein formed after injection of mRNA, owing to uncertainties about the degree of penetration of label and its dilution with endogenous amino acids. Huez *et al.* take as their measure a comparison between radioactivity in the 'endogenous' proteins and that in the peak of globin from a gel filtration column. The tacit assumption that the rate of endogenous protein synthesis is constant is very hard to test, and may not be correct.

Interesting and pertinent studies of the stability of RNA after its injection into oocytes have been made by Allende, Allende and Firtel (*Cell*, **2**, 189; 1974). They injected radioactive RNA and followed the fate of the label rather than the stability of the template activity of the mRNA. They found that the RNA was degraded at an appreciable rate, except in the cases of tRNA and poly(A) itself; however, the decay of mRNA followed biphasic kinetics. This apparently results from the interaction of mRNA with cellular components, possibly ribosomes, since the stable fraction is not seen in the presence of puromycin. These are provocative findings in the light of the extreme stability of the translational capacity of injected globin mRNA (Gurdon, Lingrel and Marbaix, *J. molec. Biol.*, **80**, 539; 1973) and also of the fact that oocytes contain respectable amounts of stored mRNA which survive from oogenesis to fertilisation (Adamson and Woodland, *J. molec. Biol.*, **88**, 263; 1974). The mechanisms ensuring on the one hand the stability of these messages, and on the other their unmasking during development are quite obscure. There were certainly no indications in Allende *et al.*'s experiments that the poly(A) played a part in the stabilisation of the injected messages; it would be interesting to repeat these experiments with radioactive globin mRNA with and without its poly(A), not an easy thing to arrange except by iodine labelling, since very high specific activities are necessary.

Taken together, these experiments suggest that removing the poly(A) may reduce the stability of the mRNA in certain circumstances; but there is little evidence from studies on intact cells to support the hypothesis that a long stretch of poly(A) confers a long life on a message. Although the poly(A) gets shorter with age (Sheiness and Darnell, *Nature new Biol.*, **241**, 265; 1973), it seems that old messages have a similar life expectancy to young ones in view of the well established exponential decay of mRNA (see for example Brandhorst and McConkey, *J. molec. Biol.*, **85**, 451; 1974). The recent description of mRNA which lacks poly(A) in HeLa cells (Milcarek, Singer and Penman, *Cell*, **3**, 1; 1974) includes data on its lifespan, and there are no indications of anything unusual about the non-adenylated species compared with the adenylated. The poly(A) of mRNA still seems to be more of a natural gift to the molecular biologists than an essential component of mRNA. Yet the refrain is always: 'It's there, so it must do something".

Histamine and the brain

from a Correspondent

AT a meeting of the Collegium Internationale Neuropsychopharmacologicum in Paris last July, ideas about the meaning of histamine in the brain were brought together and aired (*J. Pharmac. (Paris)*, **5**, *Supp.* 1, 69; 1974). From this airing, it emerged that histamine is present in the brain, although in smaller amounts than are its relatives, 5-hydroxytryptamine and noradrena-