Yanofsky's results; it would be necessary to postulate that there are special mechanisms which protect the exposed parts of T7 messengers from degradation and that these mechanisms may be selective in how they operate on different bacterial messengers. This conclusion must complicate the search to find the systems responsible for degrading messengers, but whatever these are, it seems almost certain that there will now be renewed interest in the possibility that different messengers possess distinctive structural features.

DNA REPLICATION
Starting with RNA
by our Molecular Genetics Correspondent

WHAT initiates the replication of DNA? Little enough is known about how chains of DNA are elongated, but even less certain are the processes which start them. None of the DNA polymerases found in bacteria or specified by bacteriophages seems to be able to initiate the syntheses of new chains of DNA, although they can extend free ends or repair damaged segments. One way round this impasse is to suppose that primers—short oligonucleotides of DNA—are needed to initiate synthesis. These fragments might be derived by cleavage of pre-existing chains. Another idea is that a special enzyme might be needed to start chains. And, of course, it is always possible that when the true bacterial DNA replicase is identified, it will have properties not to be predicted from those of the enzymes at present known.

But it does seem likely at present that the mechanism which initiates chains is distinct from that which elongates them. (How replication comes to an end is an open question.) An idea which has been proposed in many guises during the past few years is that there might be some sort of link between transcription and replication. Indeed, one of the popular concerns of research has been to couple different processes of macromolecular synthesis.

The notion that transcription of DNA into RNA might depend on simultaneous translation of the messenger into protein, for example, is still controversial (see Nature New Biology, 232, 161; 1971). The idea that transcription might depend on replication has been put forward in two forms. One is to suppose that genes which function at only a low level in bacteria, and possibly in other cells also, might direct the synthesis of RNA at only one point in each cell cycle, at the time when the appropriate part of the DNA is replicated. An analogous proposal has been made for the cells of higher organisms, that a "clean gene" is needed during differentiation; this theory

says that a replication of the genetic material is needed to wipe out its existing state of expression and to allow a change during embryogenesis.

The idea that replication of DNA may depend in some mechanical manner on the transcription of RNA is proposed by Brutlag, Schekman and Kornberg in the current issue of the Proceedings of the US National Academy of Science (68, 2826; 1971). They suggest that a brief transcriptional operation by RNA polymerase might provide an RNA primer for DNA synthesis. They have tested this idea by looking at the synthesis of the double stranded replicative form of the single stranded DNA bacteriophage M13 and by then following its replication. Conversion of the single stranded DNA to its duplex form relies entirely on the enzymes of the host bacterium, Escherichia coli, although replication of the double helix—which better resembles the replication of bacterial DNA—requires the synthesis of a protein specified by a gene of the phage. They have followed both these phases of DNA synthesis in conditions when rifampicin is used to inhibit initiation of RNA synthesis by RNA polymerase, or when chloramphenicol is present to inhibit translation of messenger RNA species into proteins.

Their results show that the conversion of single strands to double strands is inhibited by rifampicin but not by chloramphenicol; this shows that the effect depends directly on RNA synthesis and not on a need for the production of proteins. The replication of M13 double helical DNA is inhibited over a hundred times more forcefully by rifampicin than it is by chloramphenicol. Mutant bacterial cells which are resistant to rifampicin show neither of these effects, which confirms that replication is inhibited because there has been a change in the manner of the interaction of RNA polymerase with DNA.

How might transcription aid replication? One possibility is that the inhibition might be trivial; the RNA polymerase–rifampicin complex might inhibit replication because it is attached to DNA at some site which would otherwise be accessible to the machinery which usually initiates replication. The only argument against supposing that an accident of this sort is occurring is that rifampicin does not inhibit the continuing replication of DNA which is taking place at the same time in the host bacteria. If RNA is needed to prime transcription, Brutlag et al. think that its most likely function is a mechanical one. It might disrupt the proper structure of the DNA double helix, or it might act as a primer which is to be extended by the addition of deoxynucleotides, the original section of RNA being removed at a later stage by a nuclease.

RIBOSOMES
Pressure Strikes Again
from a Correspondent

THE controversy still rages as to whether ribosome subunits are released spontaneously from polysomes, or whether monosomes (which are then dissociated to subunits by the initiation factor F3) are an obligatory intermediate on the pathway from polysomes to subunits. Kaempfer (Proc. US Nat. Acad. Sci., 68, 2458 ; 1971) has now presented data, based on density-gradient profiles, to support the hypothesis that initiation factor F3(B) does not function as a ribosomal dissociation factor, dissociating 70S ribosomes to 30S and 50S subunits, as suggested by Subramanian and Davies (Nature, 228, 1273 ; 1970) and others, but rather functions as an anti-association factor which prevents the reassociation of 30S and 50S subunits to form synthetically inactive 70S ribosomes. Kaempfer views protein synthesis as a dynamic process controlled by F3.

In conditions favouring synthesis, subunits run off from polysomes without the formation of 70S monosomes as an intermediate. These sticky subunits are prevented by F3 from reassociating, so they rejoin only as active polysomal components. When conditions do not favour protein synthesis, the supply of subunits exceeds that of F3; the sticky nature of these subunits asserts itself, and they are sidetracked into an inactive pool of single ribosomes. These single ribosomes slowly dissociate spontaneously to subunits whose subsequent fate is dictated directly by the supply of F3, and thus by the rate of protein synthesis.

Subramanian and Davis (Proc. US Nat. Acad. Sci., 68, 2453 ; 1971) present the other side of the coin. Aware of Infante's data about the pressure-induced dissociation of ribosomes (see Nature New Biology, 233, 34 ; 1971), they explore the effect of artefactual dissociation of labelled ribosomes during centrifugation in a sucrose gradient. By first fixing ribosomes with glutaraldehyde, pressure-induced dissociation is prevented. They can demonstrate a rapid exchange of free ribosomes and subunits, an obvious contradiction to the slow dissociation postulated by Kaempfer. F3 acts reversibly, so it can not only dissociate ribosomes but also catalyses an exchange of subunits with monomeric ribosomes by its reverse action, the association of subunits to form ribosomes. In fact, they argue that there is no longer compelling evidence that polysomal dissociation to subunits does not proceed through a monosomal intermediate, which restores us full circle to the postulated role of F3 in the dissociation of monomers.